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DISTRIBUTION OF HYPERSENSITIVITY REACTIONS AMONG GARHWALI POPULATION IN A TERTIARY CARE MEDICAL COLLEGE HOSPITAL : A RETROSPECTIVE STUDY

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ABSTRACT **INTRODUCTION:** Hypersensitivity reactions (allergic) have become serious complications having increasing trend day by day around the globe. Occurs usually due to sensitization and genetic factors mediated by antigen-antibody reaction. Present study was proposed to find distribution of different hypersensitivity reactions commonly prevailing among Garhwali populations of Uttarakhand. **MATERIALS AND METHODS:** This retrospective study was carried out among 6405 confirmed patients showing hypersensitivity symptoms who visited OPD of Dermatology department at HNB Base Hospital, Srinagar (Garhwal) during January 2016 to December 2018. Hypersensitivity disorders included were Photosensitivity, Phytophotodermatitis, Polymorphous Light Eruption, Airborne contact dermatitis, Allergic contact dermatitis, Adverse Drug Reaction, Insect Bite and Urticaria. **RESULTS:** Females showed higher prevalence of 57% as compared to males. Prevailing mostly in age group of 21-30 years (22.8%). Occurrence during Summer recorded highest (29.1%) followed by rainy season (27.9%). Insect bites were more common in rainy and summer seasons and mostly among 1-10 yrs age group. Prevalence of urticaria was highest (25%) followed by photosensitivity (19.4%), allergic contact dermatitis (16.5%) whereas phytophotodermatitis showed the lowest prevalence of 1.8%. Prevalence of ABCD and Phytophotodermatitis are more common in age groups of 41-50 yrs and 51-60 yrs. **CONCLUSION:** Hypersensitive disorders have become a serious threat globally. This study has depicted a small picture about its increasing trend among Garhwali populations in this small Himalayan state of Uttarakhand.

KEYWORDS : Hypersensitivity Reactions, Garhwali Populations, Uttarakhand

INTRODUCTION

Hypersensitivity reactions (HR) are usually immune responses that are exaggerated or inappropriate against an antigen or allergen[1]. In this study, we have differentiated the commonly occurring HR prevailing among the Garhwali populations who are inhabitant of Garhwal region of Uttarakhand situated in the foot hills of Shivalik ranges of the Himalayas into different categories.

Photosensitivity (Photo)

The adverse effect shown when a patient takes drugs that shows an adverse reaction in form of phototoxicity or photo-allergy when exposed to light is known as photo sensitivity. Generation of free radicals on UVA spectrum exposure is known as phototoxic reaction whereas immune response activation by changing the structure of a drug is known as photoallergic reaction.

Nonsteroidal anti-inflammatory drugs (NSAIDs), antihypertensives, antiarrhythmics, diuretics, antidepressants, neuroleptics, various antibiotics, anticancer drugs, retinoids are mainly responsible for photosensitivity reactions[2].Three subdivisions of UV radiations are UVA(320-400nm), UVB(290-320nm), UVC(200-290nm) which are normally invisible to human eyes. The most biologically active is UVB, frequently referred to as sunburn spectrum[3]. 1% of the rays reaching the earth is UVB, which is also most energetic. UVA is lesser in energy level and consists of 99% rays reaching the earth[4]. Various biochemical mediators like IL-1, IL-10, histamine, serotonin, arachidonic acid metabolism which are released from keratinocytes, mast cells and other inflammatory cells are mainly responsible for various effects on skin[5]. IL-1, IL-6 like cytokines released from subtypes of T cells , suppressor cells, Langerhans cells are mainly responsible for the immunological changes[6-8].

Allergic reactions are abundant worldwideand prevalence shows more or less in all age groups[9-12]. In recent years such incidences have increased considerably due to complex interaction between environmental factors such as air, water, food with the genetic makeup of the particular person[12,13]. Considering all the above facts there is still a huge lacuna in proper data in epidemiological consideration about such reactions in India.[3] These poses a serious health risk among the population[14,15]. Sex has risen as one of the major factors in allergic correlation. However its role is still not fully understood[16,17]. So correlation of sex disparity and photosensitivity becomes important.

Phytophotodermatitis (Phyto)

A phototoxic dermatological reaction that occurs with exposure to ultraviolet radiation after sensitization by plant chemicals is known as Phytophotodermattis[18] which clinically manifest with hyperpigmentation, delayed erythema, bullae or vesicle formation[18,19]. Compounds like furocoumarins (plant alkaloids) are UV sensitizing compounds are main offenders for this reaction. The skin becomes reactive by UVA (ultraviolet A ray) radiation, after being sensitized by the phytochemical, leads to reaction of cutaneous type which results in vascular skin damage by linkages of nuclear DNA and associated increase in melanin production leading to hyperpigmentation. Phytophotodermatitis is mostly common in mid-to-late summer when psoralen concentrations are highest in plants and timing matches with

people being outdoors more often and less covered which increasing their surface area exposure to chemicals and UVA. Plant families Umbelliferae, Rutaceae, and Moraceae have highest concentrations of furocoumarins. Hyperpigmentation develops over 1-2 weeks, usually persists for 6-12 months. This hyperpigmentation with phytophotodermatitis appears like a drop like pattern where the UVA hits the skin after sensitization with furocoumarins. The hyperpigmentation can also be in the form of a bizarre streak or streaks[20-26].

Polymorphous Light Eruption (PMLE)

Polymorphous Light Reaction is a common photoallergic reaction whose etiology is unknown etiology. The manifestation includes papular, vesiculo-bullous and hemorrhagic type and manifest as plaque, erythema multiforme-like presentation or strophulus like reaction similar to insect bite. Lesions mainly forms on exposed area of the skin under intense sunshine for few hours or days. The main characteristic feature is always monomorphous in same patient. The rash diminishes spontaneously within several days without leaving scars[27-30].

Papular Type: The most common type of PMLE, represents as patchy erythema which are aggregation of papulovesicles or papules that disseminated or densely aggregated on a patchy erythema.

Hemorrhagic Type: Hemorrhagic lesions are seen rarely.

Strophulus/Insect bite like: Papules are like small urticarial with tiny vesicle on top. The variety is very rare and lesions are few.

Plaque Type: Mostly seen on face usually second most common variety resembles Subacute Lupus Erythematosus (SCLE). Presence of urticarial plaques, elevated, erythematous and demarcated sharply.

Erythema Multiform time: Presents as typical target lesions with less frequent occurance.

Vesiculobullous type: Type with an erythematous base with small bullae and tense vesicles. It is common in Hawaii region, rarely observed in Europe[28-30].

It has a tendency to affect fair skinned population more than dark skinned. The young female population tends to have a higher percentage of incidences irrespective of age, sex or race[30].

Airborne contact dermatitis (ABCD)

Airborne contact dermatitis is an acute or chronic dermatoses mostly affecting exposed parts of the body and caused by allergens/irritants present in atmosphere. Allergens can exist in the form of dust, sprays, pollen, volatile chemicals by airborne fumes or droplets which settle on the exposed skin of the body[31]. Airborne dermatitis commonly affects face, neck, 'V' area of chest, eyelids, axillae and forearms. This form of dermatitis can also include non exposed skin like major body folds and occasionally may be generalized in distribution[32-34]. Airborne contact dermatitis can be both plant and non-plant origin. Most common airborne dermatitis is due to compositae plant Parthenium hysterophorus. Though, cases of non-plant and industrial origin are on increasing trend especially in the developing countries[32]. In recent years there is a trend of rising incidents of ABCD[35].

The main causative factor of ABCD: 1) Pollens or dust containing particles from Parthenium hysterophorus, ragweed or certain other types medicaments or woods by delayed hypersensitivity (Type IV). 2) Other materials like glass fiber, grain dust and rock wool causing mechanical dermatitis. 3) Aerosols of different mineral oils causing irritant type of dermatitis. 4) Cement, wood dust which causes both irritant and sensitizing reactions[37,38].

The most significant allergens in Parthenium hysterophorus responsible for causing allergic contact dermatitis are Sesquiterpene lactones (SQL). They are lipophilic, and present mainly in the oleoresin fraction of the plant. Among the SQL's, Parthenin is the major sensitizer[37,38]. Parthenin belongs to pseudoguinolide class of SQL's, has an alpha methylene group exocyclic to gamma lactone, probably crucial for the induction of allergy. Apart from parthenin, other important allergens are coronopilin, hymenin, tetraneurin A etc. The other components, namely, thiopenes, monoterpenes and acetylenes are recognized to cause phytophotodermatitis. These SLs are found in other compositae plants such as genera, namely, liverwort (Frullania), tulip tree (Liriodendron, Magnoliacea) and sweetbay (Lauraceae, Laurus nobilis), which may show cross sensitivity with parthenium and vice-versa[37]. ABCD can be brought about by many methods- direct contact, like brushing of skin with plant parts, or indirect contacts or ingestion of allergens by consumption of herbal tea or application of herbal cosmetics. Dooms-Goossens classified ABCD into the following categories.

1. Airborne irritant contact dermatitis
2. Airborne allergic contact dermatitis
3. Airborne phototoxic reactions
4. Airborne photoallergic reactions
5. Airborne contact urticaria[35,39].

Allergic contact dermatitis (ACD)

Allergic contact dermatitis (ACD) is a common skin disease triggered by a T-cell-mediated immune reaction to usually innocuous allergens[40]. It is an inflammatory reaction occurring at the site of challenge with a contact allergen in sensitized individuals, characterized by redness, papules, and vesicles, followed by scaling and dry skin[41]. This disease is considered as one of the most common dermatologic diseases and the primary cause of occupational skin diseases.

ACD in childhood

Allergic contact dermatitis (ACD), rarely diagnosed in the first months of life, may be caused by rubber, vinyl sheet[42], nickel[43-46], topical antibiotics, other topical medications[45-48], and plants of the Rhus genus (includes poison ivy)[42]. Nickel induced ACD has been diagnosed in first few weeks of life but the incidence appears to be low[43,44].

ACD in young adults

Occupation is the main reason behind the incidences in this age group. This being various such as agricultural, catering, industrial etc. Clothing and its apparel is also a major source. Another important agent is cosmetics, along with environmental factor is also added. Nickel in this group rises above others as the most common culprit for this group. The main reason behind this is ear-piercing[49]. A strong correlation between ear-piercing and nickel hypersensitivity have been documented[50]. This mainly leads to the formation of jewelry rash and ear lobe rash[51].

ACD in middle age adults and elderly population

In healthy adults nickel, paraphenylenediamine, oak, poison ivy, dichromates and various rubber compounds are common culprits. In menopausal women due to clothing and dyes is a common reason for this reaction. This can be attributed to hyperhidrosis. Working class population like those in cement factories or construction workers, painters, who sets tiles and even bakers are victims of industrial type of dermatitis[42].

1). Topical Medication like for stasis ulcers is another cause of ACD in adults
2). Contact dermatitis linked to systemic eczematous, this are widespread and systemic mainly results from drugs which elderly take which can cause topical sensitization[42].
3). Old age tends to cause a decline in delayed hypersensitivity reactions by antigens contacted in earlier life[52,53]. Further, there is a decrease to development of reactions to new antigens with increase of age.
4). The epidermal Langerhans cells are involved in the processing and presentation of antigens initially in the immune system.

Adverse Drug Reaction (ADR)

An adverse drug reaction is an unwanted additional effect shown by drug beside its desirable effect. In comparison, an adverse drug event is an unexpected occurrence after coming in contact with a drug which most possibly not caused by drug[54]. Side effects of drugs are prevalent in the society after intake of drug accounting for 5% of the patients[55]. Some studies have pointed at prominently more incidences of ADR in female than male[56,57]. Similarly age related comparison shows a bias to geriatric population[58]. Although it is still unclear whether high incidence among females and elderly population is attributed to high consumption of drugs or toxicity due to metabolism variability in females and elderly[59].The common types of ADRs are:

1). Anaphylaxis- Drug related anaphylaxis is one of the most common types of ADR . The epidemiology of this reaction has been widely studied in many countries like USA, UK, rest of Europe, Australia, New Zealand, Korea, Singapore and Thailand with

simultaneous report in both adults and children. Incidence of Anaphylaxis lies between 8-50 /1000 cases/year. Still the true incidence rate of anaphylaxis is not known, even the incidence and mortality rate is still not clear. The most offending drugs causing anaphylaxis are antimicrobial mainly penicillin's, anesthetic agents. These causes IgE mediated reaction. NSAIDs and radio contrast media were frontlines for non-allegican anaphylaxis[60].

2). Severe Cutaneous Adverse Reactions (SCAR)- Steven Johnson Syndrome (SJS) or Toxic epidermal necrolysis mainly comes under this. The main offenders are cotrimoxazole- antifungal, allopurinol- for gout, carbamazepine- sedative, phenytoin- antiepileptic, phenobarbitol-barbiturate, oxicam-NSAIDs. Diarrhea, low BP, fall in blood glucose are other type of common ADRs[60].

Factors causing ADR:

1). Drug Related Factors: A drugs ability to act as hapten or a prohapten or its binding ability to immune receptor affects the immunogenicity of a drug[61]. This is in relation to certain class of drugs showing high incidence rate to ADRs than others[62].

2). Host related factors: Females seem more likely to develop drug allergies than males but this may be attributable to the overall female predominance in ADRs. Ratio of first time consults in Female and male for drug allergy was approximately2:1[63]. The incidence of self reported drug allergy generally higher in females than males[64]. Age as a responsible factor, situation is still not clear as low incidence of drug allergy in children generally prevails which may be due to the fact that children being likely to be exposed recurrently to a lesser extent to sensitizing drugs. Although in cases of chronic disease overexposure of drugs like antibiotics can lead to the child being sensitized to the particular drug[65,66].

3). Genetic Factor: Recent advancement in the field of medicines particularly genetics have brought spotlight on HLA genotypes with their association of extreme drug allergic reaction. HLA molecules presenting as antigens to the T-lymphocytes via TCR or T cell receptor generates an immune response. Among them ubiquitous molecules are HLA class I which contains HLA A, HLA B, HLA C. These are on cell surface of nucleated cells. HLA B*1502 was found to have an association with carbamazepine induced SJS/TEN[67,68]. HLA B*5801 have association with allopurinol induced SJS/TEN[69,70] and present for abacavir with HLA B*5701 is also observed but not in black population[71-73].

Insect Bite (Insct)

Insects are class of living creatures within phylum arthropods with a chitinous exoskeleton, three-part body, three pairs of jointed legs, compound eyes, and two antennae[74]. Insects (in Latin insectum, meaning "cut into sections") may be considered to "cut into" three sections, head, thorax, and abdomen. Bite is a wound produced by the mouth parts of an animal. Some animals have a special structure called sting through which they inflict wound and inject venom. All insects do not bite. Some non-biting insects are beetles, locusts, moths, and butterflies, although these may yield skin reactions by other means such as allergic reactions to their body parts, feces, or body fluids. Bees, wasps, and ants also do not bite, but produce dermatological reactions by their sting. Insect bite reactions are usually common, but evidence about their prevalence is limited. Children are more susceptible for insect bites. Insect bite reactions generally due to the following insects[75].

1). Mosquito bites: Reaction of their bite is due to allergens in saliva, but not because of toxins. The saliva has a pharmacologically active compound which can inhibit innate immune response of the body, along with causing coagulation defect, vasodilation also impairment of platelet formation[76,77].

2). Black Flies: Characterized by a small blood crust with surrounding ecchymosis. Small pruritic papules develop within a span of few hours which can last for several days to months[78].

3). Blandford flies: Produces skin swellings on bites and occasionally fever or joint pain[79].

4). Horse flies: Painful lesions with rare anaphylactic reactions are observed with generalized urticaria, itching , it can extend to paresthesia and unconsciounesness[80].

5). Louse Flies: A haematophagous louse fly of deer known as Deer ked (Lipoptena cervi L) can cause pruritic papules, usually occurs in the forest[81]. Head and neck is the prime area for the reaction, usually treatment resistant. They tend to linger for weeks to months[75].

6). Teste fly: Glossina genus spices, family is Glossinidae[82], mostly confirmed to Africa, leads to anaphylactic reaction mainly to laboratory workers[83].

7). Midges: Bites persons having favorable body odour. The non favorable persons produces a "repellent"[84]. Urticaria or delayed type of reactions mediated by IgE involving INF-γ, IL-6 and TNF-α, ulcers and bullae are formed from their bites and this persists for weeks[85,86].

8). Bugs: Belongs to Hemiptera order. These have common appendages of sucking mouth parts having smaller hind wings than forewings. They have flat and oval body with no hind wings. They do not fly as their front wings are also vestigial[75]. Types of bugs are:

I). Bed bugs: In India, abundant bed bugs are common and tropical bedbugs[74]. These are called as cimicosis. Lesions do not develop on first exposure, but develops reaction on successive exposure with substantial decrease in latency[87]. Reaction is caused by salivary protein among which first nitrophorin- a nitric-oxide liberating heme protein[88], secondly by Factor X – a 17kDa anticoagulant[89], thirdly by nucleotide binding enzyme- 40kDa apyrase-like are important immunologically[90].

ii). Mexican Chicken bugs (Haematosiphon inodorus): They cause polymorphic lesions (haematosiphoniasis) which includes wheals, papules, vesicles, pustules, and scabs[91].

iii). Assassin bugs: Their bites are defensive and extremely painful[92].

iv). Kissing bugs (Triatoma sanguisuga): Bites are painless and thus gives more time for exposure. On first sensitization reaction is not significant but with repeated exposure it cause pruritic papules with central punctum to haemorrhagic nodules and bullae may appear[93].

9). Fleas: Wingless Hematophagous ectoparasites found in birds or mammals, mainly in humans and bats cause severe pruritus and papular or maculopapular rash on bites[94,95].

10). Thrips: Bites produce tiny punta and small, pink macules or papules by bites[75,96,97].

Urticaria (Urt)

Urticaria is derived from Latin word 'urtica', which means nettle. Nettle is common variety of wild weed predominant in European regions. In medical terms, urticaria is a dermatological condition. Urticaria is a widespread debilitating condition categorized by intensely itchy, evanescent lesions known as wheals. Research have failed to yield satisfactory result as till 50% cases are of unknown etiology[98,99]. The reaction if lasting more than 6 weeks is termed as chronic urticaria (CU). The most symptom of urticaria is 'Wheel' characterized with central swelling surrounded by a reflex erythema that is itchy while the angioedema is associated with pronounced swelling of lower dermis and subcutaneous tissue with occasional involvement of mucous membranes (lips, tongue) in some patients[100]. Etiologically or clinically Acute Urticaria can be further classified into the following:

1). Immunoglobulin E (IgE)-mediated reactions- 'contact urticaria': Patients may become sensitized to a very wide range of allergens and produce specific IgE (SIgE) against these substances. Subsequent contact with relevant allergen, either directly on the skin or through mucous membranes, may result in urticaria[101].

2). Non-IgE-mediated food-related urticaria: Natural salicylates in foods and food additives ('E'numbers), including colourings (azo and nonazodyes), preservatives (sulphites, nitrates and nitrites), antioxidants [butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT)] and aspartame (an artificial sweetener), may cause urticaria[102,103], particularly in patients who develop acute allergic symptoms after taking aspirin (acetylsalicylic acid) or non-steroidal anti-inflammatory drugs (NSAIDs)[101].

3). Physical urticaria: Physical and environmental factors such as

cold, heat, sweating, exercise, pressure, sunlight, water and vibration of sound to an extend may trigger for bringing about urticaria . The symptoms of urticaria like the weal in such physical or environmental variety tend to appear for a shorter duration of time (disappear within an hour), whereas delayed pressure urticaria may takes few hours to fully develop and takes couple of days to subside[101].

4). Drug induced urticaria: Non-steroidal anti-inflammatory drugs which inhibits cyclogenase (COX) enzymes can sometimes cause urticaria[104,105]. Other drugs such as opiates, which also includes antitussive codeine can release histamine directly from mast cells[106]. In addition many over-the-counter (OTC) analgesics also in combination to various NSAIDs including aspirin, and many cough syrups contain codeine[101].

5). Infection urticaria: Many bacterial, viral or fungal infection can sometimes manifest to urticaria. Common infections causing urticaria is hepatitis[107], infectious mononucleosis[108], H.pylori infection[109], dental infections, urinary tract infections (UTI), sinusitis etc. These incidences are very low in adults, whereas children can show urticaria resulting from viral infections[101].

6). Medical conditions or diseases related urticaria: Systemic Lupus Erythematosus (SLE) and Sjögren's syndrome like auto-immune disease can manifest chronic urticaria ie Cryoglobulin-related urticaria or urticarial vasculitis. There is an increased occurrence of autoimmune thyroid disease in patients with chronic urticaria, particularly those with histamine-releasing autoantibodies – 'autoimmune urticaria'[101].

7). Hormonal influence induced urticaria: Women occasionally experience rare cyclical form of urticaria like symptoms during their menstrual cycle, which fluctuate severely in accordance to menstrual cycle known as autoimmune progesterone urticaria occurs 7-10 prior to menstruation[110]. In pregnancy urticaria often improve with a distinct clinical condition known as polymorphic eruption of pregnancy or 'pruritic urticarial papules and plaques of pregnancy' (PUPPP), in which rash starts as itchy, urticarial papules and plaques in striae on the abdomen and thighs and then spreads to affect the whole trunk and limbs, usually begins in third trimester and is most common in first pregnancies or the first multiple pregnancy[101,111].

8). Stress induced urticaria: Acute urticaria may develop in relation to particular stressful event and is recognized that financial, personal or professional stress may all worsen chronic urticaria. The condition itself may be very debilitating and it reduces quality of life[112].

9). Urticaria related to histamine-releasing autoantibodies (autoimmune urticaria): Approximately 50% of adults and children with chronic urticaria have histamine-releasing autoantibodies (IgG autoantibodies) directed against the subunit of IgE receptor on mast cells and basophils. These autoantibodies cause mast cell degranulation via activation of the classical complement pathway [113-117].

The purpose of this present study is to find relationship between age, gender and seasonal variation of common hypersensitivity reactions prevailing among populations in Garhwal Region of Uttarakhand situated in the foot hills of Himalayan Shivalik Range.

MATERIALS AND METHODS

This retrospective study was carried out among patients visited OPD of Dermatology department at HNB Base Hospital of VCSG Govt. Medical College, Srinagar (Pauri Garhwal),Uttarakhand during January 2016 to December 2018. Data was collected only from those patients showing confirmed hypersensitivity symptoms. Suspected cases or patients having other concurring diseases were excluded from the study. A total of 6405 patients were recorded during this period. The study was conducted with proper approval given by the institutional ethics committee. Age , sex, month of consultation of patients were recorded. All descriptive analysis were done by Microsoft Excel and Social Package of Social Science (SPSS) version-21 (trial).

RESULTS

Table 1: Age wise distribution with Gender

Age (Yrs)	Sex		Total (%)
	Male (%)	Female (%)	
1-10	499 (8.0)	438 (6.9)	937 (14.9)
11-20	459 (7.0)	579 (9.0)	1038 (16.0)
21-30	547 (9.0)	884 (13.8)	1431 (22.8)
31-40	400 (6.0)	743 (11.6)	1143 (17.6)
41-50	333 (5.0)	487 (7.6)	820 (12.6)
51-60	245 (3.8)	289 (4.5)	534 (8.3)
61-70	181 (2.8)	159 (2.4)	340 (5.2)
71-80	79 (1.2)	61 (1.0)	140 (2.2)
81+	10 (0.2)	12 (0.2)	22 (0.4)
Total (%)	2753 (43)*	3652 (57)*	6405 (100)*

*Statistically significant

FIG.1: AGE WISE DISTRIBUTION WITH GENDER

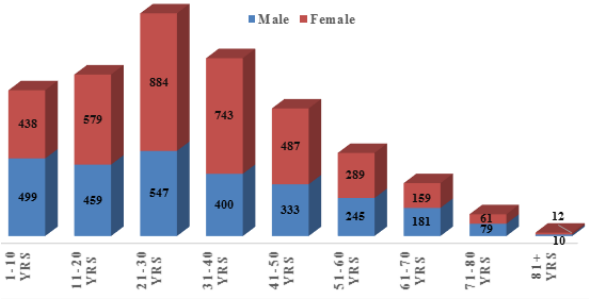

Table-1 shows relationship between various age groups and gender. The total number of cases was found 6405, out of which females showed higher percentage of 57% whereas males exhibited recorded cases of 43%. The highest prevalence of cases was found in the age group of 21-30 yrs (22.8%). Among the females and males, maximum cases were found 13.8% and 9% respectively in the same age group of 21-30 yrs. Overall the result was found to be statistically significant [Fig 1].

Table 2: Season wise Gender distribution in association to Different Diseases

Disease		ABCD	ACD	ADR	Phyto	Photo	PMLE	Insct	Urt	Total (%)
Rainy	Male	26	153	46	16	76	126	137	212	792 (12.4)
	Female	42	180	83	19	148	126	147	252	997 (15.5)
	Total (%)	68 (1.1)	333 (5.2)	129 (2.0)	35 (0.6)	224 (3.5)	252 (3.9)	284 (4.4)	464 (7.2)	1789 (27.9)
Spring	Male	20	80	25	8	140	138	48	146	605 (9.4)
	Female	31	126	52	14	287	130	61	214	915 (14.3)
	Total (%)	51 (0.8)	206 (3.2)	77 (1.2)	22 (0.3)	427 (6.7)	268 (4.2)	109 (1.7)	360 (5.6)	1520 (23.7)
Summer	Male	38	117	36	13	111	131	141	210	797 (12.4)
	Female	46	163	71	17	216	146	136	273	1068 (16.7)
	Total (%)	84 (1.3)	280 (4.4)	107 (1.7)	30 (0.5)	327 (5.1)	277 (4.3)	277 (4.3)	483 (7.5)	1865 (29.1)
Winter	Male	16	116	40	8	100	98	46	135	559 (8.7)
	Female	26	122	58	21	162	95	31	157	672 (10.5)
	Total (%)	42 (0.7)	238 (3.7)	98 (1.5)	29 (0.5)	262 (4.1)	193 (3.0)	77 (1.2)	292 (4.5)	1231 (19.2)
Total	Male	100	466	147	45	427	493	372	703	2753 (43)
	Female	145	591	264	71	813	497	375	896	3652 (57)
	Total (%)	245 (3.8)	1057 (16.5)	411 (6.4)	116 (1.8)	1240 (19.4)	990 (15.5)	747 (11.7)	1599 (25.0)	6405 (100)

FIG.2: DISEASE WISE DISTRIBUTION WITH SEASON

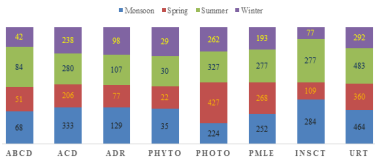

Table-2 depicts season wise distribution of various hypersensitivity cases with gender. Summer recorded the highest percentage of overall cases (29.1%) followed by rainy season (27.9%), spring (23.7%) and winter (19.2%). Normally the prevalence of all types of hypersensitive reactions in all seasons were higher among females except for PMLE during spring and winter and for insect bite (Insct) during summer where the prevalence of the males were found more [Fig 2].

Table 3: Age wise Gender distribution in association to Different Diseases

Age Group (yrs)		1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81+	Total (%)	p-value
ABCD	Male	14	7	13	9	11	20	18	7	1	100 (1.5)	0.109
	Female	8	11	21	25	29	20	19	10	2	145 (2.3)	
	Total (%)	22 (0.3)	18 (0.3)	34 (0.5)	34 (0.5)	40 (0.6)	40 (0.6)	37 (0.6)	17 (0.3)	3 (0.1)	245 (3.8)	
ACD	Male	63	75	80	70	79	41	34	21	3	466 (7.3)	0.000*
	Female	56	102	170	122	62	41	24	11	3	591 (9.2)	
	Total (%)	119 (1.9)	177 (2.8)	250 (3.9)	192 (3.0)	141 (2.2)	82 (1.3)	58 (0.9)	32 (0.5)	6 (0.1)	1057 (16.5)	
ADR	Male	26	38	38	17	11	9	6	2	0	147 (2.3)	0.021*
	Female	27	51	74	65	24	11	11	1	0	264 (4.1)	
	Total (%)	53 (0.8)	89 (1.4)	112 (1.7)	82 (1.3)	35 (0.5)	20 (0.3)	17 (0.3)	3 (0.1)	0 (0.0)	411 (6.4)	
Phyto	Male	2	5	5	8	6	8	5	5	1	45 (0.7)	0.692
	Female	2	5	11	14	17	12	6	4	0	71 (1.1)	
	Total (%)	4 (0.1)	10 (0.2)	16 (0.2)	22 (0.3)	23 (0.4)	20 (0.3)	11 (0.2)	9 (0.1)	1 (0.0)	116 (1.8)	
Photo	Male	16	55	82	82	68	58	43	19	4	427 (6.7)	0.000*
	Female	21	124	205	199	130	65	51	16	2	813 (12.7)	
	Total (%)	37 (0.6)	179 (2.8)	287 (4.5)	281 (4.4)	198 (3.1)	123 (1.9)	94 (1.5)	35 (0.5)	6 (0.1)	1240 (19.4)	
PMLE	Male	31	68	113	104	72	48	40	17	0	493 (7.7)	0.001*
	Female	24	67	122	122	80	60	17	3	2	497 (7.8)	
	Total (%)	55 (0.9)	135 (2.1)	235 (3.7)	226 (3.5)	152 (2.4)	108 (1.7)	57 (0.9)	20 (0.3)	2 (0.0)	990 (15.5)	
Insct	Male	170	83	48	27	18	12	11	2	1	372 (5.8)	0.334
	Female	168	64	51	36	28	15	8	5	0	375 (5.9)	
	Total (%)	338 (5.3)	147 (2.3)	99 (1.6)	63 (1.0)	46 (0.7)	27 (0.4)	19 (0.3)	7 (0.1)	1 (0.0)	747 (11.7)	
Urt	Male	177	128	168	83	68	49	24	6	0	703 (11)	0.000*
	Female	132	155	230	160	117	65	23	11	3	896 (14)	
	Total (%)	309 (4.8)	283 (4.4)	398 (6.2)	243 (3.8)	185 (2.9)	114 (1.8)	47 (0.7)	17 (0.3)	3 (0.1)	1599 (25)	

*Statistically Significant

Table-3 shows the relationship of different disease with various age groups in respect to gender. For ABCD, Phyto and Insct, the overall results were found to be statistically insignificant whereas for diseases ACD, ADR, Photo, PMLE and Urt were found to be statistically significant.

Table 4: Age wise distribution of Season in association to Different Diseases

Disease	Seasons	Age (Yrs)									Total (%)	p-value
		1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81+		
ABCD	Rainy	7	8	9	5	12	11	13	3	0	68 (1.1)	0.780
	Spring	6	3	9	7	9	8	1	6	2	51 (0.8)	
	Summer	6	7	10	11	10	17	18	5	0	84 (1.3)	
	Winter	3	0	6	11	9	4	5	3	1	42 (0.6)	
	Total	22	18	34	34	40	40	37	17	3	245 (3.8)	
ACD	Rainy	41	56	81	58	45	23	21	6	2	333 (5.2)	0.346
	Spring	24	29	43	41	32	18	14	4	1	206 (3.2)	
	Summer	31	62	67	48	32	18	12	10	0	280 (4.4)	
	Winter	23	30	59	45	32	23	11	12	3	238 (3.7)	
	Total	119	177	250	192	141	82	58	32	6	1057 (16.5)	
ADR	Rainy	19	28	41	22	9	5	5	0	0	129 (2)	0.524
	Spring	8	16	20	18	10	3	1	1	0	77 (1.2)	
	Summer	11	23	32	18	7	6	8	2	0	107 (1.7)	
	Winter	15	22	19	24	9	6	3	0	0	98 (1.5)	
	Total	53	89	112	82	35	20	17	3	0	411 (6.4)	
Phyto	Rainy	1	3	7	7	3	5	7	2	0	35 (0.5)	0.027*
	Spring	0	6	2	6	6	2	0	0	0	22 (0.3)	
	Summer	2	0	2	3	7	9	2	4	1	30 (0.5)	
	Winter	1	1	5	6	7	4	2	3	0	29 (0.5)	
	Total	4	10	16	22	23	20	11	9	1	116 (1.8)	
Photo	Rainy	7	30	35	52	38	33	20	8	1	224 (3.5)	0.264
	Spring	13	62	116	98	65	33	26	12	2	427 (6.7)	
	Summer	6	49	68	77	56	30	32	7	2	327 (5.1)	
	Winter	11	38	68	54	39	27	16	8	1	262 (4.1)	
	Total	37	179	287	281	198	123	94	35	6	1240 (19.4)	
PMLE	Rainy	15	32	55	57	46	29	12	6	0	252 (3.9)	0.196
	Spring	15	40	80	58	33	24	15	3	0	268 (4.2)	
	Summer	15	39	71	60	38	29	15	8	2	277 (4.3)	

	Winter	10	24	29	51	35	26	15	3	0	193 (3.1)	
	Total	55	135	235	226	152	108	57	20	2	990 (15.5)	
Insct	Rainy	114	58	42	33	16	11	7	2	1	284 (4.5)	0.532
	Spring	54	20	12	7	11	3	1	1	0	109 (1.7)	
	Summer	133	51	34	19	15	13	8	4	0	277 (4.3)	
	Winter	37	18	11	4	4	0	3	0	0	77 (1.2)	
	Total	338	147	99	63	46	27	19	7	1	747 (11.7)	
Urt	Rainy	103	98	102	59	46	34	14	7	1	464 (7.3)	0.002*
	Spring	50	69	108	56	41	22	10	3	1	360 (5.6)	
	Summer	116	59	115	84	57	38	11	3	0	483 (7.5)	
	Winter	40	57	73	44	41	20	12	4	1	292 (4.6)	
	Total	309	283	398	243	185	114	47	17	3	1599 (25)	

*Statistically Significant

Table-4 depicts the relationship of various disease in correspondence to different seasons with different age group. For ABCD, age groups of 41-50 and 51-60 yrs showed the highest number of patients in which rainy season recorded the highest number of patients in age group of 41-50 yrs and summer showed the maximum patients in age group of 51-60 yrs and overall result of ABCD was found statistically insignificant. For ACD, age group of 21-30 yrs showed the highest number of patients which contributed maximum during rainy season and overall result of ACD was found statistically insignificant. In case of ADR, age groups of 21-30 yrs again revealed highest number of patients where again rainy season recorded highest number in the same age group and overall result was found statistically insignificant. Among Phyto, highest cases was found in the age group of 41-50 yrs where summer and winter season recorded equally highest number of cases followed by age group of 31-40 yrs and result for ADR was found statistically significant**.** Among Photo, 21-30 yrs showed highest frequency where spring season recorded the highest number of patients number of patients closely followed by the age group of 31-40 yrs and overall result was found statistically insignificant**.** Among PMLE cases, the highest frequency was found in 21-30 yrs where spring season represented highest in number closely followed by age group of 31-40 yrs and of 21-30 and was found to be statistically insignificant. In Insct, age groups of 1-10 yrs showed the highest frequency with maximum prevalence in rainy season, where overall result was found statistically insignificant. Among Urt highest frequency was observed in age group of 21-30 yrs revealing higher incidence during summer season closely followed by age group of 1-10. Here all results were found statistically significant.

Table 5: Season wise frequency distribution of Different Diseases

Diseases	Seasons				Total (%)
	Rainy	Spring	Summer	Winter	
ABCD	68 (27.8)	51(20.8)	84 (34.3)	42 (17.1)	245 (3.8)
ACD	333 (31.5)	206 (19.5)	280 (26.5)	238 (22.5)	1057 (16.5)
ADR	129 (31.4)	77 (18.7)	107 (26.0)	98 (23.9)	411 (6.4)
Phyto	35 (30.2)	22 (18.9)	30 (25.9)	29 (25.0)	116 (1.8)
Photo	224 (18.1)	427 (34.4)	327 (26.4)	262 (21.1)	1240 (19.4)
PMLE	252 (25.4)	268 (27.1)	277 (28.0)	193 (19.5)	990 (15.5)
Insct	284 (38.0)	109 (14.5)	277 (37.1)	77 (10.3)	747 (11.70)
Urt	464 (29.0)	360 (22.5)	483 (30.2)	292 (18.3)	1599 (25.0)
Grand Total					**6404 (100)**

Table-5 shows the season wise frequency distribution of different hypersensitive reactions. Among all seasons, the prevalence of urticaria (Urt) was highest with 25% followed by photosensitivity (Photo) 19.4% followed by allergic contact dermatitis (ACD) 16.5% whereas phytophotodermatitis (Phyto) showed the lowest prevalence of 1.8%. The prevalence of Urt was found maximum in all seasons except spring where occurrence of Photo was found highest. For ABCD, the order of prevalence was found Summer (34.3%) > Rainy (27.8%) > Spring (20.8%) > Winter (17.1%) whereas among ACD, it was found Rainy (31.5%) > Summer (26.5%) > Winter (22.5%) > Spring (19.5%), in case of ADR showed Rainy (31.4%) > Summer (26%) > Winter (23.9%) > Spring (18.7%). Among Phyto, order of occurrence was found Rainy (30.2%) > Summer (25.9%) > Winter (25%) > Spring (18.9%) whereas in case of Photo, the order was Spring (34.4%) > Summer (26.4%) > Winter (21.1%) > Rainy (18.1%). The order in case of PMLE was found Summer (28%) > Spring (27.1%) > Rainy (25.4%) > Winter (19.5%) and insect bite (Insct) showed Rainy (38%) > Summer (37.1%) > Spring (14.5%) > Winter (10.3%) whereas Urticaria (Urt) showed the order with Summer (30.2%) > Rainy (29%) > Spring (22.5%) > Winter (18.3%).

DISCUSSION

The present study accounts that females (57%) were predominantly suffered from hypersensitive disorders in Garhwal region like that of many other articles, but in contrary C Anirudh et al. revealed about male predominance[118]. Both urban and rural populations of different age groups were represented. The major affected population was in the age group of 21-30 years. Summer recorded the highest percentage (29.1%) of various hypersensitivity cases mainly due to heat (High intensity of UV rays) and dusty environment, followed by rainy season (27.9%) due increase of communicable diseases and proliferation of plants and insects. In spring (23.7%) due to high UV radiations and high density of pollens in surrounding air manifest to higher prevalence of photosensitivity, urticaria and PMLE[119]. Prevalence of ABCD and Phytophotodermatitis are more common in age groups of 41-50 yrs and 51-60 yrs mainly due to decrease in immune-threshold and increase of sensitization which prevailed during that age and where exposure also count as compared to the older age groups. Incidence of Urticaria, Photo, ACD, PMLE and ADR showed highest frequency of hypersensitivity in age group of 21-30 years due to their increase of activity and maximum exposure. Insect bites are more prone in age groups of 1-10 yrs mainly in rainy and summer seasons where availability of insects are more and due to developing immune response and high sensitization.

CONCLUSION

Hypersensitive disorders are showing increase in trend nowadays, and Governments are promoting various activities to increase awareness, impart education, training and updates about allergic diseases among various layers of populations. Increase of allergic testing with latest technology in the field of medical research may help in proper diagnosis and efficient management of different hypersensitive reactions in future.

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