

**To study the efficacy of thymus and activation-regulated chemokine (TARC) as a diagnostic marker of atopic dermatitis and its association with the severity of the disease in the paediatric age group in the Indian context**



A dissertation submitted in partial fulfillment of the rules and regulations for M.D. Branch XX (Dermatology, Venereology and Leprosy) Examination of The Tamil Nadu Dr. M.G.R. Medical University, to be held in May 2019

## **DECLARATION**

This is to declare that the dissertation entitled- **To study the efficacy of thymus and activation-regulated chemokine (TARC) as a diagnostic marker of atopic dermatitis and its association with the severity of the disease in the paediatric age group in the Indian context-** is my original work done in partial fulfillment of rules and regulations for **M.D. degree (Branch XX) in Dermatology, Venereology and Leprosy** of **The Tamil Nadu Dr. M.G.R Medical University** to be held in May 2019.

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## **CERTIFICATE**

This is to certify that the dissertation entitled-**To study the efficacy of thymus and activation-regulated chemokine (TARC) as a diagnostic marker of atopic dermatitis and its association with the severity of the disease in the paediatric age group in the Indian context** is the bonafide original work of **Dr. Himadri**.

This study was undertaken at the **Christian Medical College, Vellore** from December 2016 to June 2018, under my direct guidance and supervision, in partial fulfillment of the requirement for the award of the **M.D. degree (Branch XX) in Dermatology, Venereology and Leprosy** of **The Tamil Nadu Dr. M.G.R Medical University**.

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## **LIST OF ABBREVIATIONS**

AD	Atopic dermatitis
ALSPAC	Avon Longitudinal Study of Parents and Children
AMP	Antimicrobial peptide
cAMP	Cyclic adenosine monophosphate
CDLQI	Children's Dermatology Life Quality Index
CGRP	Calcitonin gene-related peptide
CLDN-1	Claudin-1
DLQI	Dermatology Life Quality Index
EASI	Eczema Area and Severity Index
EDC	Epidermal differentiation complex
FLG	Filaggrin
GM-CSF	Granulocyte-macrophage colony stimulating factor
GRPR	Gastrin-releasing peptide receptor
IDQOL	Infant's Dermatitis Quality of Life Index
IFN	Interferon
IgE	Immunoglobulin E
IL	Interleukin
	International Study on Asthma and Allergies in
ISAAC	Childhood
IVIG	Intravenous immunoglobulin
LDH	Lactate dehydrogenase
NFAT	Nuclear factor of activated T-cells
PAR	protease-activated receptor
PCR	Polymerase chain reaction
PDE	Phosphodiesterase
POEM	Patient Oriented Eczema Measure
ROC	Receiver operating characteristic curve
SCORAD	SCORing Atopic Dermatitis

TARC	Thymus and activation-regulated chemokine
Th2	T-helper 2
TNF	Tumour necrosis factor
TPMT	Thiopurine methyltransferase
TSLP	Thymic stromal lymphopoietin
UV	Ultraviolet
VIP	Vasoactive intestinal polypeptide

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## INTRODUCTION

Atopic dermatitis (AD) is a pruritic, chronic inflammatory skin disease with a wide variety of clinical features, which affects upto 20% of the population in some settings.(1,2) The etiology has been linked to complex interactions between the predisposing genes, the immune system and the environment.(1,3)

AD is diagnosed based on various clinical criteria such as the Hanifin and Rajka criteria, Danish Allergy Research Centre Criteria, Schultz-Larsen criteria and the U.K. Working Party Diagnostic criteria.(4,5) The specificity of the criteria used in our study (The U.K. Working Party Diagnostic criteria) ranges from 90.4% to 98.3% and sensitivity from 10% to 95.5%.(4)

The disease can cause impairment in the quality of life and the tools used to assess the same include Quality of Life Index (IDQOL) for children below 4 years of age(6), Children's Dermatology Life Quality Index (CDLQI) for children between 4-16 years of age(6,7) and Dermatology Life Quality Index (DLQI) for those above 16 years.(8) The severity of AD is determined using several scoring systems, including SCORing Atopic Dermatitis (SCORAD), Eczema Area and Severity Index (EASI) and Patient Oriented Eczema Measure (POEM).(9)

There are several biomarkers used to assess the severity such as serum levels of thymus and activation-regulated chemokine (TARC), IL-18, lactate dehydrogenase (LDH), IgE and peripheral blood eosinophils.(10) Serum TARC levels was found to be the most reliable biomarker for AD as published in a meta-analysis in October 2015.(11)

Traditionally, the clinical disappearance of eczema and the subjective relief from pruritus have been considered as signs of remission. However, in most cases subclinical remnants persist and if the medical treatment is stopped before complete remission, chances of relapse are high.(12) Observing TARC levels is useful in improving adherence of the patients to the treatment regimens.(12,13) There are no published studies in India assessing the correlation between serum TARC levels and AD and its severity. This study was undertaken to evaluate the clinical profile of patients with AD, study the serum levels of TARC in AD compared with controls and also the relationship with the clinical severity as assessed by SCORAD index.

## **AIMS AND OBJECTIVES**

### **Primary objective:**

1. To study the efficacy of thymus and activation-regulated chemokine as a diagnostic marker of atopic dermatitis and the association with the severity of the disease in the paediatric age group in the Indian context.
2. To study the clinical profile of patients with atopic dermatitis.

### **Secondary objectives:**

To study the quality of life of patients with atopic dermatitis and its correlation with serum TARC.

## REVIEW OF LITERATURE

### **Definition:**

AD is a pruritic, chronic relapsing inflammatory skin disease usually beginning in early childhood. Its rash is characterized by itchy papules, papulovesicles, erythema, excoriations and lichenification, which occur typically in a flexural distribution.(1) It is often associated with other atopic conditions in the person or his/her family members. Asthma develops in around 30% of children with AD and allergic rhinitis in 35%.(14)

### **History:**

The earliest account of a possible AD dates back to as early as 69-140CE, as seen in the translation of the Roman historian Suetonius's book, *The Twelve Caesars*, describing a cutaneous condition affecting Emperor Augustus, although there are even earlier descriptions of itchy skin conditions. The concept of 'atopy' was initially given in 1923 by Arthur Coca and Robert Cooke when an association between asthma and allergic rhinitis was recognized by them. It was explained with a term coined from the Greek word *atopia* in 1923 by Edward Perry, a professor of Greek at Columbia University, which means 'strangeness' or 'out of place'. In 1933, Fred Wise and Marion Sulzberger introduced the term atopic dermatitis. Hanifin and Rajka published the first widely used criteria for diagnosing AD in 1980. Williams et al

modified the criteria in 1994 to develop the U.K. Working Party Diagnostic criteria.(15,16)

### **Epidemiology:**

The prevalence of AD varies widely between different countries and can affect up to 20% of children in some countries as determined in a multi-country cross-sectional study conducted by The International Study on Asthma and Allergies in Childhood (ISAAC) Steering Committee. In 6-7 year age-group, the lowest prevalence was found in Eastern Mediterranean and Indian subcontinent, while in the older age group of 13-14 years the highest prevalence was seen in Asia-Pacific, Eastern Mediterranean, Indian subcontinent and Northern and Eastern Europe. The Phase III of ISAAC study also shows that AD has plateaued in developed countries such as the United Kingdom and New Zealand but continues to increase in low-income countries.(2,17) The incidence is highest in infancy and childhood with approximately 60% of cases occurring within the first year of life and 90% within 5 years of age.(18,19)

### **Prevalence of AD in India:**

Prevalence studies from India are mostly hospital-based. In a hospital-based study in 2012 conducted across 4 hospitals in India, one from each zone, the point prevalence was found to be 6.75% with the prevalence in South India being 2.8%.(20) In ISAAC phase III, current symptom of eczema was detected in 2.7% of participating children in the Indian subcontinent, severe eczema in 0.3% children and lifetime prevalence

of 4.4% in the age group of 6-7 years. The corresponding figures in the age group of 13-14 years were 3.6%, 0.4% and 8.9%, respectively.(2,21)

### **Etiopathogenesis of AD:**

Genetic, environmental and immunological factors are implicated in the pathogenesis of AD.(3) There is a complex interplay of the immune system with the epithelium, ultimately leading to disease manifestation.

#### Genetic factors:

The risk of developing the disease is increased with loss of function mutation in the gene encoding filaggrin (FLG), an epidermal peptide that plays an important role in maintaining the skin barrier.(22) Filaggrin is encoded on chromosome 1q21 within the epidermal differentiation complex (EDC).

The risk is also influenced more by maternal disease status as compared to paternal status, though this is not universal.(23,24) The mechanisms underlying this observation could be genomic imprinting, mitochondrial transmission, interactions between the *in utero* environment and genes and exposure to the nutritional and immunologic properties of breast milk.(23)

## Environmental factors:

### *Climate:*

There are positive and negative correlations of AD symptoms with latitude and annual outdoor temperature, respectively. UV radiation, owing to its immunosuppressive effect, is an effective therapy for AD. There is a likely interplay of outdoor temperature, UV radiation, humidity and seasonal pollen counts in the pathogenesis of AD.(1)

### *Urban vs rural living:*

The burden of AD is higher in urban areas.(1)

### *Diet:*

ISAAC Phase 3 showed a protective effect of fresh fruit consumption, as opposed to fast food consumption. High fish intake during pregnancy and late infancy has also shown to confer a protective role, possibly due to the high content of anti-inflammatory *n*-3 polyunsaturated fatty acids.(1,25)

### *Breastfeeding and delayed weaning:*

The protective effect of breastfeeding in development of AD is controversial. A meta-analysis of 27 study populations published in 2009 did not show any statistically significant benefit of exclusive breastfeeding until at least 3 months of age (pooled OR 0.89, 0.76-1.04).(26) However, an earlier meta-analysis in 2001 had shown a lower incidence of AD in children who were exclusively breastfed until 3 months of

life, especially those with a family history of atopy.(27) A recent multi-centre case-control study in Italy showed lower risk of AD in children who were weaned early by 4-5 months of age as compared to those who were exclusively breastfed until 6 months.(28)

*Obesity and physical exercise:*

It is unclear whether the association between obesity and AD is causal, e.g. secondary to inflammation mediated by adipokines like leptin; or related to the diet low in antioxidants such as fruits and vegetables, which can facilitate AD via oxidative stress pathways.(1)

The hygiene hypothesis:

*Basic hygiene:*

The Avon Longitudinal Study of Parents and Children (ALSPAC) found a weak association between general hygiene measures and AD risk.(29)

*Day care:*

A cohort study in Denmark has found a reduction in risk of AD in children who attend day care centres, possibly related to increased microbial exposure. However, other studies have found an opposite effect.(30–32)

*Farm environment:*

There is no convincing protective effect but consumption of unpasteurized milk and frequent contact with farm animals has reduced AD risk in some settings.(33)

*Pets:*

A meta-analysis showed protective effect of exposure to dogs whereas the picture was less clear for cats. (34)

*Endotoxin exposure:*

Endotoxins are lipopolysaccharides on the surface of gram-negative bacilli, which may be responsible for AD risk reduction with pet exposure. However, this effect was confined to high endotoxin exposure.(33,35)

*Helminth parasites:*

The relationship between helminths and human host depends on the type, burden and timing of the parasitic infection. Schistosoma and hookworms appear to be protective against atopy. The risk of AD later in life does not seem to increase on loss of helminth exposure, supporting that perinatal priming of the immune system can protect against AD.(33,36,37) There are studies, predominantly on animals, which suggest that parasites can induce a systemic immunoregulatory effect and regulate gut dendritic cells via Toll-like receptors, induce regulatory T-cells, B-cells, dendritic cells and anti-inflammatory cytokines, which may protect against allergic responses.(1)

*Childhood vaccinations and antibiotics:*

There may be increased exposure to antigens of infectious agents through vaccinations, which can lead to Th2 immune response and increase the risk of allergic diseases. Antibiotics reduce the gut microflora and alter a child's immune system with enhanced responses to environmental antigens.(1,33)

*Gut and skin microbiome:*

Some studies have shown more *Staphylococcus aureus* and coliforms with fewer bifidobacteria and lactobacilli in early gut microflora of people who later develop AD.(38,39) The gut microbiome is influenced positively by vaginal mode of delivery and having older siblings.(40) Skin microbiome also influences the cutaneous immune system. *Staphylococcus aureus* is a well-known cause of exacerbation and chronicity in AD.(1)

Immune dysregulation:

T helper 2 (Th2) cells seem to play a crucial role in pathogenesis of AD. Th2 cytokines, IL-4 and IL-13, are increased in skin of early lesional AD, which also downregulate filaggrin expression.(1,41) In addition, IL-4 downregulates the expression of cutaneous defensins and increases the expression of bacterial adhesion molecules, which eventually facilitates colonization with *Staphylococcus aureus*.(1,42,43)

Increased levels of IL-5, GM-CSF, IL-12 and IFN- $\gamma$  are found in chronic AD lesions. IL-5 and GM-CSF promote the survival and growth of eosinophils and macrophages. IL-12 plays an important role in polarization of Th1 cells producing IFN- $\gamma$ , which induce apoptosis of keratinocytes associated with epidermal spongiosis. IL-22 is also found in high levels in chronic AD, which enhances keratinocyte proliferation, reduces antimicrobial protein expression and downregulates filaggrin expression. (1,44)

AD dendritic cells have a high expression of Fc $\epsilon$ R1, a high-affinity IgE receptor, the stabilization on cell surface of which occurs by IgE binding. Its expression, therefore, correlates with total IgE.(45,46)

Thymic stromal lymphopoietin (TSLP), a keratinocyte derived IL-7-like cytokine, causes direct neuronal triggering of itch and epidermal programming of dendritic cells to induce inflammatory Th2 cells. (47,48)

There is a deficiency of Th17 in AD skin. However, the role of IL-17 is unclear. IL-17A suppresses Th2 cytokines and TSLP expression, and IL-4 suppresses IL-17A function. This suggests that Th17 and Th2 pathways perhaps co-regulate each other. Interestingly, IL-17E (IL-25) enhances Th2 cell-mediated inflammation and downregulates filaggrin synthesis.(49)

### Food allergy:

Numerous dendritic cells expressing high-affinity IgE receptor are found on eczematous skin lesions. This enables the cells to take up a wider range of allergens.(49) This is thought to cause epicutaneous sensitization to environmental and food allergens in individuals with AD, which in turn may partly explain the relationship between food allergy, AD, allergic rhinitis and asthma, which define the 'atopic march'.(50)

### Allergic contact dermatitis:

There is no evidence currently to suggest that AD may be a yet unidentified allergic contact dermatitis, though they share clinical and histological features.(1) A hospital-based study in India observed that 7 patients with AD out of a total of 30 had co-existent allergic contact dermatitis.(51)

### Autoimmunity:

This could play a role as observed by IgE reactivity to several human protein antigens in patients with AD, which correlates with disease severity and chronicity. However, it is unclear whether autoimmunity is the primary disease mechanism or an epiphenomenon of chronic inflammation.(52)

### Sweating:

Sweating induces itching in AD. This may be due to IgE-mediated allergic response to sweat components or an altered sensation with neuropeptides that are released in

the neurogenic control of sweat glands.(1,53) Eishi *et al.* showed that sweat production via direct cholinergic effect is almost similar between patients with AD and controls, but axon reflex-induced sweating was lower in volume and had a longer latency in AD.(54)

#### Endocrine and psychological factors:

Stress causes an increased production of cortisol. However, the rise has been found to be lower in those with AD.(55) Sex-steroids also probably play a role as seen in premenstrual flare or exacerbation or amelioration of eczema in pregnancy. They possibly modify sensitivity to the anti-inflammatory effects of glucocorticoids.(56,57)

#### Pharmacological and vascular abnormalities:

There is a tendency to vasoconstriction in small blood vessels in AD as seen by various responses such as white dermographism, delayed blanch with acetylcholine, white reaction with nicotinic acid esters, abnormal reaction to histamine, low finger temperature and pronounced vasoconstriction with cold exposure.(1,58) During elicitation of itch in AD and controls, the increase in histamine concentration is the same, but tryptase is significantly increased in AD. Tryptase activates PAR-2, increased in lesional AD skin.(59,60)

Cyclic AMP (cAMP) is a key second messenger, the downstream effect of which includes increased anti-inflammatory cytokine, IL-10 production and decreased

expression of pro-inflammatory cytokine (TNF- $\alpha$ , IL-12) production in leukocytes. cAMP levels are increased by phosphodiesterase (PDE) inhibition. PDE4 inhibition mediates anti-inflammatory effects on various cell types including T lymphocytes, B lymphocytes, macrophages, monocytes, neutrophils and eosinophils.(61)

#### Pathophysiology of pruritus:

Non-histaminergic signaling is more relevant in AD. This can be mediated via PAR-2, PAR-4, neuropeptides like substance P, calcitonin gene-related peptide (CGRP), somatostatin, vasoactive intestinal polypeptide (VIP), acetylcholine (Ach) in postganglionic sympathetic fibres and neuropeptide Y.(1) *In vitro* data has demonstrated the role of NFAT signaling in keratinocyte expression of TSLP.(47) In mouse model, it has been shown that selective ablation of lamina I neurons in spinal cord, expressing gastrin-releasing peptide receptor(GRPR), led to abolition of scratch behavior with multiple pruritogens.(62)

#### **Clinical features:**

AD has a wide range of clinical features, the cardinal ones being intense pruritus and cutaneous reactivity. Acute cutaneous lesions include intensely pruritic, erythematous papules which are associated with excoriations, vesicles and serous exudate. Subacute lesions include erythematous, excoriated scaling papules. Chronic lesions include thickened plaques, lichenification and fibrotic papules or prurigo nodularis. Other findings include Dennie-Morgan folds (accentuated grooves below the lower eyelid margin), darkening beneath the eyes, also referred to as allergic

shiners, facial pallor, cheilitis, pityriasis alba, white dermographism, atopic dirty neck (reticulate pigmentation on the sides of neck) and features suggestive of filaggrin mutation which include keratosis pilaris, ichthyosis vulgaris and hyperlinearity of palms and soles, especially over the thenar eminence.(63–65) Filaggrin mutations were found in 26.7% patients with AD and 14.4.% patients without AD in a study by Morar et al.(66)

Hand eczema is another manifestation that may affect more than 50% of patients. Patchy vesicular and lichenified eczema can be seen in childhood. In more extensive disease, a diffuse, chronic lichenified eczema may be seen, which often persists into adult life. Erythroderma or exfoliative dermatitis involving more than 90% of the body surface area may be seen. Nail involvement may occur in the form of coarse pitting and ridging.(1,63)

The distribution of lesions varies according to the age of the patient and disease activity.

#### Infantile phase:

The lesions usually start on the face and there is relative sparing of the napkin area. As the child starts crawling, the exposed surfaces such as the extensor aspect of the elbows and knees become involved.(1) Facial involvement was seen in 79% infants and 74.5% children in a study by Dhar et al(67), whereas it was seen in 25% patients in another study conducted by Sehgal et al.(68)

### Childhood phase:

There is predominance of flexural eczema, especially the cubital and popliteal fossae from 18 to 24 months of age. Extensor distribution of eczema in this phase is uncommon but when present, may take longer time to remit.(1)

### Adult phase:

Flexural inflammation is less problematic than facial and hand involvement. Involvement of the lip vermilion, nipple eczema and follicular lichenified papules may be seen. Photosensitivity may also occur.(1)

### **Diagnosis and differential diagnosis:**

AD is diagnosed clinically based on the history, the morphology and distribution of lesions and other clinical signs. There are various formal set of criteria for the same such as the Hanifin and Rajka criteria, Danish Allergy Research Centre Criteria, Schultz-Larsen criteria and U.K. Working Party Diagnostic criteria.(5) The specificity of the U.K. Working Party Diagnostic criteria (Table 1) ranges from 90.4% to 98.3% and sensitivity from 10% to 95.5%.(4)

A number of diseases can mimic AD such as inflammatory skin diseases like seborrheic dermatitis, contact dermatitis, psoriasis; infections and infestations like secondary syphilis, candidiasis, scabies and HIV/AIDS related skin changes.(69)

There are also a group of relatively rare disorders with a rash similar to atopic eczema.

These include hypereosinophilic syndrome, hyper-IgE syndrome,

agammaglobulinemia, anhidrotic ectodermal dysplasia, ataxia telangiectasia, phenylketonuria, Netherton syndrome and Wiskott-Aldrich syndrome.(1)

**Table 1. The U.K Working Party Diagnostic Criteria(70)**

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Must have:  
An *itchy* skin condition (or parental report of scratching or rubbing in a child)

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Plus 3 or more of the following:

1. History of involvement of the skin creases such as folds of elbows, behind the knees, fronts of ankles or around the neck (including cheeks in children under 10).
2. A personal history of asthma or hay fever (or history of atopic disease in a first-degree relative in children under 4).
3. A history of a general dry skin in the last year.
4. Visible flexural eczema (or eczema involving the cheeks/forehead and outer limbs in children under 4).
5. Onset under the age of 2 (not used if child is under 4).

---

**Classification of severity:**

The severity of AD is determined using several scoring systems, including SCORAD, EASI and POEM. The EASI and SCORAD have been found to be the best available tools for assessing the disease severity.(9) The SCORAD index was developed by the European Task Force on Atopic Dermatitis in 1990 and consists of the an objective score which includes the extent and intensity of clinical features and a subjective score that includes sleep disturbance and pruritus.(70) The range of the objective SCORAD lies between 0 and 83 and the severity of AD can be classified as mild (<15), moderate (between 15 and 40) or severe (>40).(71,72) SCORAD index which includes the objective and subjective scores was similarly graded as mild (<25), moderate (25-50) and severe (>50).(73) In a systematic review which combined data

till October 2012, SCORAD was found to be a valid, internally consistent and interpretable composite score.(9)

### **Complications and co-morbidities:**

#### Psychosocial aspects:

The disease can cause impairment in the quality of life by causing sleep disturbance, teasing, social exclusion, depression and other behavioural disturbances. A recent study found an increased risk of mental health disorders in children with AD.(74)

There are various tools that can be used to assess the quality of life, such as IDQOL for children below 4 years of age(6), CDLQI for children between 4-16 years of age(6,7) and DLQI for those above 16 years.(8) The quality of life indices can be scored from 0 to 30, with higher score indicating higher impact on the quality of life. In addition, IDQOL has a separate score for the severity of eczema, which correlates with the overall score.(75) Studies have shown a positive correlation between QOL indices and severity as assessed by three-item severity score(76) or SCORAD.(77)

#### Growth delay:

Children with AD have a growth delay, which may be attributed to the disease and also to the use of corticosteroid therapy.(78,79)

Secondary infections:

*Bacterial infections:*

Colonization and disease exacerbation by *Staphylococcus aureus* is common in AD.

Secondary bacterial infections may also be caused by Streptococci.(1,80)

*Viral infections:*

When a virus which usually causes a localized or mild vesicular eruption causes a widespread eruption in patient with pre-existing dermatosis, it is referred to as Kaposi's varicelliform eruption. Eczema herpeticum, an acute generalized infection caused by herpes simplex virus may develop in patients with AD. The patients may present with widespread lesions and high-grade fever, or the lesions may be localized to regions of pre-existing dermatitis. Eczema vaccinatum refers to a similar eruption caused by vaccinia virus. Coxsackie infection may also cause an abnormal response.(1)

Various molecular mechanisms have been attributed to increased susceptibility for developing eczema herpeticum. Impaired mechanical skin barrier function involving both the stratum corneum and the tight junctions influenced by deficiency of claudin-1 (CLDN-1), lower levels of antimicrobial peptides (AMPs) like defensins and the cathelicidin- LL-37, Th2 predominant milieu which further reduces the expression of AMPs and reduced plasmacytoid dendritic cells have been implicated.(81,82)

### Ocular abnormalities:

Dennie-Morgan folds, conjunctival irritation and keratoconjunctivitis have been seen in children with AD. Keratoconus or conical cornea is almost always bilateral and is considered to occur due to rubbing and use of topical steroids. Both posterior and anterior subcapsular cataracts occur. Retinal detachment has also been reported.(1)

### Lymphomas:

The risk of lymphomas, both systemic and cutaneous, appears to be higher in severe AD but further studies are required to confirm the same. There is also insufficient evidence about the risk of lymphomas with the use of topical calcineurin inhibitors.(1)

### **Investigations:**

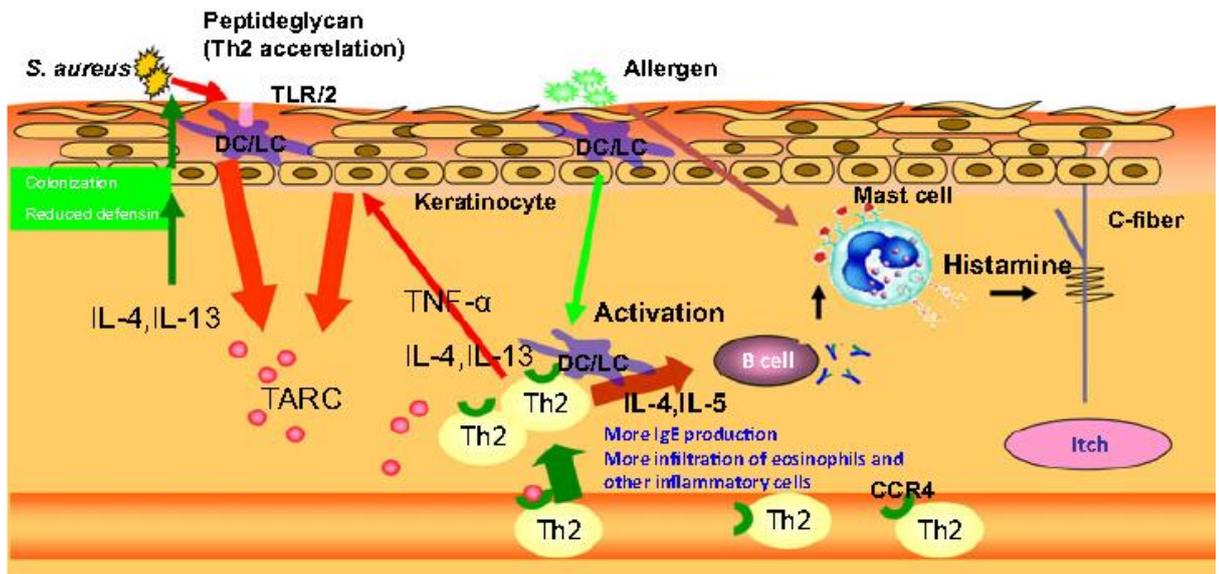
The identification of factors triggering AD is predominantly clinical. Children who have a clear allergy-like reaction such as urticaria or acute abdominal symptoms may benefit from skin prick tests or IgE antibodies against the suspect food. However, in case of eczema, the reaction may be non-IgE mediated. Pus swabs for bacterial culture and sensitivity can identify colonization or infection by *Staphylococcus aureus* or  $\beta$ -haemolytic streptococci. Herpes simplex can be identified via a Tzanck smear, polymerase chain reaction (PCR), culture, immunofluorescence slide test or electron microscopy.(1)

The role of vitamin D is increasingly being recognized in immunomodulation in different disorders. It maintains the epidermal barrier probably through increased expression of filaggrin, involucrin and antimicrobial peptides. Current evidence suggests a beneficial effect of vitamin D on AD. However, the various studies are limited by a short study duration and a small sample size. (83,84)

There are several biomarkers used to assess the severity such as serum levels of thymus and activation-regulated chemokine (TARC), IL-18, lactate dehydrogenase, IgE and peripheral blood eosinophils.(10)

### **TARC:**

Thymus and activation-regulated chemokine (TARC/CCL17) is a Th2 chemokine. It is expressed in thymus constitutively and produced by keratinocytes, endothelial cells and monocyte-derived dendritic cells. It recruits cells expressing CCR4 and CCR8 receptors and is involved in migration of Th2 cells. Its production by keratinocytes is upregulated by IL-1 $\beta$  and TNF- $\alpha$ . (85) Activation of PAR-2 (protease-activated receptor 2) by peptides also increases the transcription of TARC and therefore, proteases from mites may increase its levels via PAR-2.(86)



**Figure 1. Speculated mechanism for abnormally high TARC in AD- vicious cycles of positive feedback (88)**

Studies have shown a higher TARC level in AD compared to healthy controls and patients with other skin diseases like chronic actinic dermatitis, pustular psoriasis, prurigo nodularis, mycosis fungoides, drug eruptions etc. (87,88) Serum TARC was also found to be the most reliable biomarker for assessing severity of AD as published in a meta-analysis in October 2015, wherein a strong correlation was found with the severity of the disease in 4 longitudinal and 16 cross-sectional studies mainly from Japan (pooled correlation coefficients of 0.60 and 0.64, respectively)(11) Traditionally, the clinical disappearance of eczema and the subjective relief from pruritus have been considered as signs of remission. However, in most cases subclinical remnants persist and if the medical treatment is stopped before complete remission, chances of relapse are high. (12) TARC levels have been found to decrease

with treatment. (13,87) Observing TARC levels can, therefore, be useful in improving adherence of the patients to the treatment regimens.(12,13)

The normal values of TARC differ based on the age of a person, with highest levels in infancy (Table 2).(89) This could be due to Th2-skewed responses seen towards the common environmental antigens in all newborns.(90)

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**Table 2. Normal TARC values**

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Adult	<450 pg/mL
Infant 6–12 months	<1367 pg/mL
Infant 1–2 years	<998 pg/mL
Child 2–15 years	<743 pg/mL

---

### **Management:**

#### First line:

Patient education, reduction of trigger factors, regular emollient applications and use of topical corticosteroids to induce remission constitute the first line treatment strategies. Oral antihistamines may be added for short periods. Oral antibiotics can be given if there is a secondary bacterial infection. Oral corticosteroids like prednisolone can be used to manage severe exacerbation of the disease. Its role, though limited, is definite in such cases.(1)

Proactive therapy with local application of potent topical steroids or topical calcineurin inhibitors to the healed areas twice a week can be used for maintenance.(91)

Second line:

The compliance of the patient must be assessed in those who fail to respond to treatment. The potency of topical corticosteroids may be increased or wet wrap technique may be used. Phototherapy using either ultraviolet B (UVB) or ultraviolet A (UVA) can be given. Narrow band UVB is preferred.(1)

Third line:

*Cyclosporine:*

It suppresses the production of T-cells and IL-2. Cyclosporine significantly decreases disease activity within 2-6 weeks of initiation of treatment. The dose ranges from 3-6mg/kg/day in two divided doses. Continuous long-term regimen, upto 1 year; or intermittent short-term courses of 3-6 months can be used.(92)

*Azathioprine:*

It is a purine analogue that inhibits DNA synthesis and can be used for treatment of refractory AD. The onset of action is slower as compared to cyclosporine and improvement in disease activity may be seen over first 3 months of use. The dose needs to be adjusted according to the patient's ability to metabolise the drug, which in turn is determined by the activity of thiopurine methyltransferase (TPMT) enzyme.

TPMT levels in red blood cells should, therefore, be determined prior to initiation of azathioprine. The dose for patients with normal to high TPMT activity ranges from 1-3mg/kg/day, whereas those with low TPMT activity should be given a dose of 0.5-1mg/kg/day.(1,92)

*Methotrexate:*

It is an anti-folate metabolite that blocks the synthesis of DNA, RNA and purines and negatively affects the T-cell function. The average time to achieve maximal response is about 10 weeks.(92)

*Mycophenolate mofetil:*

It blocks purine synthesis by inhibiting inosine monophosphate dehydrogenase. The suggested dose in children ranges from 600-1200mg/ m<sup>2</sup>, which is equivalent to 40-50mg/kg/day in case of young children and 30-40mg/kg/day in case of adolescents.(92)

*Interferon gamma (IFN- $\gamma$ ):*

It is a cytokine that enhances natural killer cell production and increases macrophage oxidation. There are a few studies that show its efficacy in AD. There is no optimal dose recommended for AD but it is usually given thrice weekly as subcutaneous injections.(92)

*Biological agents:*

The data for the use of tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) inhibitors, theophylline, intravenous immunoglobulin (IVIg) for managing AD is currently insufficient. (92)

Understanding the pathogenesis of AD has led to development of targeted therapies such as Dupilumab, which is a fully human monoclonal antibody against the  $\alpha$  subunit of IL-4 receptor. It blocks IL-4 and IL-13 signalling, which are overexpressed in AD. It is given as a subcutaneous injection. Phase III trials have not identified significant safety concerns but further trials are required to establish long-term safety.(93)

Lebrikizumab, a monoclonal antibody against IL-13, also showed good tolerance and significant improvement in moderate-to-severe AD in adults in a multicentre randomised phase II trial.(94)

Crisaborole is a topical PDE-4 inhibitor, which can be used for treating mild to moderate AD.(95,96) Apremilast, an oral PDE-4 inhibitor has also been studied for treatment of AD but the results have not been as promising as in the case of psoriasis.(61)

The role of probiotics in AD:

A meta-analysis published in 2015 which included randomised trials administering probiotics to pregnant or nursing mothers or infants below the age of 3 months showed a benefit in preventing eczema in high-risk children. A mixture of

*Lactobacilli* and *Bifidobacteria* was effective rather than either strain alone.(97)

Another meta-analysis showed a reduction in SCORAD in children between 1-18 years of age who were given probiotic supplements. *Lactobacillus*, *Lactobacillus fermentum* and a probiotic mixture were effective. However, *Lactobacillus rhamnosus strain GG* and *Lactobacillus plantarum* showed no effect.(98)

## **MATERIALS AND METHODS**

### **Study design:**

This was a hospital-based, case-control study of children with AD and those with disease mimicking AD attending a tertiary care centre.

### **Setting:**

The study was done in the out-patient and inpatient departments, Department of Dermatology, Venereology and Leprosy, Christian Medical College, Vellore, a tertiary care hospital in Tamil Nadu.

### **Period of study:**

19 months (December 2016–June 2018)

### **Patient population:**

All patients (0-16 years of age) with AD, between the specified period, subject to fulfillment of the inclusion criteria were included. Controls with diseases mimicking AD were included from the patients attending the Dermatology out-patient clinic.

### **Cases:**

#### Inclusion criteria:

1. Patients with AD diagnosed by UK Working Party Diagnostic Criteria
2. Age  $\leq$  16 years

3. Patients consenting for the study

Exclusion criteria:

1. Patients not willing to participate in the study
2. Patients with age > 16 years

**Controls:**

Inclusion criteria:

1. Patients with age  $\leq$  16 years with any of the following diseases which are mimics of AD

Inflammatory Skin diseases:

- i) seborrheic dermatitis
- ii) contact dermatitis
- iii) psoriasis

Infections and infestations:

- i) candidiasis
- ii) scabies
- iii) impetigo

Exclusion criteria:

1. Age > 16 years
2. Not willing to participate in the study

## **Methodology:**

The diagnosis of AD was made based on the UK Working Party Diagnostic Criteria.

All patients, who fulfilled the inclusion criteria for cases and controls, were recruited in the study after obtaining informed consent. (Annexure-1)

The details pertaining to the study were recorded in a proforma as in Annexure 2.

## **Demographic details:**

Demographic details regarding the age at presentation, gender and address were recorded.

## **History pertaining to the AD: (Annexure 2)**

1. Antenatal and birth history were recorded. The birth order and duration of exclusive breastfeeding were also documented.
2. The age and site of onset of AD and history of involvement of other sites were obtained.
3. A history of dry skin or atopy were asked for.
4. Details of triggering factors, including seasonal variation and relieving factors, if any were also taken.
5. Details regarding complications such as cutaneous and systemic infections, behavioural changes or sleep disturbance were obtained.
6. Family history of atopy was recorded.
7. Necessary information regarding past treatment was also collected.

**Clinical examination:** (Annexure 2)

1. The anthropometric measures such as height and weight were recorded. BMI was calculated for children 2 years or older if their weight was above the 97<sup>th</sup> centile.
2. Presence of significant lymphadenopathy was documented.
3. Any ocular changes, if present, were recorded. Screening for cataract was done with torchlight examination.
4. The patient's skin, scalp, nails and mucosae were examined. Presence of acute eczematous lesions (erythema, exudation, papules, vesiculopapules, scales or crusts) or chronic lesions (infiltrated erythema, lichenification, prurigo, scales or crusts) were recorded besides other features of AD.

**Severity of AD:**

The severity of the disease was assessed clinically using the SCORAD index (Annexure-3). The objective SCORAD ranges from 0-83 and subjective SCORAD from 0-20. SCORAD index was calculated by adding objective and subjective SCORAD.

**Laboratory parameters:**

Serum TARC levels were measured for all cases and controls using enzyme- linked immunosorbent assay (Abcam's TARC Human ELISA kit). The minimum detectable dose of TARC was less than 5 pg/mL (Annexure-4). Normal TARC values decrease

with the age of the patient (89) and the published cut-off values were used for studying the correlation between different parameters in our study.

Peripheral eosinophils, serum LDH, immunoglobulin E (IgE) and vitamin D were also measured for those who were willing for the same. The cut-offs for these investigations were based on the laboratory values used in our hospital. Atopy immunoblot was done in patients with history of food allergy who were willing for the same.

### **Quality of life indices:**

The quality of life was assessed using IDQOL for children below 4 years of age and CDLQI for children between 4-16 years of age. Dermatitis severity was also assessed alongwith IDQOL for children aged under 4 years. (Annexure-5)

### **Statistical methods:**

#### Sample size:

Number of cases = 72  $\simeq$  70. Number of controls = 72  $\simeq$  70.

The sample size was calculated in the following way to show a sensitivity of serum TARC as 90% each for patients with mild AD and those with moderate to severe AD with a precision of  $\pm 10\%$ .

$$n = \frac{4pq}{d^2}$$

$$p = 90\%$$

$$q = 100 - p = 100 - 90 = 10\%$$

$$d = \pm 10\%$$

$$n_1 = \frac{4 \times 90 \times 10}{10 \times 10} = 36$$

$$n_2 = \frac{4 p' q'}{d^2}$$

$$p' = 90\%$$

$$q' = 100 - p = 100 - 90 = 10\%$$

$$d = \pm 10\%$$

$$n_2 = \frac{4 \times 90 \times 10}{10 \times 10} = 36$$

$$n_3 = n_1 + n_2$$

where,

$n_1$  = number of mild cases

$n_2$  = number of moderate/severe cases

$n_3$  = number of controls

$p$  = sensitivity of TARC for mild cases

$p'$  = sensitivity of TARC for moderate/severe cases

$d$  = precision

### Data analysis:

Data was entered in EpiData version 3.1 and analysed using SPSS version 16.0. For continuous variables mean & standard deviation or median and interquartile range were used. For categorical variables numbers and percentages were used. Chi-square test was used to find the association between age groups and TARC levels. To assess

the relationship between TARC levels and other variables like SCORAD, peripheral eosinophils, LDH, IgE, correlation coefficient and unadjusted linear regression model were used. In unadjusted analysis, the significant variables at 0.05 level were considered in the adjusted analysis.

Receiver Operating Characteristic (ROC) curve was plotted and best cut-off for serum TARC was obtained. Sensitivity and specificity with 95% confidence interval and likelihood ratios were calculated.

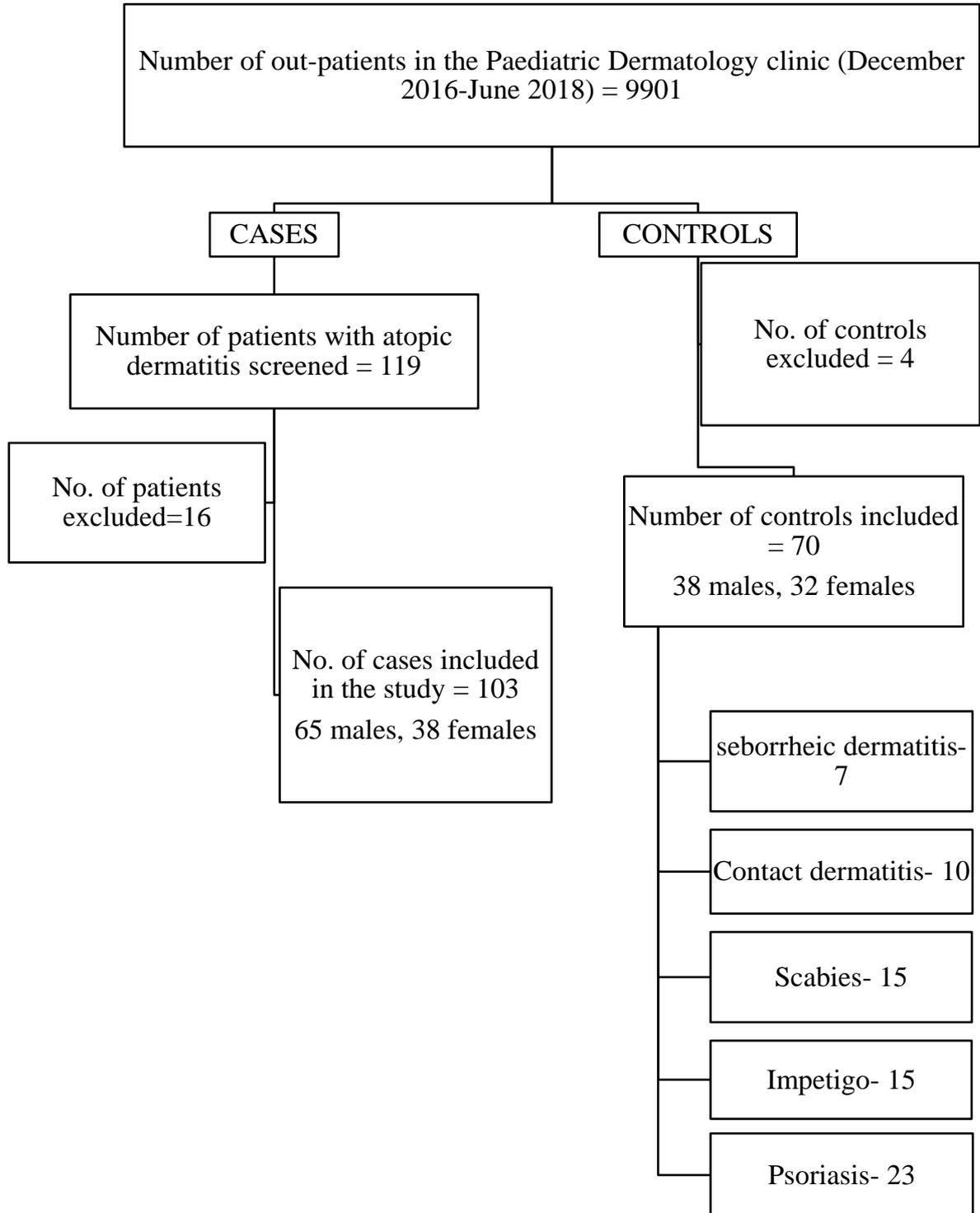
**Funding:**

The study was funded by the Fluid research grant of CMC, Vellore

**Study approval:**

The study was approved by Institutional Review Board (Research and Ethics committee) [IRB no. 10320] (Annexure 6)

## RESULTS



**Figure 2. Patient flow**

A case-control study was conducted over a period of 19 months wherein 103 cases with AD and 70 controls with diseases mimicking AD were recruited. 16 cases and 4 controls were excluded since they did not consent for investigations.

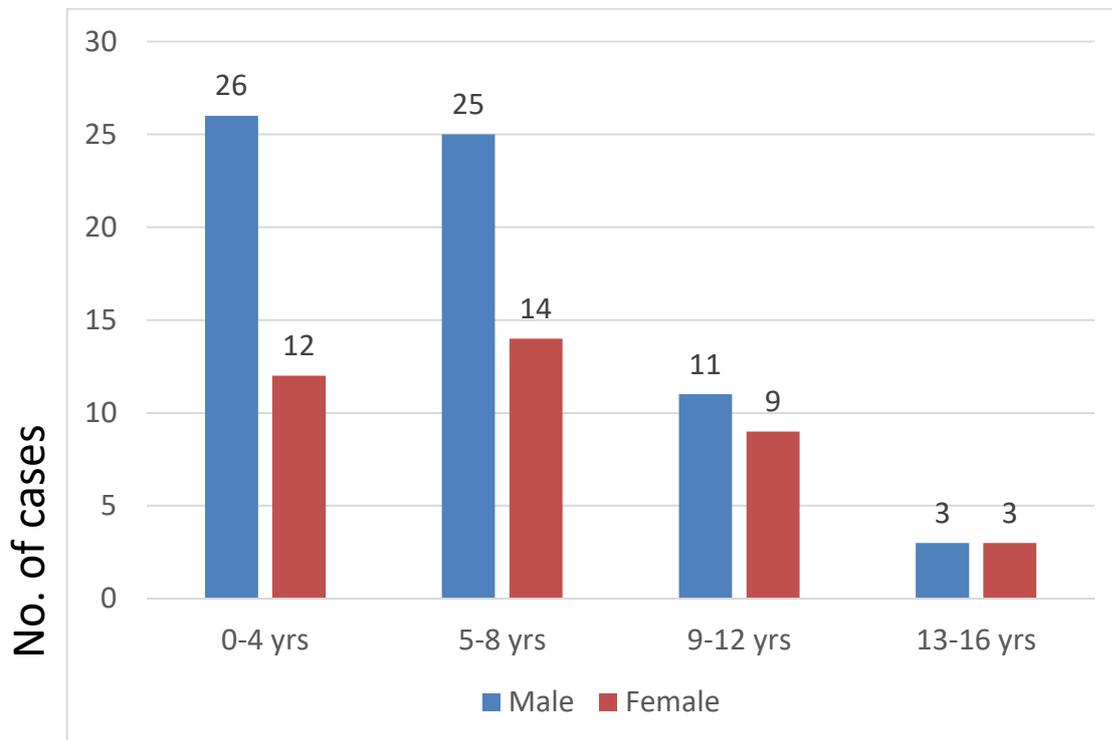
### **Demographic profile:**

#### Cases:

The age of children with AD varied from 0.13 to 16 years. The mean age and sex distribution of the cases is given in table 3. The distribution of male and female cases according to different age groups is shown in figure 3.

**Table 3. Age and sex distribution of cases**

	Atopic Dermatitis		
Gender	Male	Female	Total
Number	65	38	103
Mean age (yrs)	5.78	6.55	6.06



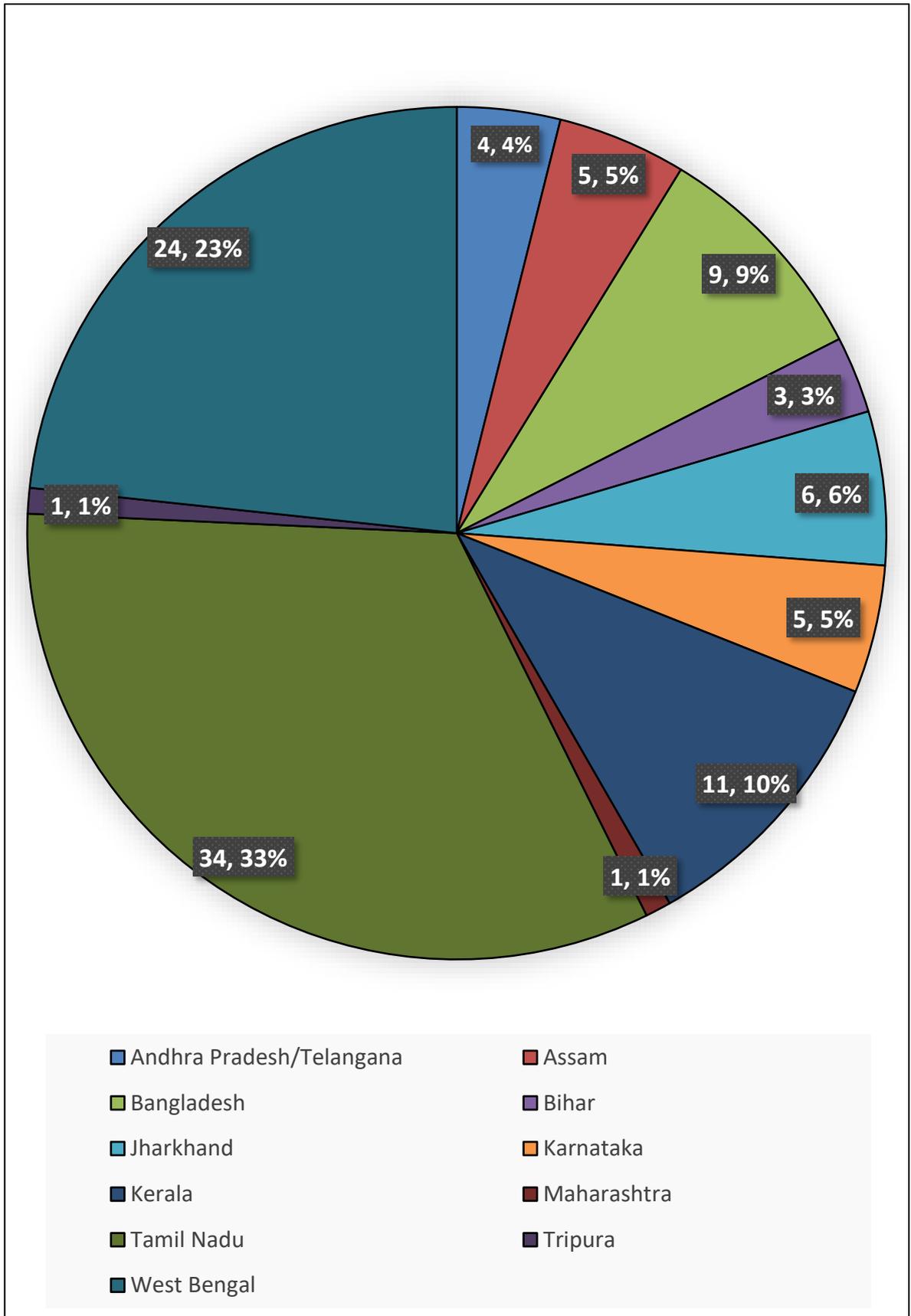
**Figure 3. Distribution of cases across different age groups**

The most common age groups were 5-8 years (n=39), followed by 0-4 years (n=38).

There were more males than females in all age groups except 13-16 year group which had equal sex distribution.

*Geographical distribution:*

The highest proportion of the cases were from Tamil Nadu (33%) followed by West Bengal (23%). (Figure 4)



**Figure 4. Geographical distribution of children with atopic dermatitis**

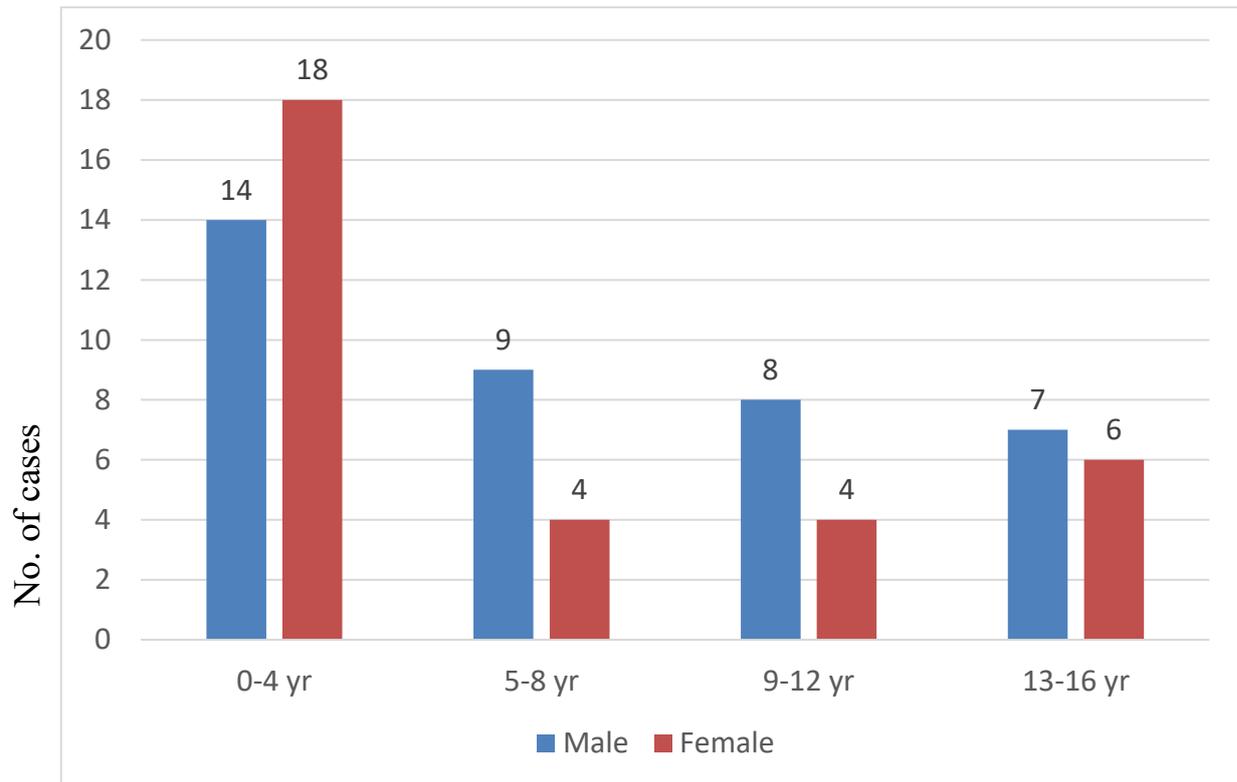
Controls:

A total of 70 children with skin disease mimicking AD were recruited. Of these, 7, 10, 15, 15 and 23 children had seborrheic dermatitis, contact dermatitis, scabies, impetigo and psoriasis, respectively. Their age ranged from 0.08 to 16 years. The age and sex distribution is shown in table 4. The gender distribution of controls in each disease category is given in table 5.

**Table 4. Age and sex distribution of controls**

Gender	Male	Female	Total
Number	38	32	70
Mean age (yrs)	7.03	5.91	6.52

The distribution of controls across various age groups is shown in figure 5. The highest number of controls were between 0 to 4 years of age.



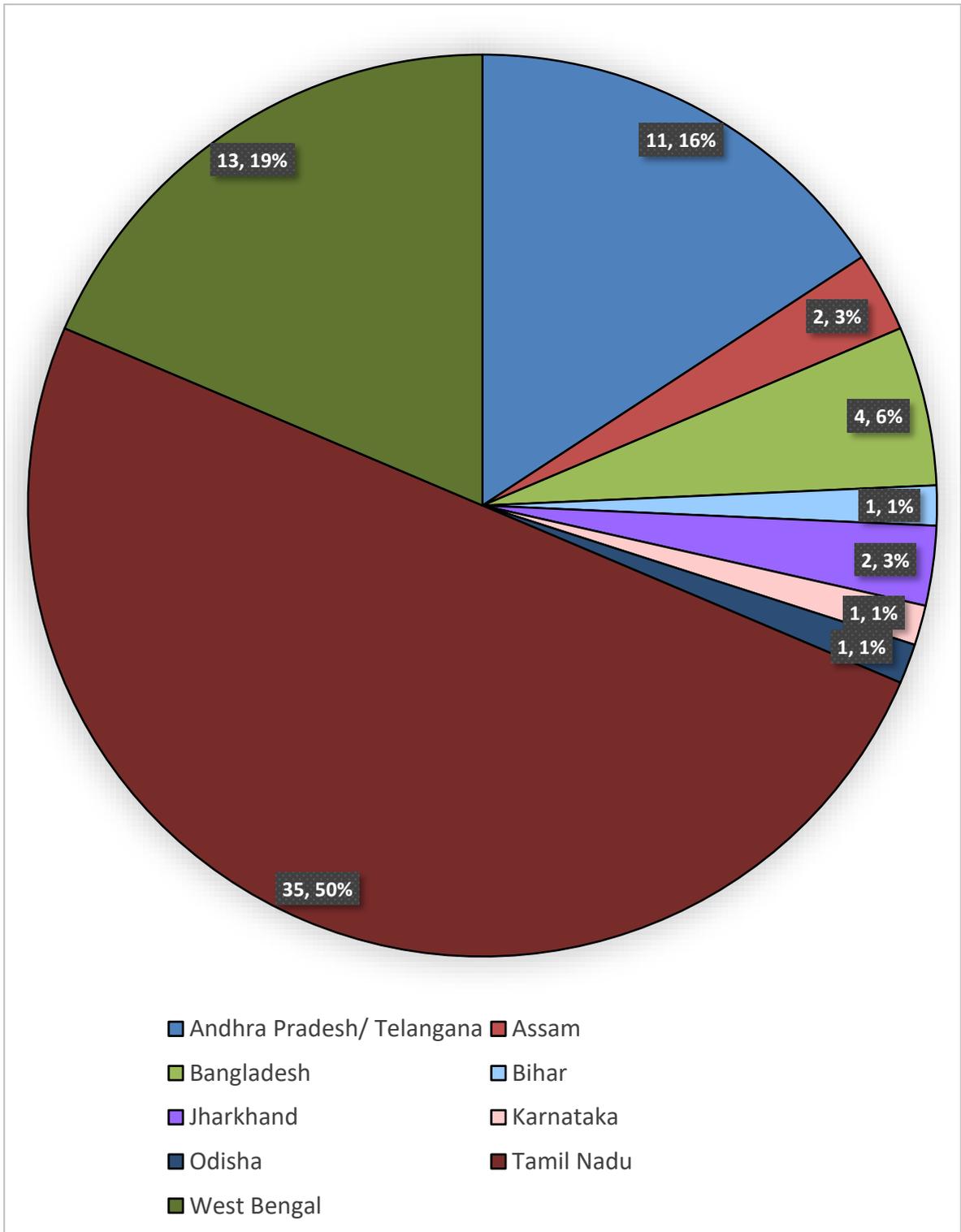
**Figure 5. Distribution of controls across different age groups**

**Table 5. Distribution of controls by diagnosis**

Diagnosis	No. of males	No. of females	Total
Seborrheic dermatitis	4	3	7
Contact dermatitis	6	4	10
Scabies	10	5	15
Impetigo	6	9	15
Psoriasis	12	11	23

*Geographical distribution:*

The highest proportion of controls were from Tamil Nadu (50%) followed by West Bengal (19%). (Figure 6)



**Figure 6. Geographical distribution of controls**

Clinical history of patients with AD:

*Birth history:*

The number of children delivered by normal vaginal delivery and Caesarean section were 60 (58.3%) and 43 (41.7%), respectively. There were 59 (57.3%) first-born, 38 (36.9%) second-born and 6 (5.8%) third-born children recruited in the study.

There were 97 (94.2%) children who had been exclusively breastfed for a duration ranging from 15 days to a maximum of 2 years. The mean duration of exclusive breast-feeding was  $5.8 \pm 3.5$  months.

*Age of onset:*

There was a wide range of age on onset of symptoms of AD ranging from 0 to 108 months, with a mean of  $20.8 \pm 26.7$  months. The onset of symptoms within first year of life was seen in 59 (57.3%) children and within the first 5 years of life in 92 (89.3%) children.

*Sites of onset and involvement as per history: (Table 6)*

Face was the site of onset for 36.9% patients followed by cubital fossae (32%) and popliteal fossae (26.5%).

Amongst the sites involved, 80.6% patients had facial involvement, followed by cubital fossae (79.6%) and popliteal fossae (74.8%). Of these 23.3% had more than 1 site of involvement.

**Table 6. Sites affected in AD**

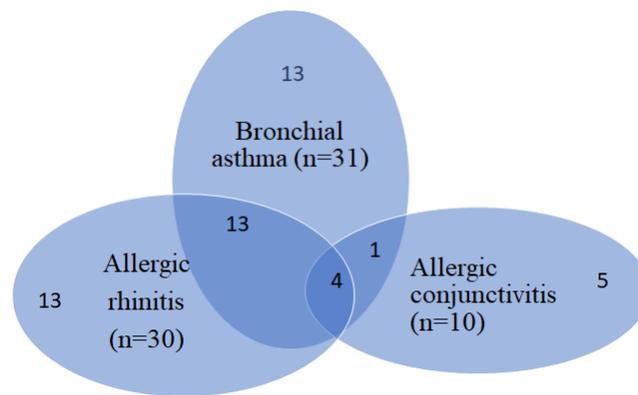
Sites affected	Frequency	Percentage
Face	83	80.6
Neck	32.9	55.3
Upper limb (Flexure)	82	79.6
Upper limb (Extensor)	42	40.8
Lower limb (Flexure)	77	74.8
Lower limb (Extensor)	45	43.7
Trunk	59	57.3
Scalp	44	42.7
Mucosa	2	1.9
Nails	2	1.9

*Symptoms pertaining to the skin:*

Dryness of skin was reported by 94.2% of the cases.

*Symptoms of mucosal allergy:*

Mucosal allergy was present in 48 children (46.6%) out of whom 64.6% had asthma, 62.5% had allergic rhinitis and 20.8% had a history of allergic conjunctivitis. Figure 7 shows the number of children with each of the three conditions.



**Figure 7. Personal history of mucosal allergy**

*Triggers and relieving factors:*

Seasonal variation was noticed by parents in 68% of the patients, with a majority of them reporting exacerbation in the winter season (61.4%). A worsening of the skin condition in the summer season was seen in 41.4% of patients, followed by 8.7% and 1.4% in the rainy and spring seasons, respectively. Exacerbation in 2 seasons was seen in 9 (8.7%) patients.

Other triggers reported by parents included examination-related stress (2.9%), skin infections (1%), food allergens (36.9%), airborne allergens, including dust and cement exposure (17.5%), sweating (39.8%) and woollen clothing (32%). Amongst the 38 children who reported food triggers, atopy immunoblot testing was done in 23 (60.5%) children and was positive in 15 (39.5%) of them. Habitual scratching was noticed as an aggravating factor in 6.8% patients.

Bathing was reported as a relieving factor in 13 (12.6%) children, an air-conditioned environment in 4 (3.9%) children and distraction in 5 (4.9%) children.

*Exposure to pets:*

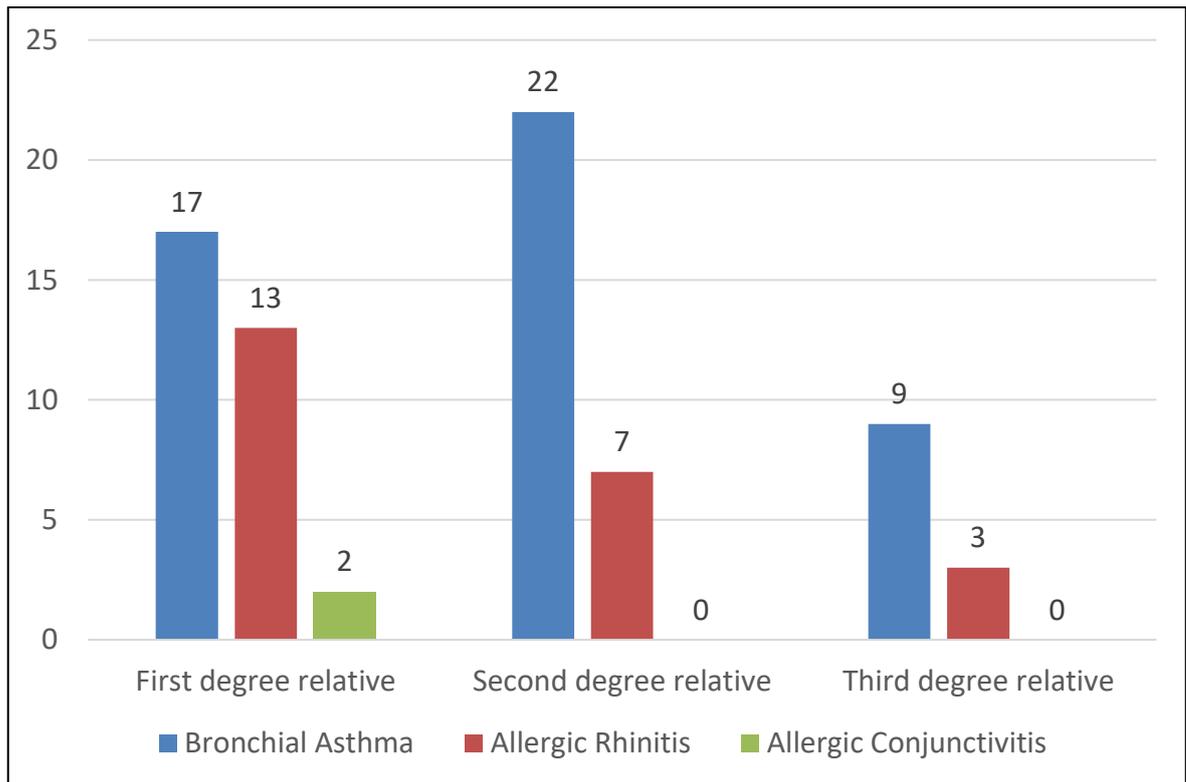
Only 9 (8.74%) cases had exposure to domestic pets with equal number of cases being exposed to dogs (5, 55.56%) and cats (5, 55.56%). 1 patient was exposed to both dogs and cats.

*Treatment history:*

Of the 103 cases, 3 did not have previous treatment details and 12 children had not taken any dermatological treatment in the past. A total of 88 patients had taken some form of dermatological treatment, with 80.7% having used topical steroids and only 21.6% topical calcineurin inhibitors. Amongst the systemic agents, 23, 5 and 2 patients had used systemic steroids, cyclosporine and methotrexate, respectively. Phototherapy was given to 3 patients.

*Family history:*

A family history of atopy was present in 68 children, bronchial asthma being the most common (48, 46.6%) followed by allergic rhinitis (23, 22.3%). (Figure 8)



**Figure 8. Family history of atopy**

*Complications and comorbidities as per history:*

Sleep disturbance was present in 56.3% children and 12 cases (11.7%) also had behavioural disturbances owing to the disease, in the form of excessive irritability, anger or aggressiveness.

A history of skin infections was present in 34 cases (33%), all of whom reported a bacterial infection. Of these, 20 (58.8%) patients had a history of recurrent infections. However, only 7 (20.6%) out of the 34 cases had a documented pus culture, all of which showed *Staphylococcus aureus*. The bacterial swabs of 2 of these children also showed *Klebsiella*, *Pseudomonas* and non-fermenting gram negative bacilli.

None of the study patients had a history suggestive of eczema herpeticum or eczema vaccinatum. A small number of patients (7, 6.8%) also reported systemic infections in the form of respiratory infections (6) and post infectious glomerulonephritis (1).

Two patients had Wiskott-Aldrich syndrome and one had anhidrotic ectodermal dysplasia. One patient had concomitant vitiligo.

#### Clinical profile of cases:

##### *Anthropometry:*

Table 7 shows the distribution of height and weight percentiles across various age groups. Majority of the patients had height and weight between 3<sup>rd</sup> to 97<sup>th</sup> centile. There were 11.65% children with a height below the 3<sup>rd</sup> centile and 12.62% children with a weight below the 3<sup>rd</sup> centile.

**Table 7. Height and Weight centiles**

	Height		Weight	
	No. of cases	Percentage	No. of cases	Percentage
<b>Below 3rd centile</b>				
<1 yr	0	0	0	0
1-2 yrs	2	13.33	2	13.33
> 2 yrs	10	12.82	11	14.1
Total	12	11.65	13	12.62
<b>3rd to 97th centile</b>				
<1 yr	10	100	9	90
1-2 yrs	10	66.67	13	86.67
> 2yrs	61	78.21	58	74.36
Total	81	78.64	80	77.67
<b>Above 97th centile</b>				
< 1 yr	0	0	1	10
1-2 yrs	3	20	0	0
> 2 yrs	7	8.97	9	11.54
Total	10	9.71	10	9.71
< 1 yr (n=10), 1-2 yrs (n=15), >2 yrs (n=78)				

Of the 9 children whose weight was above the 97<sup>th</sup> centile, 2 (2.6%) children were overweight and 7 (8.9%) were obese based on the BMI centile for their age.

*Cutaneous features:*

The various morphological types seen in our patients are presented in table 8 and the distribution in table 9.

**Table 8. Morphology of lesions in infantile and childhood AD**

Feature	Infantile AD (n=15)		Childhood AD (n=88)		p values
	Number	Percentage	Number	Percentage	
Acute eczema	14	93.3	56	63.6	<b>&lt;0.001</b>
Follicular eczema	2	13.3	2	2.3	0.065
Erythroderma	1	6.7	5	5.7	0.880
Lichenification	4	26.7	52	59.1	0.068
Prurigo	-	-	2	2.3	-
Psoriasiform	-	-	3	3.4	-

p value for chronic lesions (lichenification+prurigo+psoriasiform) = **0.042**

The significant values are highlighted in bold.

Patients were categorized into infantile AD (< 18 months) and childhood AD (> 18 months).(1)

### **Infantile AD:**

Amongst the children under 18 months of age (n=15), acute eczematous lesions were the most common morphological type seen in 14 (93.3%) cases. Localized lesions were present in 3 (20%) children, all of whom had lesions over the face. Extensor distribution of lesions was seen in 7 children of whom it was the only site involved in 2 (13.3%). 5 (33.3%) patients had involvement of the cubital fossae and 6 (40%) had involvement of the popliteal fossae. Both flexural and extensor involvement was seen in 5 (33.3%) cases. Overall, involvement of the face, trunk and extensor aspect of extremities was more common in the infantile phase as compared to the childhood phase. (Table 9) Erythroderma was seen in 1 (6.7%) case.

Chronic lesions in the form of lichenification were seen in 4 (26.7%) cases, all of whom also had features of acute eczema. Extensor involvement was seen in 3 (20%) cases. Flexural involvement was seen in only 1 (6.7%) case.

**Table 9. Distribution of lesions in infantile phase & childhood phase**

Sites affected	Infantile AD (n=15)				Childhood AD (n=88)			
	Acute eczematous lesions		Chronic lesions		Acute eczematous lesions		Chronic lesions (Lichenification/ Prurigo/Psoriasiform*)	
	No. of cases	% of cases	No. of cases	% of cases	No. of cases	% of cases	No. of cases	% of cases
Face	13	86.7	1	6.7	34	38.6	9	10.2
Neck	5	33.3	1	6.7	20	22.7	18	20.5
Cubital fossa	5	33.3	0	0	34	38.6	41	46.6
Popliteal fossa	6	40.0	1	6.7	36	40.9	38	43.2
Axilla	2	13.3	0	0	11	12.5	0	0
Extensor of upper limb	7	46.7	3	20.0	22	25.0	16	18.2
Extensor of lower limb	6	40.0	3	20.2	24	27.3	20	22.7
Trunk	9	60.0	1	6.7	24	27.3	9	10.2

\*Prurigo in 2 patients involving extensor aspects of upper & lower limbs in both and trunk & flexor aspect of lower limb in 1.

### **Childhood AD:**

Amongst children above 18 months of age (n= 88), acute eczematous lesions were most common, similar to the infantile phase, seen in 56 (63.6%) cases. (Table 8) Localized lesions were present in 9 (10.2%) children with 6 (6.8%) having involvement of the face and 1(1.1%) each having involvement of the cubital fossae and extensor aspect of upper and lower limbs, respectively. Ear lobe involvement was seen in 2 (2.3%) children. Cubital fossae were involved in 34 (38.6%) cases and popliteal fossae in 36 (40.9%) cases. Extensor distribution alone was seen in 5 (5.7%) children with 3 (3.4%) children having both upper and lower limb involvement. Both

flexural and extensor involvement was seen in 27 (30.7%) children. Erythroderma was seen in 5 patients.

Chronic lesions in the form of lichenification were seen in 52 (59.1%) children, prurigo in 2 (2.3%) children and psoriasiform lesions in 3 (3.4%) children. Psoriasiform lesions involved the extensor aspect of upper and lower limbs in all of them, face in 2 (2.3%) children and trunk in 1 (1.1%) child. Among these, 24 (27.3%) had only lesions of chronic AD and the rest had features of both acute and chronic. Overall, localized lesions of chronic AD were seen in 11 (12.5%) children with involvement of the face, cubital fossae, flexor and extensor aspects of the lower limbs in 3 (3.4%), 6 (6.8%), 1 (1.1%) and 1 (1.1%) cases, respectively. Flexural involvement was seen in 47 (53.4%) children. Extensor involvement was seen in 22 (25.0%) children.

Overall, acute eczema was more common in infants as compared to children and chronic lesions were more common in children, both being statistically significant (p value of <0.001 and 0.042, respectively). (Table 8) Chronic lesions in the flexural aspects of extremities were more common in childhood phase as compared to the infantile phase, though not statistically significant (p value- 0.032). (Table 9)

**Other cutaneous features:**

Dennie-Morgan folds were observed in 20 (19.4%) patients. Xerosis was seen in 88 (85.4%) patients.

Clinical features suggestive of filaggrin mutation such as palmar hyperlinearity, keratosis pilaris and ichthyosis vulgaris were seen in 71 (68.9%), 24 (23.3%) and 20 (19.4%) patients, respectively. All 3 features were seen in 10 (9.7%) cases and any 2 of the 3 features in 29 (28.2%) cases.

Follicular prominence was seen in 9 (8.7%) patients. Excoriations were observed in 61 (59.2%) children. Nipple eczema was not seen in any of our patients.

*Other findings:*

Nail changes were seen in the form of transverse or longitudinal ridges, Beau's lines, leukonychia and perionychial papules in 5 children. Cheilitis was present in 2 (1.9%) patients.

*Lymphadenopathy:*

Lymphadenopathy was present in 22 (21.4%) children with cervical, axillary and inguinal lymphadenopathy in 16.5%, 4.9% and 4.9%, respectively. More than 1 lymph node group was involved in 5 (4.9%) children.

*Complications at the time of induction into the study:*

A height below the 3<sup>rd</sup> centile was seen in 11.6% (12) cases and weight below the 3<sup>rd</sup> centile in 12.6% (13) children.

A minority of the patients had ocular changes, with 1 patient each with amblyopia, blepharitis, watering, redness, refractory error and squint. Children were not sent for routine ophthalmological screening in this study.

Four (3.9%) patients also had acanthosis nigricans and all of them were obese (BMI above 95<sup>th</sup> centile).

Secondary bacterial infection of the skin was seen in 18 (17.5%) patients, with 7 having a documented Staphylococcal infection. Other organisms isolated from pus cultures included beta-hemolytic Streptococcus (2), Klebsiella (2), Pseudomonas (1) and non-fermenting gram negative bacilli (1). Nasal swab was done in 28 (27.2%) children, out of which 22 (78.6%) children showed Staphylococcal carriage.

#### Laboratory parameters and biomarkers:

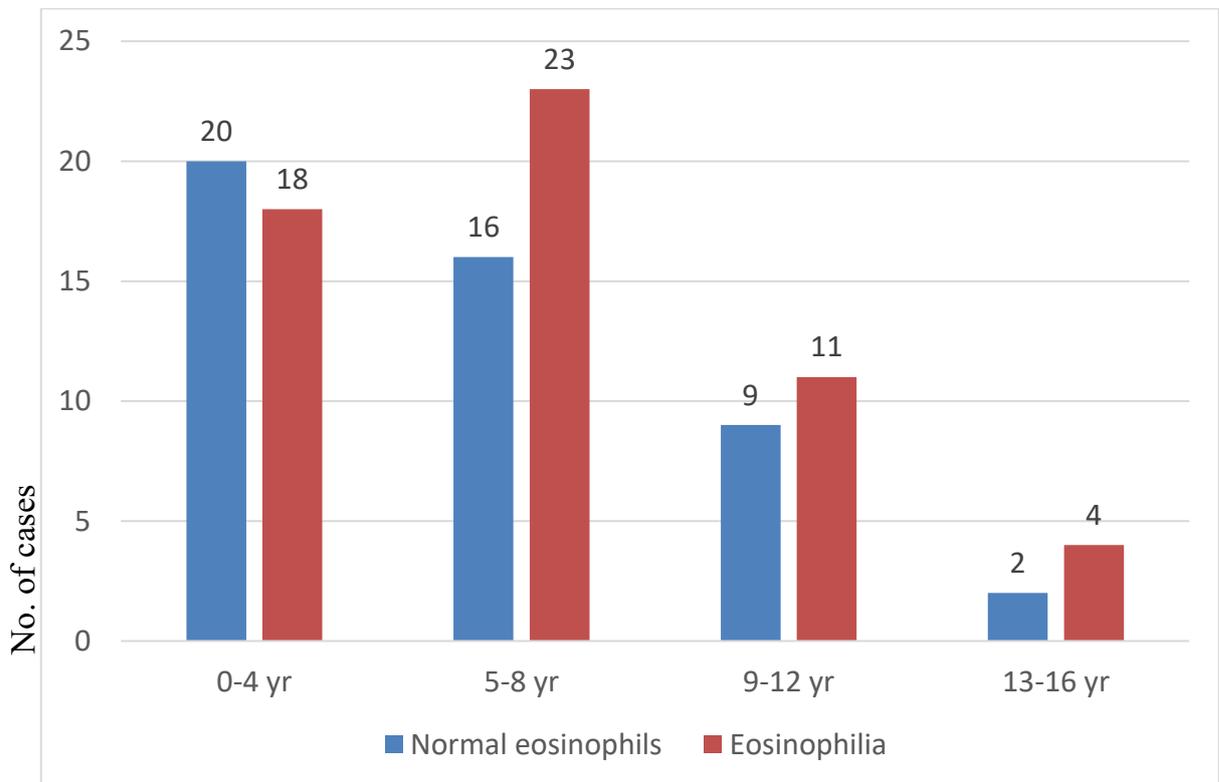
The laboratory parameters which have been previously shown to correlate with disease severity were done for those willing and the results are as follows:

##### *Eosinophilia:*

Peripheral eosinophilia, as defined by peripheral eosinophils above 6%, was present in 56 (54.4%) patients out of all 103 patients for whom it was done. The values ranged from 0 to 31%. The mean peripheral eosinophils in different age groups is shown in table 10 and the number of children with elevated eosinophils is shown in figure 9.

**Table 10. Peripheral eosinophilia in different age groups**

Age group (years)	Mean peripheral eosinophils (%)
0-4	8.18 $\pm$ 6.28
5-8	8.69 $\pm$ 5.86
9-12	8.35 $\pm$ 6.36
13-16	10.33 $\pm$ 6.62
Total	8.53 $\pm$ 6.09



**Figure 9. Distribution of eosinophilia across different age groups**

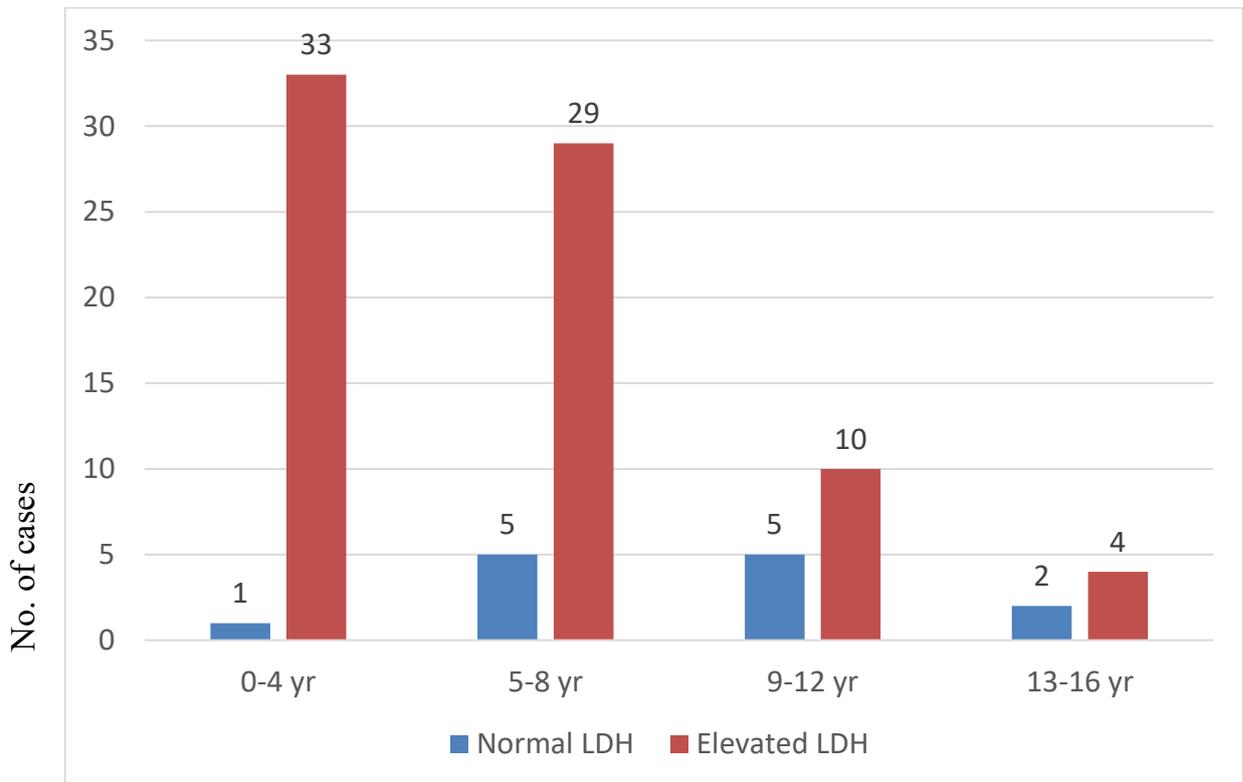
The highest number of cases with eosinophilia was found in the age group of 5 to 8 years.

**LDH:**

LDH levels were done for 89 cases and was elevated (>460 units/L) in 76 (85.4%) patients (range- 359 to 1320 units/L). The mean LDH in different age groups is shown in table 11 and the number of children with elevated values is shown in figure 10.

**Table 11. Mean LDH for different age groups**

Age groups (years)	Mean LDH (units/L)
0-4	699.12±143.14
5-8	643.26±223.91
9-12	576.33±174.45
13-16	660.00±299.26
Total	654.45±195.64

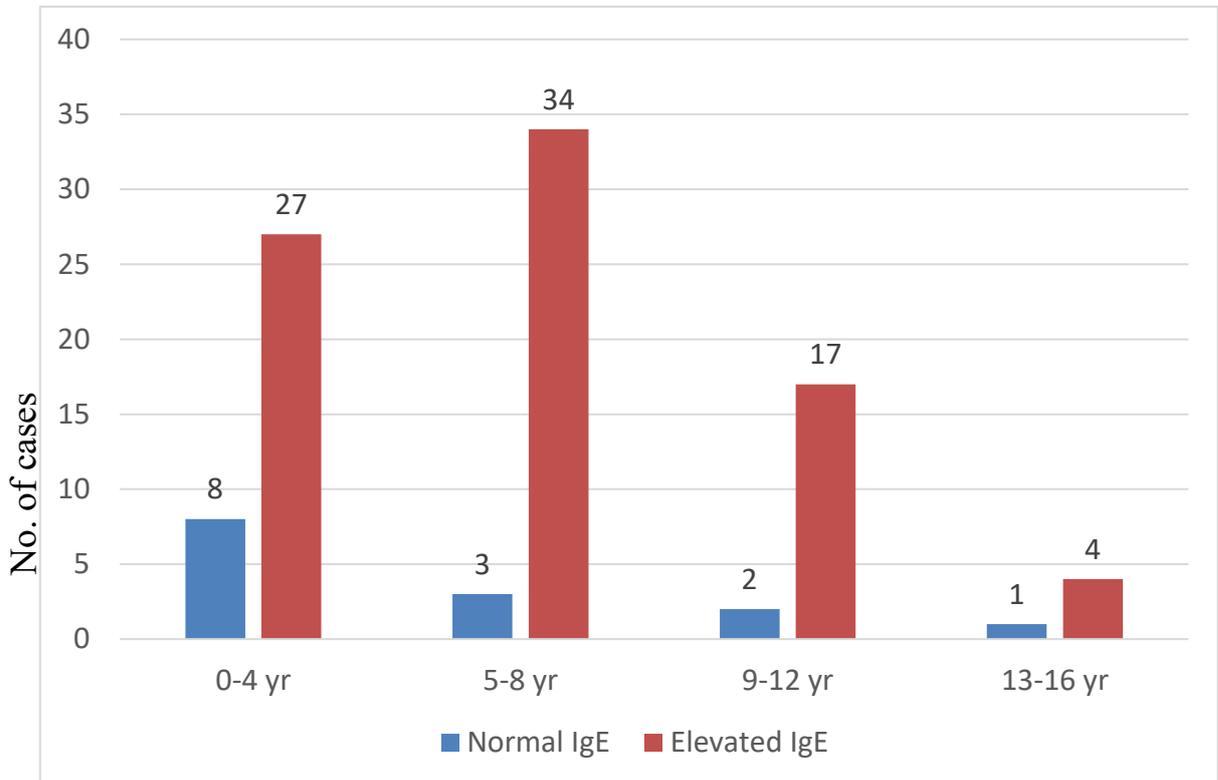


**Figure 10. Distribution of normal and elevated LDH across different age groups**

The highest number of cases with elevated LDH was found in 0-4 year age group.

*Serum IgE:*

Serum IgE ranged from 1.5 to 15,488 units/mL and was elevated in 82 (85.4%) out of 96 patients for whom it was done, based on the age specific cut-offs (0-1 yr: 1-29 units/mL; 1-3 yrs: 1-49 units/mL and above 3 yrs: 5-100 units/mL). The number of children with normal and elevated IgE is shown in figure 11.



**Figure 11. Distribution of normal and elevated IgE across different age groups**

The highest number of cases with elevated IgE was found in 5-8 year age group.

*Vitamin D:*

Hypovitaminosis D was present in 62 (92.5%) out of the 67 children for whom it was measured. The mean vitamin D level was  $17.36 \pm 8.54$  ng/mL, which was below normal of 30.0 ng/mL. It also correlated inversely with SCORAD index ( $r = -0.13$ ) which was statistically not significant ( $p$  value- 0.29). There was no significant correlation between vitamin D and TARC values in the age groups of 1-2 years ( $n=7$ ,  $r = -0.18$ ,  $p$  value= 0.70) and above 2 years ( $n=58$ ,  $r = 0.06$ ,  $p$  value = 0.64). The correlation was not assessed for children below 1 year of age since vitamin D was tested in only 2 infants.

*TARC:*

As the published values of TARC levels (89) are available for age groups of less than 1 year, 1-2 years and above 2 years, all patients were classified into these age groups to assess the relationship with other parameters.

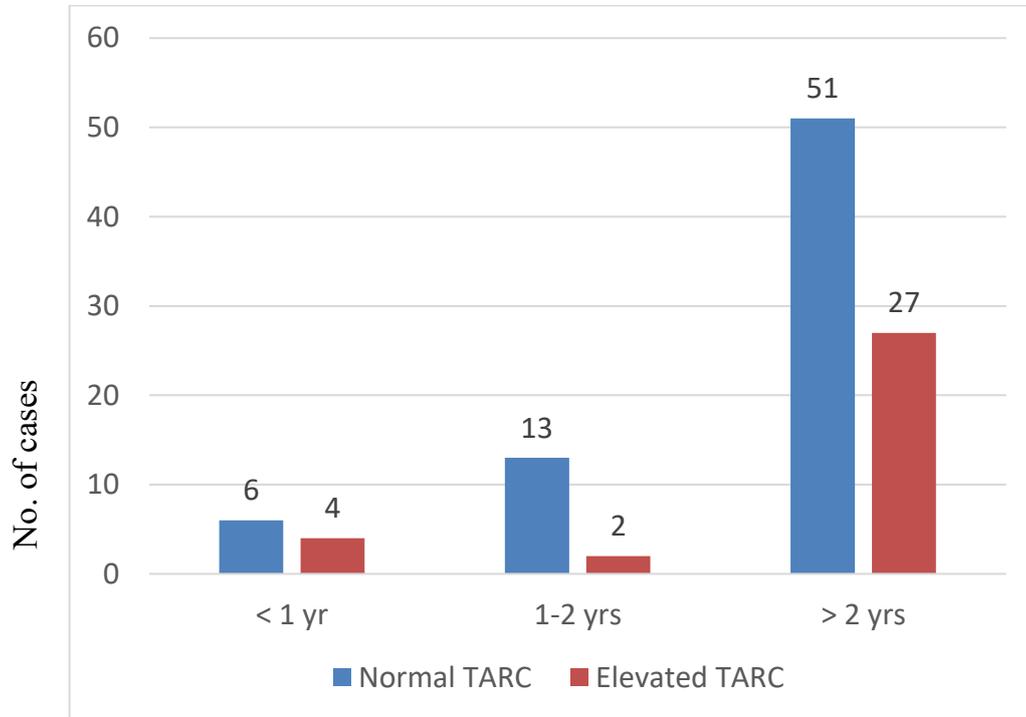
TARC values in cases ranged from 14pg/mL to 2503pg/mL with a mean of  $862.83 \pm 782.19$ .

Age specific mean TARC values and the range of values are recorded in table 12.

**Table 12. Mean TARC values in different age groups of cases**

Age group	Normal TARC(89) (pg/mL)	Mean TARC (pg/mL)	Median (pg/mL)	Range (pg/mL)
< 1 yr (n=10)	< 1367	1,186.90	993.50	372-2500
1-2 yr (n=15)	< 998	814.40	703.00	170-2500
>2 yrs (n=78)	< 743	830.60	467.50	14-2503

It was elevated in 33 (32%) cases based on the existing cut-off values (89), with the highest proportion in those above 2 years (27, 81.8%) (Figure 12)



**Figure 12. Distribution of normal and elevated TARC in AD**

TARC values in controls ranged from 46 pg/mL to 2500 pg/mL with a mean of 531.53  $\pm$  491.21. It was within the normal range in 60 (85.7%) controls. (Table 13)

**Table 13. Distribution of serum TARC levels in controls**

Diagnosis	Mean TARC (pg/mL)	Range of TARC (pg/mL)	No. with normal TARC	No. with elevated TARC	% with elevated TARC
Seborrheic dermatitis	669.86 $\pm$ 685.02	107-1,841	5	2	28.57
Contact dermatitis	625.50 $\pm$ 344.14	313-1,129	9	1	10
Scabies	561.80 $\pm$ 512.28	108-1,646	13	2	13.33
Impetigo	572 $\pm$ 383.80	181-1,683	14	1	6.67
Psoriasis	402.61 $\pm$ 538.90	46-2,500	19	4	17.39
Total	531.53 $\pm$ 491.21	46-2,500	60	10	14.29

Seborrheic dermatitis (2/7 patients) and psoriasis (4/23 patients) were associated with elevated TARC levels. The highest serum TARC level was seen in a patient with psoriasis. (Table 19) The patient was not known to have an atopic diathesis.

The mean and median TARC values for cases and controls in different age groups is shown in table 14.

**Table 14. Mean and median TARC values amongst cases and controls**

Age group	Cases		Controls	
	Mean (pg/mL)	Median	Mean	Median
<1 yr (n=10)	1,186.90	993.50	1,064.80	1,117.50
1-2 yrs (n=15)	814.40	703.00	531.17	532.50
>2 yrs (n=78)	830.60	467.50	420.52	249.50

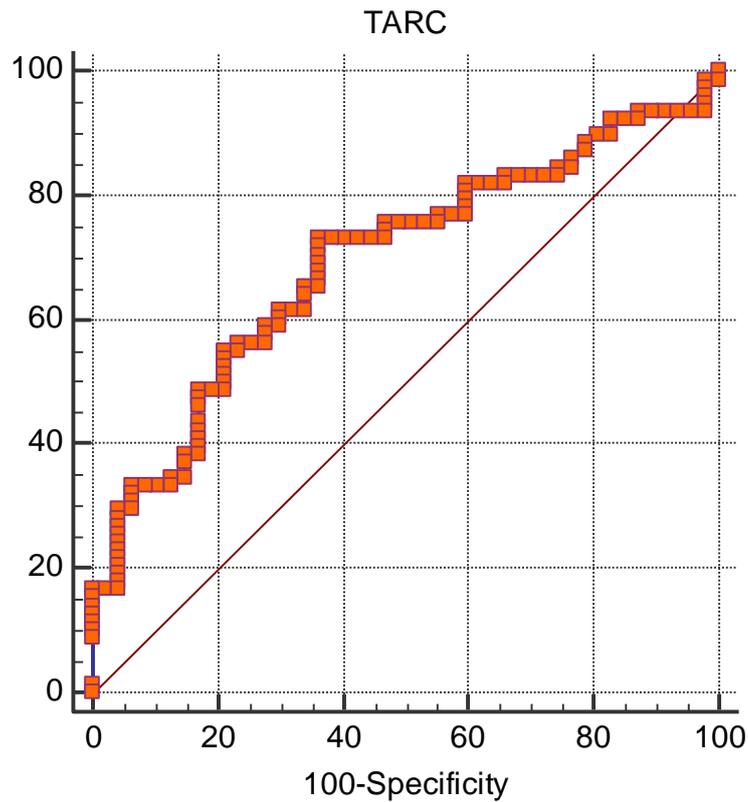
The difference between the median TARC values amongst the cases and controls was statistically significant (p value= 0.004).

The median TARC level was lower in patients on systemic therapy (390 pg/mL) compared to the other cases (469 pg/mL) (p value = 0.04)

Sensitivity and specificity of serum TARC:

Since the number of children under 1 year and between 1-2 years were few, ROC curves were not drawn for them.

ROC curve for serum TARC levels for those above 2 yrs of age (after excluding an outlier with TARC value of 2500 pg/mL) is as shown in figure 13.



**Figure 13. ROC curve for children above 2 years**

In our study, the optimal cut-off level for TARC for the diagnosis of AD in children above 2 years was 365 pg/mL with a sensitivity of 57.7% and specificity of 72.3%. The positive predictive value was 77.6% (C.I- 64.7% to 87.5%) and negative predictive value was 50.8% (C.I- 38.2% to 63.2%). Using this value, the number of patients with TARC levels of  $\geq 365$  pg/mL was 46.

Table 15 shows the relationship between TARC levels and SCORAD, QOL indices and other biomarkers.

**Table 15. Pearson correlation coefficient(r) between serum TARC levels and SCORAD, QOL indices and other biomarkers**

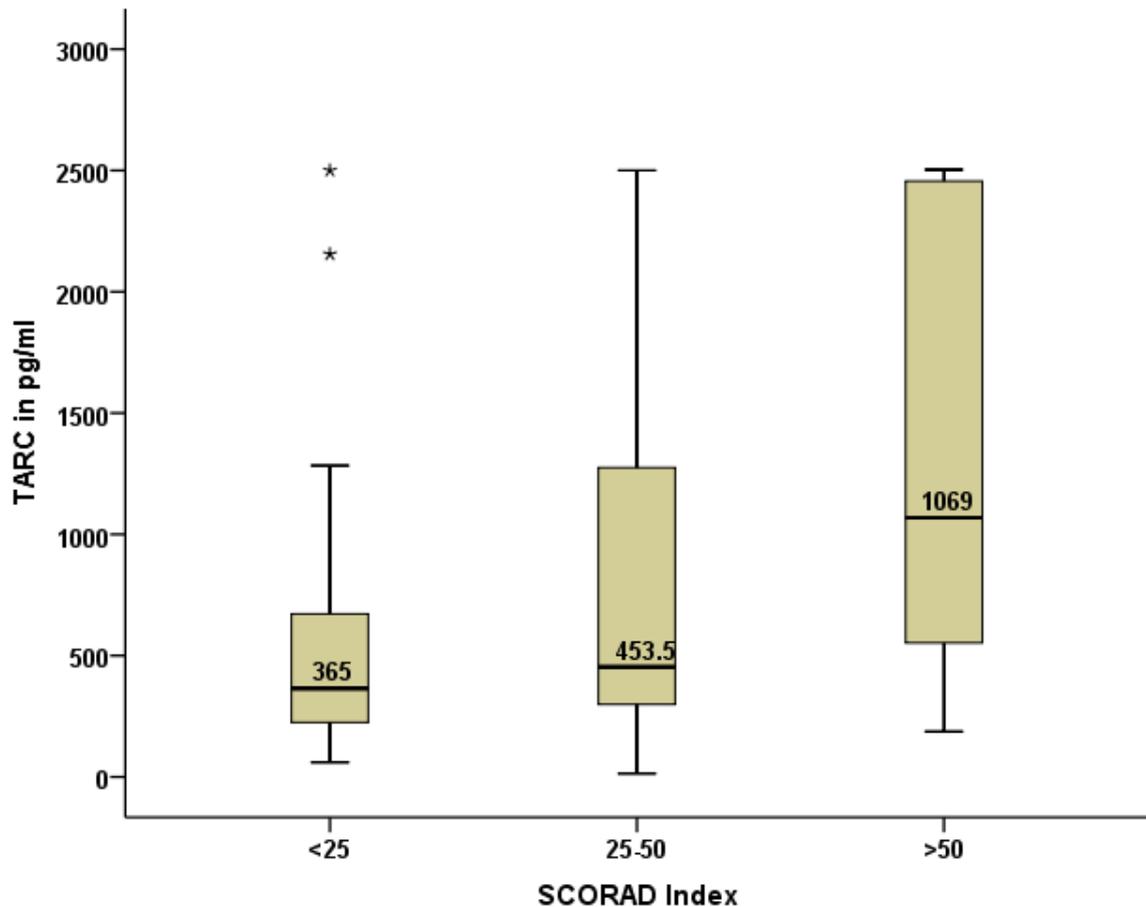
Parameter	< 1 yr		1-2 Yrs		>2 yrs	
	r	p value	r	p value	r	p value
1. Objective SCORAD	0.353	0.317	-0.176	0.530	<b>0.524</b>	<b>&lt;0.001</b>
2. SCORAD index	0.320	0.367	-0.230	0.410	<b>0.538</b>	<b>&lt;0.001</b>
3. Peripheral eosinophils	-0.083	0.819	0.162	0.565	<b>0.583</b>	<b>&lt;0.001</b>
4. LDH	-0.549	0.100	0.440	0.133	<b>0.550</b>	<b>&lt;0.001</b>
5. IgE	0.510	0.161	0.094	0.759	0.169	0.150
6. IDQOL	0.391	0.263	-0.190	0.497	<b>0.823</b>	<b>0.003</b>
7. CDLQI	NA		NA		<b>0.380</b>	<b>0.001</b>

The significant correlations are highlighted in bold. (p value < 0.05)

NA- not applicable

There was a statistically significant correlation of serum TARC levels with objective SCORAD, SCORAD index, peripheral eosinophils, LDH, IDQOL and CLDQI in children above 2 years of age.

The increase in the levels of serum TARC with rise in SCORAD indices (mild <25, moderate 25-50, and severe >50) is shown in figure 14.



**Figure 14. TARC values with SCORAD index**

### **TARC values vs mucosa allergy**

There was no statistically significant difference in serum TARC values amongst those with or without a history of atopy.

### **TARC values vs phenotypic features of filaggrin mutation**

The correlation between serum TARC levels in children older than 2 years and phenotypic features of filaggrin mutation were studied. The TARC levels in those with (mean TARC  $241.67 \pm 194.57$  pg/mL) and without (mean TARC  $907.42 \pm$

812.19 pg/mL) all 3 features of filaggrin mutation (n=10, 9.7%) were significant (p value= 0.003) with higher TARC values in those without the mutation. No significant difference was found when only 2 of the 3 features were present.

Severity scoring:

The mean objective SCORAD was  $28.9 \pm 18.3$  with the lowest and highest scores of 1.6 and 75.6, respectively (Objective SCORAD, minimum-0, maximum-83). The mean subjective SCORAD was  $8.3 \pm 5.2$  (Subjective SCORAD, minimum-0, maximum-20). The highest SCORAD was seen in the age group of 9-12 years, followed by 13-16 years. (Table 16)

**Table 16. Age-wise distribution of mean SCORAD**

Age group (years)	Mean objective SCORAD	Mean SCORAD index (Objective + Subjective)
0-4	28.8	36.0
5-8	27.6	36.4
9-12	31.5	41.0
13-16	30.0	37.0

The correlation coefficient between objective SCORAD or SCORAD index and serum TARC levels, peripheral eosinophils, LDH, IgE and quality of life scores are given in tables 13 and 14.

**Table 17. Pearson correlation coefficient(r) between objective SCORAD & SCORAD index and other clinical and laboratory parameters**

Parameter	Objective SCORAD					
	< 1 yr (n=10)		1-2 yrs (n=15)		>2 yrs (n=78)	
	r	p value	r	p value	r	p value
TARC	0.353	0.317	-0.176	0.530	<b>0.524</b>	<b>&lt;0.001</b>
Peripheral eosinophils	0.569	0.086	<b>0.595</b>	<b>0.019</b>	<b>0.368</b>	<b>.001</b>
LDH	-0.445	0.198	0.091	0.767	<b>0.546</b>	<b>&lt;0.001</b>
IgE	0.423	0.257	-0.135	0.660	<b>0.306</b>	<b>0.008</b>
IDQOL	0.515	0.128	0.227	0.415	<b>0.882</b>	<b>0.001</b>
CDLQI	NA*				<b>0.480</b>	<b>&lt;0.001</b>

The significant correlations are highlighted in bold. (p value < 0.05)

\*NA-not applicable for age < 4 yrs

**Table 18. Pearson correlation coefficient(r) between SCORAD index and other clinical and laboratory parameters**

Parameter	SCORAD index					
	<1yr (n=10)		1-2yrs (n=15)		>2yrs (n=78)	
	r	p value	r	p value	r	p value
TARC	0.320	0.367	-0.230	0.410	<b>0.538</b>	<b>&lt;0.001</b>
Peripheral eosinophils	0.578	0.080	<b>0.609</b>	<b>0.016</b>	<b>0.397</b>	<b>&lt;0.001</b>
LDH	-0.434	0.221	0.067	0.828	<b>0.582</b>	<b>&lt;0.001</b>
IgE	0.490	0.181	-0.046	0.881	<b>0.331</b>	<b>0.004</b>
IDQOL	0.622	0.055	0.362	0.185	<b>0.926</b>	<b>&lt;0.001</b>
CDLQI	NA				<b>0.541</b>	<b>&lt;0.001</b>

The significant correlations are highlighted in bold (p value < 0.05)

\*NA- not applicable for age < 4 yrs

As seen in the above tables, the following investigations had a significant positive correlation with objective SCORAD and SCORAD index:

- 1-2 year age group: Peripheral eosinophils
- Above 2 years: Serum TARC, peripheral eosinophils, LDH and IgE; with highest correlation with serum LDH, followed by serum TARC.

Quality of life indices also correlated significantly with SCORAD in children above 2 years of age.

Quality of life indices:

Quality of life for 35 children, who were below 4 years of age was assessed using IDQOL (minimum and maximum IDQOL score of 0 and 30, respectively and dermatitis severity score of 0 and 4, respectively). The mean score was  $9.4 \pm 5.84$ , ranging from a score of 1 to 27. The mean of IDQOL and dermatitis severity in different age groups is presented in Table 19.

**Table 19. Mean IDQOL and dermatitis severity**

Age (in years)	Mean IDQOL	Mean Dermatitis Severity score
< 1 yr (n=10)	8.4	2.3
1-2 yrs (n=15)	9.3	2.3
>2 yrs (n=10)	10.6	2.2
Total	9.4	2.3

The correlation coefficients and p values of various laboratory markers with IDQOL are presented in table 20.

**Table 20. Pearson correlation coefficient between IDQOL and laboratory markers**

Parameter	< 1 yr		1-2 yrs		>2 yrs	
	r	p value	r	p value	r	p value
TARC	0.391	0.263	-0.190	0.497	<b>0.823</b>	<b>0.003</b>
Peripheral eosinophils	0.527	0.117	0.513	0.050	<b>0.682</b>	<b>0.030</b>
LDH	-0.571	0.085	0.006	0.984	0.583	0.100
IgE	<b>0.760</b>	<b>0.018</b>	0.050	0.871	0.308	0.386

The significant values are highlighted in bold (p value < 0.05)

There was a significant correlation between IDQOL and serum TARC levels & peripheral eosinophils in children above 2 years. There was also a significant correlation of IDQOL with IgE in children below 1 year of age.

CDLQI was done to assess the quality of life of children who were 4 years of age or older (CDLQI, minimum and maximum scores of 0 and 30, respectively). The mean CDLQI score was  $12.5 \pm 7.2$ , ranging from 0 to 27. Its correlation with laboratory parameters is given in table 21.

**Table 21. Correlation between CDLQI and laboratory parameters**

Parameter	Age 4-16 yrs	
	r	p value
TARC	<b>0.380</b>	<b>0.001</b>
Peripheral eosinophils	<b>0.414</b>	<b>&lt;0.001</b>
LDH	<b>0.363</b>	<b>0.006</b>
IgE	0.234	0.062

The significant values are highlighted in bold (p value < 0.05)

There was a significant correlation of CDLQI with serum TARC levels, peripheral eosinophils and serum LDH.

A



B



**Figure 15. Eczema on cheeks in an (A) infant and (B) child**



**Figure 16. Follicular eczema**



**Figure 17. Involvement of the scalp in a child with AD**

A. Centrofacial sparing



B



**Figure 18. Erythroderma secondary to AD**



**Figure 19. Flexural lichenification in a child with AD**



**Figure 20. Psoriasiform lesions**



A



B



C

**Figure 21. Features of filaggrin mutation: (A) Palmar hyperlinearity  
(B) Keratosis pilaris (C) Ichthyosis vulgaris**



A)

**Mild AD:**

*SCORAD*

*index = 13.6*



B)

**Moderate AD:**

*SCORAD*

*index = 43.5*



C)

**Severe AD:**

*SCORAD*

*index = 50.5*



**Figure 22 . Mild (A), moderate (B) and severe (C) AD**



**A**



**B**

**Figure 23. Complications in AD: (A) Secondary bacterial infection  
(B) Acanthosis nigricans in a child with obesity**



A



B

**Figure 24. Mimics of AD: (A) Seborrheic dermatitis (B) Psoriasis**



**Figure 25. Scabies**

## DISCUSSION

AD is a chronic relapsing pruritic condition, which usually starts in childhood. It presents with a wide variety of clinical features.(1) The ISAAC committee noted a wide variation in the prevalence of AD across countries. (2) Various biomarkers have been studied to assess the severity such as serum levels of TARC, IL-18, LDH, IgE and peripheral blood eosinophils.(10) There are several studies on the demographic and clinical profile of AD from India in the paediatric age group (67,68) however, there are no Indian studies assessing the efficacy of TARC to predict the diagnosis or severity of the disease. Serum TARC was found to be the most reliable biomarker for AD according to a meta-analysis published in October 2015.(11)

In this study, in addition to the clinical profile of AD in the paediatric age group, we evaluated the efficacy of TARC as a diagnostic marker and for assessment of disease severity in the Indian subcontinent using a case-control design. Quality of life impairment was also studied.

The demographic details of our study were compared with that of previous studies published on AD and are shown in table 22.

**Table 22. Comparative profile of the demographic and clinical data between the present study versus previous studies**

Parameter	Present study	Kay et al.(99)	Dhar et al.(67)	Sehgal et al.(68)
Country & year	India (2016-2018)	England (1989-1990)	India (1987-1994)	India (2010-2011)
Number of patients with AD	103	218	672	100
Type of study	P	P	P	P
Duration of study	1 yr 7 months	12 months	7yrs 6 months	1 yr 8 months
Mean age of onset	Infants- 1.98 months Children-1.98 yrs	Median- 6 months	Infants-4.2 months Children-4.1 yrs	3.63 ± 1.42 yrs
Personal history of atopy	46.6% (Asthma-64.6% Allergic rhinitis-62.5% Allergic conjunctivitis-20.8%)	Asthma-38%	10.86% (Infants-0.09% Children-15.37%)	Asthma-37% Allergic rhinitis-42%
Family history of atopy	66.02%	-	36.9%	-

P- prospective

Symptoms of AD occurred within the first year of life in 57.3% cases and within 5 years of age in 89.3% cases. This was similar to the study done by Kay et al. wherein approximately 60% of cases occurred within the first year of life and 90% within 5 years of age.(18) However, the age of onset of disease was lower in our study when compared to other Indian studies.(67,68)

Among precipitating and exacerbating factors in our study, sweating was the most common followed by food allergens, woollen clothing and dust-mites. Habitual scratching was reported by 6.8%. Werfel et al. compiled data from 8 studies and found a prevalence of food allergy varying between 33 to 63%.<sup>(100)</sup> Moderate to marked deterioration was observed in mildly involved skin of one-third patients with AD with positive skin-prick tests to house dust-mites when challenged with *D. pteronyssinus* in an earlier study.<sup>(101)</sup> Sweating and stress were reported as provoking factors in 96% and 81% patients, respectively in a study on 85 adult patients with AD.<sup>(102)</sup>

In our study, seasonal variation was observed in 68% cases with 61.4% reporting a winter exacerbation, which was comparable to other studies from India and the West. Dhar and Kanwar reported it in 67.14% amongst the infantile AD and 58% amongst childhood AD,<sup>(67)</sup> while Sehgal et al. found the same in 70% patients <sup>(68)</sup>. A study conducted in Germany on 39 children with eczema showed that 21 (53.8%) of them had aggravation in the winter season while 18 (46.2%) in the summer season.<sup>(103)</sup>

At induction into the study, eczema on the face was observed in 86.7% cases in infantile AD but only 38.6% in childhood AD. This was similar to the study by Dhar et al. in case of infants where face was involved in 79%. However, it was much lower for childhood AD when compared to 74.5% children in the same study by Dhar et al.<sup>(67)</sup> It was higher than that found in the study by Sehgal et al. where 25% had facial involvement and 45% had involvement of the flexures<sup>(68)</sup>. Chu et al. also

found highest involvement of head and neck region in infantile AD (25.3%).(104) In our study, both in infantile and childhood AD, acute eczema (93.3% and 63.6%, respectively) was the most common morphological type but chronic lesions were seen in a much higher number of children (57, 64.8%) when compared to infants (26.7%). Dhar et al.(67) had also found a high number of infants with acute eczema (52.7% ), while in children predominant lesions were chronic involving 47.4% cases. This is in confirmation with the widely accepted opinion of acute lesions being more common in infants and chronic in children.(1,63,105) Erythroderma was seen in 6 (5.8%) cases. Previous Indian studies have reported a prevalence of erythroderma of about 15% in children with AD.(106,107)

Growth retardation, as assessed by height and weight below the 3<sup>rd</sup> centile was observed in 11.65% and 12.62% cases, respectively. Of these only 2 (15.4%) children with weight below 3<sup>rd</sup> centile and 4 (33.3%) with a height below 3<sup>rd</sup> centile had history of use of systemic steroids. This was similar to the study by Kristmundsdottir et al. wherein 10% children had a height lower than 3<sup>rd</sup> centile.(108) However, the growth retardation in cases recruited in our study was lower than the study by Dhar et al. where height and weight were below the 3<sup>rd</sup> centile in 34% and 42% children, respectively.(109) An association of central obesity with children suffering from AD has previously been described, wherein 15% children with AD had obesity.(110) In our study, there were 10 (9.7%) cases with weight above the 97<sup>th</sup> centile; 7 (70%) of them had obesity and 4 (40%) also had acanthosis nigricans.

Most common cutaneous bacterial infection reported in AD is *Staphylococcus aureus*, (80,111) which was the most frequent organism isolated in our study as well. Other studies have reported eczema herpeticum in the paediatric age group,(111) which was not seen in our study.

Traditionally, severity assessment of AD is done by clinical scores such as SCORAD index, EASI and POEM. Recently, various biomarkers have been studied to help in assessing the severity of the disease. TARC is an important Th2 chemokine involved in homing CCR4 expressing T-cells to the skin and its production is upregulated by IL-1 $\beta$  and TNF- $\alpha$ .(85) Its levels have been found to correlate with disease severity elsewhere and we found a similar correlation with SCORAD in children above 2 years of age. (Table 23)

**Table 23. Correlation coefficients (r) of severity scores versus laboratory parameters.**

	Present study		Kataoka (89)		Kou et al.(10)		Thijs et al.(11)*			
Age of patients	>2yrs		Adult		18-75yrs					
Type of study	Case-control		Cross-sectional		Cross-sectional		Longitudinal		Cross-sectional	
	r	p value	r	CI#	r	p value	r	CI#	r	CI#
Severity score	SCORAD index		EASI		SCORAD index		SCORAD in 59.4% studies			
TARC	0.538	<0.001	0.673	0.55-0.77	0.794	<0.001	0.60	0.48-0.70	0.64	0.57-0.70
Peripheral eosinophils	0.397	<0.001	0.226	-	0.459	<0.001	-	-	-	-
LDH	0.582	<0.001	0.449	0.27-0.60	0.454	<0.001	-	-	0.51	0.38-0.62
IgE	0.331	0.004	0.326	0.14-0.50	0.305	<0.01	0.33	0.08-0.64	0.45	0.32-0.57

\*Meta-analysis

#CI= Confidence interval (95%)

We found the highest correlation of SCORAD index with LDH ( $r=0.582$ ) followed by serum TARC levels ( $r=0.538$ ). Peripheral eosinophils and serum IgE also positively correlated with SCORAD index, though the relationship was lesser than with TARC ( $r=0.397$  and  $0.331$ , respectively). This was different from Japanese studies wherein TARC had the highest correlation with the severity score. However, LDH is non-specific and is released from tissues during damage, explaining the rise in its levels in many conditions like AD, malignancies, hemolysis etc.(11) Therefore, TARC levels being more specific for AD, is a more reliable biomarker.(11)

Sensitivity and specificity of serum TARC measured by ELISA elsewhere ranged from 83-85% and 92-96%, respectively.(90) Normal serum TARC levels reported by Kataoka was 743 pg/mL for children above 2 years.(89) In our study, using the ROC curve as a tool for evaluation of TARC level as a diagnostic tool for AD, we found the cut-off to be 365pg/mL, which is lower than that reported by Kataoka.(89) The sensitivity and specificity in our study was found to be 57.7% and 72.3%, respectively. The positive and negative predictive values were 77.6% and 50.8%, respectively for our sample, though these will differ based on the prevalence of disease in a population.

The median TARC value was 519pg/mL (range 14 to 2503pg/mL) in cases and 319pg/mL (range 46 to 2500pg/mL) in controls, the difference being statistically significant ( $p$ -value 0.004). This was in conformation with the finding of Hijnen et al., who had shown statistically significant difference ( $p$  value of  $<0.001$ ) between

patients with AD versus those without any allergic disease or with only a respiratory allergy (bronchial asthma, allergic rhinitis or both).(87) Therefore, it can be used as an adjunct to the clinical diagnosis of AD to differentiate diseased from the non-diseased population.

The role of vitamin D has also been implicated in the severity and pathogenesis of AD. Peroni et al. found higher vitamin D levels in mild AD compared to severe AD.(112) However, Chiu et al. did not find any significant correlation ( $r = -0.001$ ,  $p = 0.99$ ).(113) Our study showed an inverse relationship between the levels of vitamin D and severity assessed by SCORAD index ( $r = -0.13$ ) which was statistically not significant ( $p$  value 0.29).

Severity of AD also correlated positively with QOL indices for children above 2 years in our study. A comparison with other studies is shown in table 24. This implies that children with a severe disease require psychosocial support since their quality of life is significantly impaired.

**Table 24. Severity of AD versus QOL indices**

	Present study (Above 2 yrs)		Cheng et al(77)		Djurović et al(76)
Severity score	SCORAD index		SCORAD index		Three-item severity score
	r	p value	r	p value	Spearman's correlation coefficient ( $\rho$ )
IDQOL	0.926	<0.001	0.358	<0.05	0.31-0.74
CLDQI	0.541	<0.001	0.386	<0.05	0.31-0.69

In children above 2 years of age, a significant correlation was found between serum TARC levels and objective SCORAD, SCORAD index, IDQOL and CDLQI scores. It also correlated with other objective markers of severity such as peripheral eosinophils and LDH. We did not find a similar correlation for children under 2 years. However, the number studied was small (n=25). A comparison of correlation of TARC levels with other clinical and laboratory parameters in children older than 2 years with another study in Japan is given in table 25.

**Table 25. Correlation coefficient between serum TARC levels and other clinical and laboratory parameters**

Parameter	Present study (for age > 2yrs)		Kakinuma et al.(85)	
	r	p value	r	p value
1. Objective SCORAD	<b>0.52</b>	<b>&lt;0.001</b>	<b>0.60</b>	<b>&lt;0.001</b>
2. SCORAD index	<b>0.54</b>	<b>&lt;0.001</b>	-	-
3. Peripheral eosinophils	<b>0.58</b>	<b>&lt;0.001</b>	<b>0.61</b>	<b>&lt;0.001</b>
4. LDH	<b>0.55</b>	<b>&lt;0.001</b>	-	-
5. IgE	0.17	0.19	<b>0.57</b>	<b>&lt;0.001</b>

The significant values are highlighted in bold

TARC levels correlated with SCORAD, peripheral eosinophils and LDH similar to the study by Kakinuma et al.

In summary, the clinical profile of our patients was similar to other studies, in terms of age of onset, precipitating and exacerbating factors, morphology of lesions and secondary bacterial infections. The complications of growth retardation, obesity and secondary viral infections were lower in our study. There was a significant difference in levels of TARC in AD and controls, suggesting the usefulness of TARC to aid in the diagnosis of AD. We also found a positive correlation of serum TARC levels with SCORAD index, quality of life indices and other biomarkers in children above 2 years of age, which indicates that TARC levels may be used as an objective marker of disease severity. This is in confirmation to most other studies conducted elsewhere.(11)

## CONCLUSION

- In this hospital-based case-control study, the mean age of children with AD was 5.78 years in males and 6.55 years in females. The majority of children were older than 2 years and the ratio of male: female was 1.7:1, which was similar to other Indian studies.(67,68)
- AD manifested by 1 year of age in 57.3% and by 5 years in 89.3% of children.
- Sweating was the most common exacerbating factor followed by food allergens, woollen clothing and dust-mites.
- Face was the most common site affected (83,80.6%) irrespective of the age group.
- Acute eczema was the most common morphological type present in 70 out of 103 patients (68%) with or without lichenification (56,54.3%). Erythroderma was seen in 6 (5.8%) cases. The prevalence of acute eczema was significantly higher in the infantile group (<18 months) as compared to childhood group (>18 months) (p value of <0.001). On the other hand, chronic AD comprising of lichenification, prurigo and psoriasiform lesions was more common in the childhood group (p value of 0.042).
- Growth retardation was not significant in our sample as majority of the cases were between 3<sup>rd</sup> to 97<sup>th</sup> centile of height (78.64%) and weight (77.67%). Obesity was seen in 8.9% children.

- TARC levels were elevated in 33 (32%) cases. The median TARC value was 519pg/mL (range 14-2503pg/mL) in cases and 319pg/mL (range 46-2500pg/mL) in controls (p-value 0.004).
- The cut-off obtained for TARC level in AD by the ROC curve analysis was 365pg/mL (for children above 2years), with a sensitivity of 57.7%, specificity of 72.3%, positive predictive value of 77.6% and negative predictive value of 50.8%.
- The mean SCORAD index was  $37.21 \pm 22.0$ . This correlated with TARC levels in children above 2 years ( $r= 0.52$ , p-value  $<0.001$ ) and with other biomarkers like LDH ( $r=0.55$ ), serum IgE ( $r=0.31$ ) and peripheral eosinophils ( $r=0.37$ ).
- TARC levels correlated significantly with QOL indices in children above 2 years (IDQOL:  $r=0.823$ , p-value= $0.003$  and CLDQI:  $r=0.380$ , p-value= $0.001$ ).
- Our study has shown that serum TARC can be used as an adjunct to the clinical criteria for the diagnosis of AD and correlates with disease severity as assessed by SCORAD.

## **LIMITATIONS**

- The study is from a single centre and hence the sample may not be representative of a large population.
- The number of children below 1 year and between 1-2 years were very limited and hence we could not determine a definite relationship between the clinical and laboratory parameters or plot the ROC curve in these groups.
- Patients were examined only once during the study period, therefore we could not study the effect of treatment on the level of biomarkers and its effectiveness as a prognostic marker.

## **RECOMMENDATIONS**

- Multicentre studies are needed to study the efficacy of serum TARC as a diagnostic marker and to assess its relationship with the disease severity.
- Prospective studies are required to study its efficacy as a prognostic marker to prevent undue early termination of treatment.

## SUMMARY

### **Background:**

Atopic dermatitis (AD) is a pruritic, chronic inflammatory skin disease which is diagnosed by clinical criteria such as the Hanifin and Rajka criteria, the U.K. Working Party Diagnostic criteria etc. Its severity is determined using clinical scoring systems, such as SCORing Atopic Dermatitis (SCORAD), Eczema Area and Severity Index (EASI) and Patient Oriented Eczema Measure (POEM). There are several biomarkers also to assess the severity such as serum thymus and activation-regulated chemokine (TARC), IL-18, lactate dehydrogenase (LDH), IgE and peripheral blood eosinophils, of which TARC has shown promising results elsewhere. There are no published studies in India assessing the correlation between serum TARC levels and AD and its severity. This study was undertaken to evaluate the same in the Indian subcontinent.

### **Objectives:**

Our primary objective was to study the efficacy of TARC as a diagnostic marker of AD and its association with the severity of the disease in the paediatric age group in the Indian context and to study the clinical profile of patients with AD. Secondary objective was to study the quality of life of patients with AD and its correlation with serum TARC.

## **Methods:**

A hospital-based case-control study was conducted in the department of Dermatology, Venereology and Leprosy, Christian Medical College, Vellore over a period of 19 months from December 2016 to June 2018, with approval from the Institutional Review Board (IRB. No. 10320). 103 patients aged 0-16 years with AD and 70 controls with diseases mimicking AD (psoriasis, scabies, contact dermatitis, seborrheic dermatitis, impetigo) were recruited after an informed written consent. Data was entered into a standard clinical proforma. The UK Working Party Diagnostic Criteria was used to diagnose AD. TARC levels were measured using Abcam's Human ELISA kit. Other laboratory parameters tested included LDH, serum IgE and peripheral eosinophils. Severity of AD was assessed by calculating SCORAD index. Quality of life was assessed using IDQOL for children below 4 years and CDLQI for those above 4 years. Receiver-operating-characteristic curve was plotted for optimal cut-off value for TARC and correlation was determined using Pearson-correlation-coefficient and linear regression.

## **Results:**

103 (65-males,38-females) cases and 70 (38-males,32-females) controls were recruited with mean age (years) of 6.06 and 6.52, respectively. AD manifested by 1 year of age in 57.3% and by 5 years in 89.3% of children, the face being the most common site affected (83,80.6%). In infantile AD (n=15), 14 (93.3%) cases had acute eczema and 4 (26.7%) had lichenification in addition. In childhood AD (n=88), 56 (63.6%) cases had acute eczema, 52 (59.1%) had lichenification, 2 (2.3%) had prurigo

and 3 (3.4%) had psoriasiform lesions. Erythroderma was seen in 6 (5.8%) cases. All features of filaggrin mutation were seen in 10 (9.7%) cases. Xerosis was seen in 88 (85.4%) patients. Dennie-Morgan folds were seen in 20 (19.4%) cases. The median TARC value was 519pg/mL (range 14-2503pg/mL) in cases and 319pg/mL (range 46-2500pg/mL) in controls (p-value 0.004). A cut-off of 365pg/mL was obtained in AD (children>2years) using the ROC curve (sensitivity-57.7%, specificity-72.3%, positive-predictive-value-77.6%, negative-predictive-value-50.8%). The mean SCORAD index was  $37.21 \pm 22.0$ . This correlated with TARC levels in children >2years ( $r= 0.52$ , p-value <0.001) and also with other biomarkers like LDH ( $r=0.55$ ), serum IgE ( $r=0.31$ ) and peripheral eosinophils ( $r=0.37$ ). TARC levels correlated significantly with QOL indices in children >2 years (IDQOL- $r=0.823$ , p-value=0.003 and CLDQI- $r=0.380$ , p-value=0.001).

### **Conclusion:**

The clinical profile of our patients was similar to previous studies. Our results suggest that serum TARC is a useful adjunct to the clinical criteria for the diagnosis of AD and correlates with the severity of disease as well and can, therefore, provide an objective assessment of severity in AD.

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## ANNEXURES

### ANNEXURE-1 : CONSENT FORMS, CHILD ASSENT FORMS & PATIENT INFORMATION SHEETS

Informed Consent form to participate in a clinical trial

**Study Title: To study the efficacy of thymus and activation-regulated chemokine (TARC) as a diagnostic marker of atopic dermatitis and its association with the severity of the disease in the paediatric age group in the Indian context**

**Study Number:**

**Subject's Initials:** \_\_\_\_\_ **Subject's Name:**

**Date of Birth / Age:** \_\_\_\_\_

- (i) I confirm that I have read and understood the information sheet dated \_\_\_\_\_ for the above study and have had the opportunity to ask questions. [ ]
- (ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]
- (iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]
- (iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]
- (v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Signatory's Name: \_\_\_\_\_ Signature:

Or

R  
D

Signatory's Name: \_\_\_\_\_

Signature of the Investigator: \_\_\_\_\_

Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Study Investigator's Name: \_\_\_\_\_

Signature (or) thumb impression of the Witness: \_\_\_\_\_

Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Name and Address of the Witness: \_\_\_\_\_

### शोध अध्ययन में भाग लेने के लिए सूचित सहमत पत्र

अध्ययन शीर्षक: एटॉपिक डर्मेटाइटिस से पीड़ित बच्चों (०-१६ वर्ष) के थाइमस एंड एक्टिवेशन-रेगुलेटेड कीमोकाइन (TARC) का सीरम स्तर और बीमारी की गहनता से उसका सम्बन्ध

अध्ययन संख्या:

प्रतिभागी का नाम: \_\_\_\_\_

जन्मतिथि / उम्र : \_\_\_\_\_

१) मैं इस बात की पुष्टि करता हूँ कि मैंने दिनांक \_\_\_\_\_ सूचना पत्र को उपरोक्त अध्ययन के लिए पढ़ा और समझा है, और मुझे प्रश्न पूछने का मौका मिला है।

२) मैं इस बात को समझता हूँ कि इस अध्ययन में मेरी भागीदारी स्वैच्छिक है। मैं किसी भी समय बगैर कोई कारण बताए, तथा मेरी चिकित्सा में बिना कोई बाधा आए, या कानूनी अधिकार बिना प्रभावित हुए, इस अध्ययन को छोड़ सकता हूँ।

३) मैं समझता हूँ कि आचार समिति और नियामक अधिकारियों को मेरे स्वास्थ्य अभिलेखों के वर्तमान अध्ययन और इस संबंध में भविष्य में होने वाले अनुसंधानों के लिए मेरी अनुमति की जरूरत नहीं होगी, चाहे मैं इस से अपनी भागीदारी वापस ले लूँ। मैं इस बात से सहमत हूँ।

हालाँकि, मैं समझता हूँ मेरी पहचान का खुलासा तीसरे पक्ष को दी गई किसी भी जानकारी अथवा प्रकाशन में नहीं किया जाएगा

४) मैं इस बात के लिए सहमति देता हूँ कि इस अध्ययन से उत्पन्न हुए परिणामों को वैज्ञानिक प्रायोजन के लिए प्रदान करने से इंकार नहीं करूँगा।

५) मैं उपरोक्त अध्ययन में भाग लेने के लिए सहमत हूँ।

हस्ताक्षर या अंगूठे का निशान (विषय / कानूनी तौर पर स्वीकार्य प्रतिनिधि):

हस्ताक्षरकर्ता का नाम: \_\_\_\_\_ दिनांक: \_\_\_\_ / \_\_\_\_ /

\_\_\_\_\_

अन्वेषक के हस्ताक्षर: \_\_\_\_\_

दिनांक: \_\_\_\_ / \_\_\_\_ / \_\_\_\_

अध्ययन जांचकर्ता का नाम: \_\_\_\_\_

गवाह के हस्ताक्षर या अंगूठे का निशान: \_\_\_\_\_

दिनांक: \_\_\_\_ / \_\_\_\_ / \_\_\_\_

गवाह का नाम व पता: \_\_\_\_\_

மருத்துவ ஆராய்ச்சியில் பங்கெற்பத்தற்கான ஒப்புதல் படிவம்

ஆய்வின் தலைப்பு: தைமஸ் மற்றும் டி ஏ ஆர் ஸி யின் இரத்த அளவு ஏட்டோப்பிக் டெர்மடைடிஸ் உள்ள குழந்தைகளில் ஆராய்ந்து அதற்கும் நோயின் தீவிரத்திற்கும் உள்ள உறவையும் குறித்து ஆராய்தல்.

எண்:

பங்கெற்பவரின் கையொப்பம்:

பங்கெற்பவரின் பெயர்:

பிறந்த தேதி/ வயது:

(i) இந்த ஆராய்ச்சியில் நான் தகவல் படிவதிலுள்ள எல்லா விவரங்களையும் படித்து அறிந்துக்கொண்டேன். கேள்விகள் கேட்க வாய்ப்பளிக்கப்பட்டது.

(ii) இந்த ஆராய்ச்சியில் பங்குகோள்வது என் விருப்பம்சார்ந்தது என்றும், இவ்வாராய்ச்சியில் இருந்து எப்போது வேண்டுமானாலும், எக்காரணமுமின்றி விலகிக்கொள்ளலாம் என்றும் புரிந்து கொண்டேன். என்னுடைய விலகல் என் மருத்துவ சிகிச்சைக்கான எந்த ஒரு உரிமையையும் பாதிக்காது என்பதையும் புரிந்துகொண்டேன்.

(iii) இந்த ஆராய்ச்சி சம்பாந்தமான பொறுப்பில் உள்ளவர்கள் சட்டப்பூர்வமான குளுவைச்சார்ந்தவர்கள் மற்றும் ஒழுங்குமுறைக் குழுவைச் சார்ந்தவர்கள் என்றும் என்னுடைய மருத்துவ பதிவேடுகளை என் அனுமதியில்லாமல் பயன்படுத்தலாம் என்பதற்கு முழு சம்மதம் தெரிவிக்கிறேன். இந்த ஆய்விலிருந்து நான் விலகினாலும் அவர்கள் என் பதிவேடுகளை பயன் படுத்தலாம் என்றும் ஆய்வு முடிவுகள் வெளியிடப்படும் பொது என் பெயரும் எண்ணைக் குறித்த தகவல்களும் வெளியிடப்படாது என்பதை நன்கு அறிவேன்.

(iv) இந்த ஆராய்ச்சியில் பெறப்படும் தகவல்களை அறிவியல் சம்மந்தமாக பயன்படுத்துவதில் எனக்கு எந்த மறுப்பும் இல்லை.

இரகசியத்தன்மை:

இந்த ஆய்வில் உங்கள் பெயரோ அல்லது முகவரியோ எந்த இடத்திலும் குறிப்பிட படாது. இந்த ஆய்வின் பொழுது உங்களைப் பற்றி பெறப்பட்ட அனைத்து தகவலும் மிகவும் பாதுகாப்பாகவும், இரகசியமாகவும் வைக்கப்படும். மேலும் இத்தகவலை தேவைப்படும் பொது சட்டவிதிமுறைக்குட்பட்டே பயன்படுத்தப்படும்.

பங்குபெறுவது:

இந்த ஆய்வில் நீங்கல் பங்குபெறுவது அல்ல பங்குபெற மறுப்பது உங்கள் விருப்பமே. இந்த ஆய்வின் பொழுது எந்த நேரத்திலும் அந்த காரணத்தினாலும் தானகவே விலகிக்கொள்ளலாம். மேலும் நீங்கள் விலகினாலோ அல்ல பங்குபெற மறுத்தாலோ அதனால் தாங்கள் பெறும் மருத்துவ சிகிச்சையில் எந்த வித பாதிப்பும் ஏற்படாது.

அணுகவும்:

டாக்டர். ஹிமாத்ரி ஸின்ஹா  
பாலியல் மற்றும் தொழு நோய் பிரிவு - 1  
கிறிஸ்துவ மருத்துவக் கல்லூரி  
வேலூர்

கையெழுத்து:  
கையெழுத்திட்டவரின் பெயர்:  
தேதி:

ஆய்வாளரின் கையெழுத்து:  
ஆய்வாளரின் பெயர்:  
தேதி:

சாட்சியாளரின் கையெழுத்து:  
சாட்சியாளரின் பெயர் மற்றும் முகவரி:

কককনককল টকয়কল গববষণকয় অঅশগহবণর কলকখাত অননমকাত পত

সককড কশবরকনকম :

এটটপপক ডটরটটটটটটটটট চররটটটটটটট আকটন ০-১৬ বছর বয়সস পশশটদর রটক ' থটইটস ও এপকটভশন পনয়পনত ককটরটকটইন (TARC) ' নটরক পদটটথরর রটতট সরসকট কটর এই করটটগর তসবতটর সটঙ তটর সমকর পনররয়

গববষণক অননকমকঙ :

অঅশগহরকটরসর নটটরর আদদকর : \_\_\_\_\_

অঅশগহরকটরসর নটর: \_\_\_\_\_

জনপতপথ / বয়স \_\_\_\_\_ হটসপটতটল নন \_\_\_\_\_

পটক পচপহত করন :

i . এই গটবষনটর তথদপত আপর পটডপছ এবঅ সমমররভটটব ববটবাপছ, এবঅ তট সঅকটন পশ করটর আরটটক সরয় ও সবটয়টগ কদয়ট হয়টছ | ( )

ii . এই গটবষরটয় আপর কসছটয় অঅশগহন করপছ | কয় ককটটনট রবহটতর আপর চটইটল এর কথটক অনবরপত পতদটহটর কটর

পনটত পটপর এবঅ তটর ককটনরকর পভটব এই হটসপটতটল আরটর বতর রটন বট আগটরস পচপকৎসটয় বট আইপন অপধকটটরর

উপর পডটব নট | ( )

iii . এই অঅশগহটন সমপত থটকটর ফটল আরটর সমটন সঅগহ করট তথদটপদ বদবহটর করটত গটবষনটকতর টর আর ককটটনট

অনবরপত লটগটব নট, পকন আরটর পপরচয় ককটটনট তত তসয় কতর টটক জটনটটনট হটব নট, এবঅ ককটথটও পকটশ করট হটব নট |

( )

iv . এই গটবষনটর ককটটনট তথদটপদ ও ফলটফল বদবহটটর আপর ককটনরকর বটধট কদব নট, যপদ তট ববজটপনক কটটজর

ককটত বদবহত হয় | ( )

v . এই গটবষরটয় অঅশগহন করটত আপর সমত | ( )

সটকর / পটপ সই ( অঅশগহনকটরসর / আইনত গহরটয়টগদ পপতপনপধ র )

সটকরকটরসর নটর : \_\_\_\_\_ তটপরখ : \_\_\_\_/\_\_\_\_/\_\_\_\_

তদনকটরসর সটকর

তদনকটরসর নটর : \_\_\_\_\_

তটপরখ : \_\_\_\_/\_\_\_\_/\_\_\_\_

সটকসর সটকর / পটপ সই

তটপরখ : \_\_\_\_/\_\_\_\_/\_\_\_\_

সটকসর নটর ও পঠকটনট : \_\_\_\_\_

## **CHILD ASSENT FORMS**

Title of the study: **To study the efficacy of thymus and activation-regulated chemokine (TARC) as a diagnostic marker of atopic dermatitis and its association with the severity of the disease in the paediatric age group in the Indian context**

Protocol number:

Principal investigator: Dr. Himadri

Address: Department of Dermatology, Venereology and Leprosy Unit 1, Christian Medical College (CMC), Vellore. Phone no: 0416-2283527

Location where the study will be conducted: Department of Dermatology, Venereology and Leprosy Unit I, Christian Medical College, Vellore

We want to tell you about a study we are doing. A research study is a special way to find out more about a disease. We are trying to find out the relationship between serum levels of TARC and a disease called atopic dermatitis. You are being asked to join the study because we feel that you are a ideal subject for the causes being studied.

The doctor will examine your skin thoroughly and take down the details in a special proforma. If felt necessary she would click photographs of the skin lesions. For some tests, blood would need to be withdrawn. We would see you only once in the study period. Follow ups are welcome though not absolutely necessary for this study.

### **Can anything bad happen to me?**

We want to tell you about some things that might hurt or upset you if you are in this study.

The most common side effects from blood drawing include:

- Pain
- Bleeding at the puncture site
- Slight possibility of infection or fainting

### **Can anything good happen to me?**

We don't know if being in this research study will help you feel better or get well. But we will be able to tell you something which can be used for monitoring the treatment of your disease.

### **Will anyone know I am in the study?**

We will not tell anyone that you took part in this study. When the study is completed, we will write a report about what we find out. We won't use your name in the report.

**What happens if I get hurt?**

There is a negligible risk of getting hurt and your parents/ guardians have been informed about the same.

**What if I do not want to do this?**

You don't have to be in this study. It is entirely your wish. If you agree now, but refuse

later, that is okay too. All you need to do is to tell us.

If you want to participate in this study, please sign below –

**Yes, I want to be a part of this study**

**No, I do not want to be a part of this study**

Name of the child:

Signature/ thumb impression of the child:

Date:

**Witness mediator**

Name:

Signature/thumb impression:

Date:

**Person obtaining Assent:**

I have explained the research at a level that is understandable by the child and believe

that the child understands what is expected during the study.

Name of the investigator: Dr Himadri

Signature:

Date:

**Witness mediator**

Name:

Signature:

Date:

## बाल सहमति पत्र

शोध का शीर्षक: एटॉपिक डर्मेटाइटिस से पीड़ित बच्चों (०-१६ वर्ष) के थाइमस एंड एक्टिवेशन-रेगुलेटेड कीमोकाइन (TARC) का सीरम स्तर और बीमारी की गहनता से उसका सम्बन्ध प्रोटोकॉल संख्या:

प्रधान अन्वेषक: डॉ. हिमाद्रि

अध्ययन का स्थान: डर्मेटोलॉजी, वेनेरेओलोजि और कुष्ठ रोग विभाग, क्रिस्टियन मेडिकल कॉलेज, वेल्लोर। दूरभाष: ०४१६-२२८३५२७

हम आपको इस अध्ययन के बारे में बताना चाहते हैं। एक रोग के बारे में अधिक जानकारी प्राप्त करने के लिए शोध किया जाता है। हम एटॉपिक डर्मेटाइटिस नामक बीमारी और TARC के सीरम स्तर के बीच का सम्बन्ध ढूँढने का प्रयास कर रहे हैं। आपसे अनुरोध किया जाता है कि आप इस शोध का हिस्सा बनें क्योंकि हमारा मानना है कि आप इस अध्ययन के लिए उपयुक्त कर्ता हैं। डॉक्टर आपकी त्वचा की पूर्ण रूप से जांच करने के पश्चात् एक विशेष प्रोफॉर्मा में विवरण लिखेंगी। आवश्यकता पड़ने पर आपकी त्वचा की तस्वीर ली जा सकती है। कुछ जांच के लिए आपके खून का नमूना लिया जायेगा। हम आपको अध्ययन के दौरान केवल एक बार देखेंगे। पुनर्निरीक्षण अनिवार्य नहीं है किन्तु अपेक्षित है।

### क्या इस अध्ययन में भाग लेने से मुझे कुछ नुकसान पहुँच सकता है?

हम आपको कुछ बात बताना चाहते हैं जिससे आप विचलित हो सकते हैं। खून निकालने की संभावित जटिलताएं निम्नांकित हैं:

- दर्द
- पंक्चर के स्थान रक्त स्राव
- इन्फेक्शन या बेहोश होने की सम्भावना

### इस अध्ययन में भाग लेने से मुझे क्या फायदा होगा?

हम नहीं जानते कि इस अध्ययन में भाग लेने से आपके स्वास्थ्य में कोई सुधर आएगा या नहीं। परंतु हम आपको कुछ जानकारी दे पाएंगे जिससे आपकी बीमारी के इलाज की निगरानी संभव होगी।

### क्या किसी और को पता चलेगा कि मैं इस अध्ययन का हिस्सा हूँ?

हम किसी को नहीं बताएँगे कि आपने इस अध्ययन में भाग लिया। अध्ययन समाप्त होने पर हम एक रिपोर्ट तैयार करेंगे जिसमें हम आपका नाम नहीं लिखेंगे।

### यदि मुझे चोट लगी तो क्या होगा?

आपको चोट लगने की सम्भावना नगण्य है। किन्तु आपके माता-पिता को सूचित कर दिया गया है कि यदि आपको किसी प्रकार की परेशानी हो तो वे तुरंत आपको डॉक्टर के पास दिखाएं।

**यदि मैं इस अध्ययन में भाग न लेना चाहूँ तो मुझे क्या करना पड़ेगा?**

अध्ययन में भाग लेने का निर्णय आपका है। यदि आप इसमें शामिल होने से सहमत होकर फिर शामिल न होना चाहें तब भी कोई मुश्किल नहीं है। आपको केवल अपना निर्णय हमें बताना है। यदि आप इस अध्ययन में भाग लेना चाहते हैं तो कृपया नीचे हस्ताक्षर करें।

[ ] हाँ, मैं इस अध्ययन में भाग लेना चाहता/चाहती हूँ

[ ] नहीं, मैं इस अध्ययन में भाग नहीं लेना चाहता/चाहती हूँ

बच्चे का नाम:

हस्ताक्षर/ अंगूठे का निशान:

दिनांक:

**गवाह मध्यस्थ**

नाम:

हस्ताक्षर/ अंगूठे का निशान:

दिनांक:

**स्वीकृति प्राप्त करने वाला व्यक्ति**

मैंने इस अध्ययन के बारे में बच्चे को उसके द्वारा समझने वाले स्तर पर समझाया है। मेरा विश्वास है की बच्चा यह समझ गया है कि अध्ययन में भाग लेने से उसे क्या करना पड़ेगा।

शोधकर्ता का नाम: डॉ. हिमाद्री

हस्ताक्षर:

दिनांक:

ஒப்புதல் படிவம்

ஆராய்ச்சியின் தலைப்பு : தைமுஸ் சுரப்பியும் அதன் செயல்பாடை நிர்ணயிக்கும் கீமொக்கைனும் எட்டொப்பிக் டெர்மடைடிஸ் வியாதியில் செயல்படும் விதம்

படிவ எண்:

ஆராய்சியாளர்: மருத்துவர் ஹிமாத்திரி ஸின்ஹா

விலாசம்: தோல் நோய் பிரிவு, பாலியல் மற்றும் தோல் நோய் பிரிவு எண்: 1, கிறீஸ்துவ மருத்துவக் கல்லூரி, வெல்லூர்.  
தொடர்பு எண்: 0416 2283527

ஆராய்ச்சி செய்யப்படும் இடம்: பாலியல் மற்றும் தோல் நோய் பிரிவு எண்:1, கிறீஸ்துவ மருத்துவக் கல்லூரி, வெல்லூர்.

நாங்கள் தங்களுக்கு நாங்கள் செய்யும் ஆராய்ச்சியை பற்றி கூற விரும்புகின்றோம். ஆராய்ச்சி என்பது ஒரு வியாதியை குறித்து மேலும் அறிந்து கொள்வதற்கான ஓர் நல்ல வழியாகும். நாங்கள் இப்போது ஏட்டொப்பிக் டெர்மடைடிஸ் என்கின்ற வியாதிக்கும் டிஏஆர்ஸி என்கின்ற திரவம் இரத்தத்தில் இருப்பதற்கும் உள்ள சம்பந்தத்தை அறிய விரும்புகின்றோம். தாங்கள் எங்கள் ஆராய்ச்சிக்கு உதவியாக இருப்பீர்கள் என்று கருதுகிறோம்.

இதற்க்காக, மருத்துவர் தங்கள் சருமத்தை நன்றாக சோதனை செய்து கண்டுபிடிப்புகளை ஒரு தனி தாளில் எழுதுவார்கள்.

தேவை பட்டால் தோலில் உள்ள புண்களை புகைப்படம் பிடிப்பார்கள். சில ஆய்வுக்காக இரத்தம் எடுக்கப்படும். இந்த ஆராய்ச்சிக்காலம் முழுதிலும் நாங்கள் உங்களை ஒரு முறை மட்டுமே சந்திக்க தேவை உண்டு. ஆனாலும், தாங்கள் விரும்பப்பட்டால் எங்களை மீண்டும் வந்து சந்திக்க அனுமதி உள்ளது.

எனக்கு ஏதெனும் சிரமம் உண்டாகுமா?

இரத்தம் எடுத்தலால், சிறிது வலி, இரத்தக் கசிவு, மயக்கம், ஆகியவை உண்டாக வாய்ப்பு உள்ளது.

எனக்கு நல்லது ஏதெனும் நடக்குமா?

இதன் மூலமாக தினசரி வாழ்க்கையில் பயன் இல்லாவிட்டாலும், இதன் மூலமாக கிடைக்கும் செய்திகளை பயன்படுத்தி நாங்கள் தங்கள் நோயைக் குறித்து பல விஷயங்களை அறிந்து கொள்ள முடியும்.

இதை பற்றி யாருக்காவது தெரிய வருமா?

நீங்கள் இந்த ஆராய்ச்சியில் பங்குபெற்றது குறித்து நாங்கள் யாருக்கும் சொல்ல மாட்டோம். மேலும் இதில் சேகறித்த விவரங்களை வெளியீடு செய்யும் போது தங்கள் பெயரை இட மாட்டோம்.

எனக்கு அடி பட வாய்ப்பு உள்ளதா?

இருக்கும் சிறிய வாய்ப்பு தங்கள் பெற்றொரிடம் சொல்ல பட்டுள்ளது.

எனக்கு பங்குபெற விருப்பம் இல்லையென்றால்?

இது முழுக்க முழுக்க தங்கள் விருப்பத்துக்கு உற்பட்டதே. தாங்கள் எப்போது வேண்டுமானாலும் பங்குபெற மறுக்கும் வசதி உள்ளது.

இதில் பங்கு பெற விருப்பம் இருந்தால் கீழே கையொப்பமிடவும்.

ஆம், பங்குபெற விருப்பப்படுகிறேன்: [   ]

இல்லை, பங்குபெற விருப்பமில்லை:[   ]

குழந்தையின் பெயர்:

குழந்தையின் கையொப்பம்:

தேதி:

சாட்சியாளர்:

பெயர்:

கையொப்பம்:

தேதி:

ஒப்புதல் வாங்குபவர்:

நான் குழந்தைக்கு அதற்கு புரியும் மொழியில், புரியும் வண்ணத்தில் கூறியுள்ளேன். குழந்தை, ஆராய்ச்சியைக் குறித்த சரியான தகவல்களை பெற்று இருக்கிறது என்று நம்புகிறேன்.

ஆராய்ச்சியாளர் பெயர்:

கையொப்பம்:

தேதி:

சாட்சியாளர்:

பெயர்:

கையொப்பம்:

தேதி

শশশর সমশত পত

সসডড ডশররসনসম :

এটটটশপক ডটরটটটটইশটস চররটটটটগ আকটন ০-১৬ বছর বয়সস শশশটদর রটক ' খটইরটস  
ও এশকটভশন

শনয়শনত ককটটটটটইন (TARC) ' নটরক পদটটটথরর রটতট সরসকট কটর এই করটটটগর  
তসবতটর সটঙ তটর সমকর

শনররয়

পপসরটসকল সসখখস :

পধসন তদনকসরর : ডড ডহমসদর

ডঠকসনস : চমরররসগ , পযযনররসগ ও কক ষ পরসগ ডবভসগ, ইউডনট 1 ( DVL 1 ) , ডখসসন

পমডডরকল করলজ , পভরলসর

পফসন নাড 0416- 2283527

গরবষণস পযখসরন হরব পসখসনকসর ডঠকসনস : চমরররসগ , পযযনররসগ ও কক ষ পরসগ ডবভসগ,  
ইউডনট 1 ( DVL 1 ) , ডখসসন

পমডডরকল করলজ , পভরলসর

পতসমসরক আমরস একডট গরবষণসর বখসপসরর বলরত চসই , পযডট আমরস এখসরন করডছ | গরবষণস  
মসরন হরচ একডট ডবরশষ উপসয়

, পকসরনস পরসগ-এর বখসপসরর যসরত আমরস আরস পবডশ জনরত পসডর | আমরস এরটসডপক

ডসমরসটসইডটস পরসগ এর সসরখ TARC

নসরমর ররক পসওয়স একডট পদসরথরর পযসগসরযসগ পবসরসর পচযস করডছ এই গরবষণসয় | পতসমসরক আমরস এই  
গরবষণসয় পযসগ ডদরত

বলডছ কসরণ আমসরদর ধসরণস পয পয পরসগডট ডনরয় আমরস কসজ কররবস, এটসর গরবষণসর জনখ তক

ডম আদশর পসথরর |

একজন ডসকসর পতসমসর সসরস শররররর তক ভসরলসভসরব পররকস করর পদরখ একডট ডবরশষ ফরমর

তস ডলরখ পনরবন | যডদ তসর

দরকসর মরন হয় তসহরল পস পতসমসর চসমডসয় হওয়স ফক স্কক ডড, ঘস এগডলর ছডব ও তক লরত

পসররন | ডকছক পটস কররত রক

পররকস করসর দরকসর ও পডরব | এই গরবষণসর জনখ পতসমসরক আমসরদর কসরছ খসডল একবসরডট

আসরত হরব, তসর পর আসসর

দরকসর পনই ডকন তক ডম চসইরল আবসর আসরত সসগত , যডদও এই গরবষণসর জনখ তসর পসভসরব

পরয়সজন পনই |

এই গটবষরটয় ভটগ শনটল আরটর শক শকছছ খটরটপ হটত পটটর ?

এই গৱবষণসয় ভসগ ডনৱল এমন ডকছক যসৱ কসৱৱণ পতসমসৱ বখসথস বস কষ হৱত পসৱৱ , তসৱ  
বখসপসৱৱ পতসমসৱক আমৱস জসনসৱত

চসই।

সবৱচৱয় সসখসৱণভসৱব ৱক পৱৱকস কৱসৱ ফৱল এগডল হৱত পসৱৱ -

- বখসথস

- ৱক পৱৱকসৱ জসয়গসয় ৱক পবৱৱসৱনস

- সসকমণ হওয়সৱ বস অজসন হৱয় যসওয়সৱ হসলকস সমসবনস

এই গটবষৱটয় ভটগ শনটল আৱটৱ শক শকছছ লটভ হটত পটটৱ ?

এই গৱবষণসৱ কসৱৱণ পতসমসৱ পৱসগ ভসৱলস হওয়সৱ পকৱত পকসৱনস লসভ হৱব ডকনস তস আমৱস  
এখৱনস জসডননস ডকন এৱ পথৱক

পসওয়স ফলসফল ডদৱয় আমৱস পতসমসৱ পৱসগডটৱ ডচডকৎসসৱ পযৱৱবকণ কৱৱত পসৱৱবস।

অনন ককউ শক জটনটত পটৱটব কয আশৱ এই গটবষৱটয় ভটগ শনটয়শছ ?

নস, এইটস আমৱস কসউৱক জসনৱত পদব নস পয তক ডম এৱত ভসগ ডনৱয়ৱছস। গৱবষণসৱ পশৱষ  
ফলসফল ডনৱয় আমৱস একটস ডৱৱপসটৱ

ডলখৱবস। এই ডৱৱপসটৱ এ পতসমসৱ নসম পকসশ কৱস হৱবনস।

আৱটৱ ককটটনট কশত হটল শক হটব?

## **PATIENT INFORMATION SHEET**

**Study Title: To study the efficacy of thymus and activation-regulated chemokine (TARC) as a diagnostic marker of atopic dermatitis and its association with the severity of the disease in the paediatric age group in the Indian context**

We are inviting you to take part in a research study. Before you decide it is important for you to understand why we are doing the research and what it will involve. Please read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you want more information. Take time to decide whether you wish to take part or no .

### **Purpose of research:**

We are going to do a study on the relationship between a blood test, TARC, and atopic dermatitis and other skin conditions like seborrheic dermatitis, contact dermatitis, candidiasis, scabies and impetigo. There are different blood tests which correlate with the severity of atopic dermatitis. One of them, TARC, has been found to be the most specific for this. We want to do research on this topic because there is little information on this in India. This study will provide data on this topic and help for better understanding of markers of disease severity. This will be useful for optimum management of the disease.

### **Expected duration of the Subject's participation:**

You will be examined by the doctor only once in the study period.

### **Description of the procedures:**

The doctor will do detailed examination and note down the information in a special form.

Relevant blood investigations which include TARC, peripheral eosinophils, Immunoglobulin E(IgE) and lactate dehydrogenase(LDH) will be done depending on the clinical diagnosis and extent of disease. At the end of the study, we will analyse all the data obtained so far.

### **Risks or discomforts to the Subject:**

Small amount of blood will be collected from peripheral vein. The most common side effects from blood drawing include:

- Pain
- Bleeding at the puncture site
- Slight possibility of infection or fainting

We are not doing any additional tests apart from the standard protocol

### **Benefits to the Subject:**

We are going to study the features of the disease and do tests like complete blood count, TARC, LDH, IgE. In this study we are going to know the association between TARC levels and various skin diseases and the severity of atopic dermatitis. This will be helpful in making a decision regarding treatment and the way in which the disease affects you.

**Benefits to others:**

Overall data about TARC levels and atopic dermatitis is very little in India. This study will provide data on this topic and help for better understanding of different clinical presentations of atopic dermatitis and its association with TARC. This will be useful for optimisation of duration of management of such conditions.

**Confidentiality:**

Your name and address will not be revealed at any point of time. All information which is collected about you during the course of the research will be kept strictly confidential unless we are required by law to share any information

**Participation:**

It is up to you to decide whether to take part or not. You are still free to withdraw from the study at any time, without giving any reason. A decision to withdraw, or a decision not to take part, will not affect the standard of care you receive.

**Contact person:**

Dr. Himadri,  
Post Graduate resident,  
Department of Dermatology, Venereology, Leprosy  
Christian Medical College,  
Vellore.  
Mobile- 9003237239  
Office-04162283527

रोगी सूचना पत्र

अध्ययन शीर्षक: एटॉपिक डर्मेटाइटिस से पीड़ित बच्चों (०-१६ वर्ष) के थाइमस एंड एक्टिवेशन-रेगुलेटेड कीमोकाइन

**(TARC)** का सीरम स्तर और बीमारी की गहनता से उसका सम्बन्ध

हम आपको एक शोध अध्ययन में भाग लेने के लिए आमंत्रित कर रहे हैं। इससे पहले कि आप कुछ तय कर सकें आपके लिए

यह समझना महत्वपूर्ण है कि हम यह शोध क्यों कर रहे हैं, और इसमें क्या शामिल किया गया है। कृपया निम्न जानकारी को ध्यानपूर्वक पढ़ें और यदि आप चाहें तो दूसरे लोगों से भी इस विषय में चर्चा करें। यदि इसमें कुछ स्पष्ट नहीं है अथवा इस बारे में आप अधिक जानकारी चाहते हैं तो हमसे पूछें। आप यह तय करने में समय लें कि आप इसमें हिस्सा लेना चाहते हैं या नहीं।

शोध का उद्देश्य: हम एक रक्त परीक्षण, **TARC**, और एटॉपिक डर्मेटाइटिस तथा अन्य त्वचा के रोग जैसे सेबोरिक

डर्मेटाइटिस, कांटेक्ट डर्मेटाइटिस, कैंडिडिआसिस, स्केबीज़ और रोज़ा के बीच संबंध पर एक अध्ययन करने जा रहे हैं।

विभिन्न रक्त परीक्षण एटॉपिक डर्मेटाइटिस की गहनता से सम्बंधित हैं। उनमेंसे **TARC** सबसे अधिक विशिष्ट पाया गया है। भारत में इस पर कम जानकारी है इसलिए हम इस विषय पर शोध करना चाहते हैं। इस अध्ययन से इस विषय पर अधिक जानकारी प्राप्त होगी और रोग की गंभीरता के मार्कर की बेहतर समझ के लिए मदद मिलेगी। इससे रोग का बेहतर इलाज संभव होगा।

रोगी की भागीदारी की अवधि:

अध्ययन काल में चिकित्सक के द्वारा केवल एक बार आपकी जांच की जाएगी।

प्रक्रियाओं का विवरण:

डॉक्टर विस्तृत शारीरिक परीक्षण करके सारी जानकारी को एक पत्र में लिखेंगे। परीक्षण नैदानिक निदान के आधार पर

प्रासंगिक रक्त जांच जैसे **TARC**, इओसिनोफिल्स, इम्युनोग्लोब्यूलिन इ (**IgE**) तथा लैक्टेट डीहैड्रोजेन्स (**LDH**)

परीक्षण किये जायेंगे। अध्ययन के अंत में हम अब तक प्राप्त सभी डाटा का विश्लेषण करके रोग की गंभीरता के साथ उसके

सम्बन्ध का अध्ययन करेंगे। एटॉपिक डर्मेटाइटिस के अलावा जो मरीज़ अध्ययन में भाग लेंगे, **TARC** उनके लिए

निःशुल्क किया जायेगा।

रोगी की असुविधा तथा जोखिम:

रक्त की थोड़ी सी मात्रा परिधीय नस से एकत्र की जाएगी। खून निकालने की संभावित जटिलताएं निम्नांकित हैं:

- दर्द
- पंक्चर के स्थान रक्त स्राव
- इन्फेक्शन या बेहोश होने की बहुत थोड़ी सम्भावना

हम मानक प्रोटोकॉल के अलावा कोई भी अतिरिक्त परीक्षण नहीं कर रहे हैं।

रोगी को लाभ:

हम इस त्वचा की बीमारी के विभिन्न रूप तथा रक्त परीक्षण जैसे पूर्ण रक्त प्रोफाइल, **TARC**, **LDH**, इज का

अध्ययन करने जा रहे हैं। इस अध्ययन से हमें **TARC** के सीरम स्तर तथा एटॉपिक डर्मेटाइटिस व अन्य त्वचा के रोगों की गहनता के बीच संबंध ज्ञात होगा। इससे रोग की गंभीरता का मार्गदर्शन करके उसके उपचार के बारे में फैसला लेने में मदद मिलेगी।

दूसरों को लाभ:

भारत में एटॉपिक डर्मेटाइटिस और **TARC** के बारे में बहुत कम जानकारी है। यह अध्ययन इस विषय पर डाटा प्रदान

करेगा जिससे एटॉपिक डर्मेटाइटिस के विभिन्न लक्षण तथा **TARC** से बीमारी की गहनता के सम्बन्ध को बेहतर तरीके से समझने में मदद मिलेगी। इससे रोग के उत्तम उपचार के बारे में निर्णय लेने में सहायता मिलेगी।

गोपनीयता:

किसी भी समय आपके नाम और पते का खुलासा नहीं किया जायेगा। अनुसन्धान के दौरान जो भी जानकारी आपके द्वारा

एकत्रित की जाएगी उसे सख्ती से गोपनीय रखा जायेगा, जब तक की उस जानकारी को साझा करना कानून द्वारा आवश्यक न हो।

भागीदारी:

यह तय करना आपके ऊपर निर्भर करता है कि आप इसमें हिस्सा लें या न लें। आप किसी भी समय बिना कोई कारण बताये इस अध्ययन से अपनी भागीदारी वापिस ले सकते हैं। भाग न लेने का निर्णय अथवा अपनी भागीदारी वापिस लेने का निर्णय आपकी देखभाल के मानक को प्रमाणित नहीं करेगा।

संपर्क करें:

डॉ. हिमाद्रि

पोस्ट ग्रेजुएट रेसिडेन्ट

त्वचा विज्ञान, रतिजरोग, कुष्ठ रोग विभाग

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वेल्लोर

मोबाइल: **9003237239**

कार्यालय: **04162283527**

### **பங்குபெறுபவர் தகவல் படிவம்:**

ஆய்வின் தலைப்பு:

டி ஏ ஆர் ஸி என்ற கீமோகைன் இரத்த அளவை, ஏட்டோப்பிக் டெர்மடைடிஸ் உள்ள குழந்தைகளில் ஆராய்ந்து, அதற்கும் நோயின் தீவிரத்திற்கும் உள்ள உறவையும் குறித்து ஆராய்தல்.

ஆய்வின் காரணம்:

நாங்கள் தங்களுக்கு நாங்கள் செய்யும் ஆராய்ச்சியை பற்றி கூற விரும்புகின்றோம். ஆராய்ச்சி என்பது ஒரு வியாதியை குறித்து மேலும் அறிந்து கொள்வதற்கான ஓர் நல்ல வழியாகும். நாங்கள் இப்போது ஏட்டோப்பிக் டெர்மடைடிஸ் என்கின்ற வியாதிக்கும் டிஏஆர்ஸி என்கின்ற திரவம் இரத்தத்தில் இருப்பதற்கும் உள்ள சம்பந்தத்தை அறிய விரும்புகின்றோம். நாங்கள் இந்த ஆய்வில் செபோரிக் டெர்மடைடிஸ், கான்டக்ட் டெர்மடைடிஸ், கன்டிடையாஸிஸ், ஸ்கேபிஸ், இம்பெடைகோ போன்ற நோய்களையும் ஆய்வு செய்கிறோம். தாங்கள் எங்கள் ஆராய்ச்சிக்கு உதவியாக இருப்பீர்கள் என்று கருதுகிறோம்.

பங்கு பெறுபவரின் ஆய்வின் காலம்:

இந்த ஆராய்ச்சிக்காலம் முழுதிலும் நாங்கள் உங்களை ஒரு முறை மட்டுமே சந்திக்க தேவை உண்டு.

ஆய்வின் வழிமுறை:

இதற்க்காக, மருத்துவர் தங்கள் சருமத்தை நன்றாக சோதனை செய்து கண்டுபிடிப்புகளை ஒரு தனி தாளில் எழுதுவார்கள். தேவை பட்டால் தோலில் உள்ள புண்களை புகைப்படம் பிடிப்பார்கள். சில ஆய்வுக்காக இரத்தம் எடுக்கப்படும். இந்த ஆராய்ச்சிக்காலம் முழுதிலும் நாங்கள் உங்களை ஒரு முறை மட்டுமே சந்திக்க தேவை உண்டு. ஆனாலும், தாங்கள் விருப்பப்பட்டால் எங்களை மீண்டும் வந்து சந்திக்க அனுமதி உள்ளது. ஏட்டோப்பிக் டெர்மடைடிஸ் இல்லாத குழந்தைகளுக்கு டி ஏ ஆர் ஸி ரத்த பரிசோதனை இலவசமாக செய்யப்படும்.

ஆய்வினால் உண்டாகும் சங்கடம்:

இரத்தம் எடுத்தலால், சிறிது வலி, இரத்தக் கசிவு, மயக்கம், ஆகியவை உண்டாக வாய்ப்பு உள்ளது.

ஆய்வினால் நோயாளிக்கு உண்டாகும் பயன்:

இதன் மூலமாக தங்கள் தினசரி வாழ்க்கையில் பயன் இல்லாவிட்டாலும், இதன் மூலமாக கிடைக்கும் செய்திகளை பயன்படுத்தி நாங்கள் தங்கள் நோயைக் குறித்து பல விஷயங்களை அறிந்து கொள்ள முடியும். அதன் காரணமாக இந்த வியாதியால் சிரமப்படும் பொதுமக்களுக்கு எங்களால் உதவ இயலும்.

ஆய்வினால் பிறருக்கு உண்டாகும் பயன்:

இந்த வியாதியை பற்றி பல புதிய தகவல்களை அறிந்து கொள்ளலாம். அதன் காரணமாக இந்த வியாதியால் சிரமப்படும் பலருக்கு எங்களால் உதவ இயலும்.

ஆய்வின் நம்பகத்தன்மை:

நீங்கள் இந்த ஆராய்ச்சியில் பங்குபெற்றது குறித்து நாங்கள் யாருக்கும் சொல்ல மாட்டோம். மேலும் இதில் சேகறித்த விவரங்களை வெளியீடு செய்யும் போது தங்கள் பெயரை இட மாட்டோம்.

தங்கள் பங்களிப்பு:

இது முழுக்க முழுக்க தங்கள் விருப்பத்துக்கு உற்ப்பட்டதே. தாங்கள் எப்போது வேண்டுமானலும் பங்குபெற மறுக்கும் வசதி உள்ளது. நீங்கள் பங்குபெற மறுத்தாலும் உங்கள் வைத்தியத்தில் எந்த விதமான வேறுபாடும் ஏற்படாது.

ஆய்வாளர்

டாக்டர். ஹிமாத்ரி

பாலியல் மற்றும் தொழு நோய் பிரிவு - 1

கிறிஸ்துவ மருத்துவக் கல்லூரி

வேலூர்

04162283527

স্বাস্থ্যসেবা নাম: ০-১৬ বছর ~~ক~~ বয়সি যাহাদিক্ত স্বাস্থ্য সেবা গ্রহণ করে; টি-১  
আর-ডি-১ পরিকল্পনা নির্দেশ করা হবে, তার সাথে চর্মরোগের সংক্রমণ নির্দেশ করা,

আরও আশঙ্কাজনক এই স্বাস্থ্যসেবা যেমন নিচে উল্লেখ করা হল, তার আর আশঙ্কাজনক  
জনক প্রয়োজন যে কোন হবে; যেহেতু এই স্বাস্থ্যসেবা করা হবে, নিম্নে উল্লেখিত  
দ্রব্য যত ভালোভাবে পূরণ হবে; দরকার হলে আনুষঙ্গিক সামগ্রী আনয়ন করতে পারবে,  
যদি কিছু স্ক্র্যাব না পাওয়া যায় বা আরও উন্নত স্ক্র্যাব চাই, তবে আশঙ্কাজনক হিসাবের  
অনুযায়ী পূরণ করা (প্রস্তুত হিসাব নিকা) যে এই স্বাস্থ্যসেবা আনয়ন  
অসম্ভব হতে পারে তা।

স্বাস্থ্যসেবা উদ্দেশ্য:

এই স্বাস্থ্যসেবা কার্যক্রম আশ্রয় দেয়া হবে চর্ম রোগের একটি উপকার টি-১-আর-ডি-১  
আর-ডি-১ চর্মরোগের, যেমন 'এমিউসিওসিস', 'অস্টিওসিস', 'কন্ড্রোমিউসিস',  
'ক্যালসিফিয়ারসিস', 'স্ট্রোফিউসিস' এবং 'ইম্মুণোডিফেন্স' জাতীয় সংক্রমণ জন্ম দিবে না,  
যদিও আশ্রয় উপকার দ্বারা এমিউসিওসিসের সংক্রমণ নির্দেশ করা যায়,  
যদিও আরও টি-১-আর-ডি-১ কে স্ক্র্যাব নির্দেশ করা হবে কারণ এই নির্দেশ স্বাস্থ্যসেবা  
করলেই হয়নি এবং আশঙ্কাজনক এই স্বাস্থ্যসেবা কার্যক্রম আশ্রয় যে উন্নত স্ক্র্যাব  
পারবে, তা আশঙ্কাজনক এই চর্মরোগের সংক্রমণ জন্ম দিবে না এবং, আরও  
স্বাস্থ্যসেবা এই জাতীয় চর্মরোগের কারণে পারবে।

স্বাস্থ্যসেবা যেমন নিচে বলা হয়েছে সেখানে নিচে দেওয়া:

স্বাস্থ্যসেবা কার্যক্রমের আশঙ্কাজনক স্ক্র্যাবের প্রথম পরীক্ষা করবে,

টিউবের পরীক্ষা করা হবে:

স্বাস্থ্যসেবা কার্যক্রমের পরীক্ষা করা হবে যে সংক্রমণ উন্নত পারবে, তা একটি  
নির্দেশিত স্বাস্থ্যসেবা নির্দেশ দেবে এবং, কিছু এক পরীক্ষা করলে আশঙ্কাজনক স্ক্র্যাবের  
উপস্থিতি লক্ষ্য করা যায়। (আর-ডি-১-আর-ডি-১, প্রতিকারসহ ইমিউনোডিফেন্স, ইম্মুণোডিফেন্স







Non dermatological:

Dermatological:

Drug	Duration of treatment	Last taken on
Emollients		
Topical steroids		
Topical calcineurin inhibitors		
Antihistamines		
Systemic steroids		
Antibiotics		
Cyclosporine		
Azathioprine		
Methotrexate		
Phototherapy		
Biologicals		
Others		

Family history of atopy: Yes/No                      If yes : Asthma/ Allergic rhinitis/ Allergic conjunctivitis

1<sup>st</sup> degree/2<sup>nd</sup> degree/3<sup>rd</sup> degree

**Examination:**

Height-            cm (centile-            )    Weight-            kg (centile-            )

Significant lymph nodes: Cervical/ Axillary/ Inguinal

Ocular changes: Keratoconjunctivitis/ Keratoconus/ Cataract/ Others/ Nil

Dennie-Morgan folds: Present/Absent

Sites involved: Face/ Neck/ upper limbs- flexor-cubital fossa/axilla; extensor/ Lower limbs-flexor-popliteal fossa; extensor/ Trunk/ Scalp/ Mucosa/ Nails/ Hair

Type of lesion: Eczema/ Prurigo/ Psoriasiform/ Excoriation/ Xerosis/ Secondary infection/ Lichenification / Keratosis pilaris/ Palmar hyperlinearity/Others

SCORAD: Objective: \_\_\_\_\_                      Subjective: \_\_\_\_\_                      Total: \_\_\_\_\_

**Investigations:**

Serum TARC:

Peripheral eosinophils (%):

Serum Lactate dehydrogenase (units/L):

Immunoglobulin E (units/mL):

**Quality of life:**

IDQOL: \_\_\_\_\_ Dermatitis severity: \_\_\_\_\_

CDLQI: \_\_\_\_\_

### ANNEXURE-3: SCORAD

#### **SCORAD (SCORing Atopic Dermatitis) Index:**

Area	Percentage affected
Head and neck	
Upper limbs	
Lower limbs	
Anterior trunk	
Back	
Genitals	
Total (A)	

**Intensity:** A representative area of eczema is selected and the intensity of each of the following signs is assessed as none (0), mild (1), moderate (2) or severe (3).

	Intensity score
Redness	
Swelling	
Oozing / crusting	
Skin thickening (lichenification)	
Scratch marks	
Dryness (assessed in an area without inflammation)	
Total (B) (maximum 18)	

#### **Subjective symptoms:**

	Score
No itch (0) to worst imaginable itch (10)	
No sleeplessness (0) to worst imaginable sleeplessness (10)	
Total (C)	

Total score:  $A/5 + 7B/2 + C =$

Objective SCORAD was graded as mild (<15), moderate (15-40) and severe (>40).

SCORAD index which included the objective and subjective scores was graded as mild (<25), moderate (25-50) and severe (>50).

#### **ANNEXURE-4: SERUM TARC LEVEL DETERMINATION**

Serum TARC levels were determined by using *enzyme-linked immunosorbent assay* (Abcam's TARC Human ELISA kit)

##### **PRINCIPLE:**

This assay employs an antibody that is specific for Human TARC and is coated on a 96-well plate. Standards as well as samples are pipetted into the wells. TARC gets bound to the wells by the immobilized antibody. The wells are washed and biotinylated anti-Human TARC antibody is added. After washing away unbound biotinylated antibody, HRP-conjugated streptavidin is pipetted to the wells. The wells are again washed, a TMB substrate solution is added to the wells and colour develops in proportion to the amount of TARC bound. The Stop Solution changes the colour from blue to yellow, and the intensity of the colour is measured at 450 nm.

##### **SAMPLING AND STORAGE:**

Serum is separated from blood sample collected by venepuncture and stored at -20°C .The kit is also stored at -20°C.

##### **REAGENTS:**

20X Wash Buffer Concentrate

Recombinant Human TARC Standard

Assay Diluent C

5X Assay Diluent B

Biotinylated anti-human TARC

400X HRP-Streptavidin Concentrate

TMB One-Step Substrate reagent

Stop Solution

**REAGENT PREPARATION:**

All reagents are equilibrated to room temperature (18-25°C) prior to use.

*1X Assay Diluent B:*

5X Assay Diluent B is diluted 5-fold with deionized or distilled water.

*1X Wash Solution:*

20mL of 20X Wash Buffer Concentrate is diluted with deionized or distilled water to yield 400mL of 1X Wash Buffer.

*1X Biotinylated TARC Detection Antibody:*

100µL of 1X Assay Diluent B is added into the vial to prepare a detection antibody concentrate. The detection antibody concentrate is diluted 80-fold with 1X Assay Diluent B prior to use.

*1X HRP-Streptavidin Solution:*

HRP-Streptavidin concentrate is diluted 400-fold with 1X Assay Diluent B prior to use.

**STANDARD PREPARATION:**

50ng/mL of Stock Standard is prepared by adding 400µL of Assay Diluent C into the vial of TARC Standard.

Standard #1 is prepared by adding 30µL of 50ng/mL Stock Standard to 570µL of Assay Diluent C into tube #1. 300µL of Assay Diluent C is pipetted into the remaining tubes.

Standard #2 is prepared by adding 200 $\mu$ L Standard #1 to tube #2 and so on as given below:

Standard #	Volume to dilute ( $\mu$ L)	Diluent ( $\mu$ L)	Total Volume ( $\mu$ L)	Starting Conc. (pg/mL)	Final Conc. (pg/mL)
1	30	570	600	50,000	2,500
2	200	300	500	2,500	1,000
3	200	300	500	1,000	400
4	200	300	500	400	160
5	200	300	500	160	64
6	200	300	500	64	25.6
7	200	300	500	25.6	10.2
8	0	300	300	0	0

#### SAMPLE PREPARATION:

Assay Diluent C should be used for dilution of serum, the optimal dilution factor being determined by the investigator.

#### PROCEDURE:

1. 100 $\mu$ L of each standard and sample is added into appropriate wells, and then incubated for 2.5 hours at room temperature or overnight at 4°C with gentle shaking.
2. The solution is discarded and washed 4 times with 1X Wash Solution.
3. 100 $\mu$ L of 1X Biotinylated TARC Detection Antibody is added to each well and incubated for 1 hour at room temperature with gentle shaking.
4. The solution is discarded and washed as in step 2.
5. 100 $\mu$ L of 1X HRP-Streptavidin solution is added to each well and incubated for 45 minutes at room temperature with gentle shaking.
6. The solution is discarded and washed as in step 2.

7. 100 $\mu$ L of TMB One-Step Substrate Reagent is added to each well and incubated for 30 minutes at room temperature in the dark with gentle shaking.
8. 50 $\mu$ L of Stop Solution is added to each well and reading is done at 450nm.

CALCULATIONS:

The results are calculated by a microplate reader, capable of measuring absorbance at 450nm.

SENSITIVITY:

The minimum detectable dose of TARC was less than 5 pg/mL.

# ANNEXURE-5 : CDLQI & IDQOL

## CHILDREN'S DERMATOLOGY LIFE QUALITY INDEX

Hospital No

Name:

Diagnosis:

CDLQI  
SCORE:

Age:

Address:

Date:

**The aim of this questionnaire is to measure how much your skin problem has affected you OVER THE LAST WEEK. Please tick ✓ one box for each question.**

- |   |  |   |
|---|--|---|
| <p>1. Over the last week, how <b>itchy</b>, "<b>scratchy</b>", <b>sore</b> or <b>painful</b> has your skin been?</p>  | <p>Very much <input type="checkbox"/><br/>Quite a lot <input type="checkbox"/><br/>Only a little <input type="checkbox"/><br/>Not at all <input type="checkbox"/></p>  | <p><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/></p>  |
| <p>2. Over the last week, how <b>embarrassed</b> or <b>self conscious</b>, <b>upset</b> or <b>sad</b> have you been because of your skin?</p>   | <p>Very much <input type="checkbox"/><br/>Quite a lot <input type="checkbox"/><br/>Only a little <input type="checkbox"/><br/>Not at all <input type="checkbox"/></p>  | <p><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/></p>  |
| <p>3. Over the last week, how much has your skin affected your <b>friendships</b>?</p>  | <p>Very much <input type="checkbox"/><br/>Quite a lot <input type="checkbox"/><br/>Only a little <input type="checkbox"/><br/>Not at all <input type="checkbox"/></p>  | <p><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/></p>  |
| <p>4. Over the last week, how much have you changed or worn <b>different</b> or <b>special clothes/shoes</b> because of your skin?</p>  | <p>Very much <input type="checkbox"/><br/>Quite a lot <input type="checkbox"/><br/>Only a little <input type="checkbox"/><br/>Not at all <input type="checkbox"/></p>  | <p><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/></p>  |
| <p>5. Over the last week, how much has your skin trouble affected <b>going out</b>, <b>playing</b>, or <b>doing hobbies</b>?</p>  | <p>Very much <input type="checkbox"/><br/>Quite a lot <input type="checkbox"/><br/>Only a little <input type="checkbox"/><br/>Not at all <input type="checkbox"/></p>  | <p><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/></p>  |
| <p>6. Over the last week, how much have you avoided <b>swimming</b> or <b>other sports</b> because of your skin trouble?</p>  | <p>Very much <input type="checkbox"/><br/>Quite a lot <input type="checkbox"/><br/>Only a little <input type="checkbox"/><br/>Not at all <input type="checkbox"/></p>  | <p><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/></p>  |
| <p>7. <u>Last week,</u>  was it <b>school time</b>?</p> <p style="text-align: center;"><b>OR</b></p> <p>was it  <b>holiday time</b>?</p>  | <p><b>If school time:</b> Over the last week, how much did your skin problem affect your <b>school work</b>?</p> <p><b>If holiday time:</b> How much over the last week, has your skin problem interfered with your enjoyment of the <b>holiday</b>?</p> | <p>Prevented school <input type="checkbox"/><br/>Very much <input type="checkbox"/><br/>Quite a lot <input type="checkbox"/><br/>Only a little <input type="checkbox"/><br/>Not at all <input type="checkbox"/></p> <p>Very much <input type="checkbox"/><br/>Quite a lot <input type="checkbox"/><br/>Only a little <input type="checkbox"/><br/>Not at all <input type="checkbox"/></p> |
| <p>8. Over the last week, how much trouble have you had because of your skin with other people <b>calling you names</b>, <b>teasing</b>, <b>bullying</b>, <b>asking questions</b> or <b>avoiding you</b>?</p> | <p>Very much <input type="checkbox"/><br/>Quite a lot <input type="checkbox"/><br/>Only a little <input type="checkbox"/><br/>Not at all <input type="checkbox"/></p>  | <p><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/><br/><input type="checkbox"/></p>  |
| <p>9. Over the last week, how much has your <b>sleep</b> been affected by your skin problem?</p>  | <p>Very much <input type="checkbox"/><br/>Quite a lot <input type="checkbox"/></p>   | <p><input type="checkbox"/><br/><input type="checkbox"/></p>  |

10. Over the last week, how much of a problem has the **treatment** for your skin been?

- Only a little
- Not at all
  
- Very much
- Quite a lot
- Only a little
- Not at all

**Please check that you have answered EVERY question. Thank you.**

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बाल त्वचारोग जीवन गुणवत्ता सूची

हॉस्पिटल क्रमांक:

नाम :

रोग निदान:

सीएलडीक्यूआई स्कोर

उम्र:

दिनांक:

पता:

इस प्रश्नोत्तरी का उद्देश्य यह नापना है कि आपकी त्वचा की परेशानी ने गत सप्ताह में आपके जीवन पर कितना प्रभाव डाला है। कृपया हर प्रश्न के लिए एक बॉक्स पर टिक करें।

1. गत सप्ताह, आपकी त्वचा में कितनी खुजली, पीड़ा, दर्द या चुभन लग रहा था?
 

बहुत ज्यादा	<input type="checkbox"/>
बहुत	<input type="checkbox"/>
थोड़ा	<input type="checkbox"/>
बिलकुल नहीं	<input type="checkbox"/>
2. गत सप्ताह, अपनी त्वचा के कारण आपने कितने शर्मसार, स्व चैतन्य
 

बहुत ज्यादा	<input type="checkbox"/>
बहुत	<input type="checkbox"/>
थोड़ा	<input type="checkbox"/>
बिलकुल नहीं	<input type="checkbox"/>
3. गत सप्ताह, आपकी त्वचा ने आपकी दोस्ती पर कितना प्रभाव डाला?
 

बहुत ज्यादा	<input type="checkbox"/>
बहुत	<input type="checkbox"/>
थोड़ा	<input type="checkbox"/>
बिलकुल नहीं	<input type="checkbox"/>
4. गत सप्ताह, आपकी त्वचा ने आपके कपड़े/जूते पहनने पर कितना प्रभाव डाला?
 

बहुत ज्यादा	<input type="checkbox"/>
बहुत	<input type="checkbox"/>
थोड़ा	<input type="checkbox"/>
बिलकुल नहीं	<input type="checkbox"/>
5. गत सप्ताह, आपकी त्वचा ने आपके सामाजिक जीवन या फुरसत के समय की गतिविधियों या खेलकूद पर कितना प्रभाव डाला?
 

बहुत ज्यादा	<input type="checkbox"/>
बहुत	<input type="checkbox"/>
थोड़ा	<input type="checkbox"/>
बिलकुल नहीं	<input type="checkbox"/>
6. गत सप्ताह, आपकी त्वचा ने तैराकी या आपके अन्य खेलकूद के लिए कितनी मुश्किलें खड़ी कीं?
 

बहुत ज्यादा	<input type="checkbox"/>
बहुत	<input type="checkbox"/>
थोड़ा	<input type="checkbox"/>
बिलकुल नहीं	<input type="checkbox"/>
7. गत सप्ताह,  
क्या विद्यालय यदि विद्यालय का समय: गत सप्ताह, आपकी त्वचा ने आपकी पढ़ाई में कितनी रूकावट डाली?
 

विद्यालय जाने से रोका	<input type="checkbox"/>
बहुत ज्यादा	<input type="checkbox"/>
बहुत	<input type="checkbox"/>
थोड़ा	<input type="checkbox"/>
बिलकुल नहीं	<input type="checkbox"/>

या

क्या छुट्टी का समय था? यदि छुट्टी का समय: गत सप्ताह, आपकी त्वचा ने आपकी छुट्टी का आनन्द लेने पर कितना प्रभाव डाला?

बहुत ज्यादा	<input type="checkbox"/>
बहुत	<input type="checkbox"/>
थोड़ा	<input type="checkbox"/>
बिलकुल नहीं	<input type="checkbox"/>
8. गत सप्ताह, क्या आपकी त्वचा की वजह से लोगों ने आपको चिढ़ाया, मज़ाक उड़ाया, प्रश्न किये या आपसे परहेज किया?
 

बहुत ज्यादा	<input type="checkbox"/>
बहुत	<input type="checkbox"/>
थोड़ा	<input type="checkbox"/>
बिलकुल नहीं	<input type="checkbox"/>
9. गत सप्ताह, क्या आपकी त्वचा ने आपकी नींद पर कितना प्रभाव डाला?
 

बहुत ज्यादा	<input type="checkbox"/>
बहुत	<input type="checkbox"/>
थोड़ा	<input type="checkbox"/>

10. गत सप्ताह, आपकी त्वचा के उपचार ने आपके लिए कितनी मुश्किलें खड़ी कीं?  बिलकुल नहीं
- बहुत ज़्यादा
- बहुत
- थोड़ा
- बिलकुल नहीं

कृपया देख लें कि आपने हर प्रश्न का उत्तर दे दिया है। धन्यवाद।

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3) கடந்த ஒரு வாரத்தில் உங்கள் குழந்தையின் சருமம் நெகிழ்வா பரிகரித்தது?

- மிகவும் அதிகம்
- அதிகம்
- சிறிது
- ஒன்றும்மில்லை

4) கடந்த ஒரு வாரத்தில் உங்கள் குழந்தையின் சருமத்தில் சுவர் சருமம் எவ்வளவு அதிகமாகம் விளங்கியது?

- மிகவும் அதிகம்
- அதிகம்
- சிறிது
- ஒன்றும்மில்லை

5) கடந்த ஒரு வாரத்தில் உங்கள் குழந்தையின் விண்ணாய்வு சருமம் எவ்வளவு பரிகரித்தது?

- மிகவும் அதிகம்
- அதிகம்
- சிறிது
- ஒன்றும்மில்லை

6) கடந்த வாரத்தில் உங்கள் குழந்தையின் சருமம், நீச்சல் மற்றும் டிரைவிங் விளையாட்டுகளை சருமம் பரிகரித்தது?

- மிகவும் அதிகம்
- அதிகம்

- சிறிது
- ஒன்றாயில்லை

7) கடிந்த வாரத்தில் உங்கள் குழந்தையின் சருமம் சிறிது மீட்டர் அளவுக்கு எவ்வளவு மாற்றம்?

- மிகவும் அதிகம்
- அதிகம்
- சிறிது
- ஒன்றாயில்லை

8) கடிந்த வாரத்தில் உங்கள் குழந்தையின் சருமத்தின் காரணமாக உங்கள் குழந்தையை கிண்டல் செய்யும் தனிப்பட்டவருக்கு நிகழ்ந்ததா?

- மிகவும் அதிகம்
- அதிகம்
- சிறிது
- ஒன்றாயில்லை

9) கடிந்த வாரத்தில் உங்கள் குழந்தையின் சருமம் சிறிது குறைந்ததை எவ்வளவு மாற்றம்?

- மிகவும் அதிகம்
- அதிகம்
- சிறிது
- ஒன்றாயில்லை

1) கட்டிட வாய்ப்பில், உங்கள் படுமருள்  
சிகிச்சை எவ்வளவு சிறந்ததை அளிக்க?

- மிகவும் சிறந்த
- சிறந்த
- சிறந்த
- சீர்தரமற்றவை

எல்லா கேள்விகளுக்கும் விடையளிப்பீர்களா  
என்று சீர்பார்க்கும் வகையிலும்

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শিশুর চর্মরোগে সুস্থতা ও জীবনের মানের সূচক

হাসপাতাল নং :  
নাম :  
বয়স :  
ঠিকানা :

বোগ :  
তারিখ :

CDLQL score : \_\_\_\_\_

এই প্রশ্ন সমূহের উদ্দেশ্য হলো চর্ম সমস্যা বিগত এক সপ্তাহে আপনার ( শিশুর ) জীবনকে কতটা প্রভাবিত করেছে তা নির্ণয় করা । প্রত্যেকটি প্রশ্নের যে কোনো একটি অপশনের পাশের বাক্সে টিক - চিহ্ন দিন ।

1.	বিগত সপ্তাহে আপনার স্বকে কতটা চুলকানি , চুলকানি ডাব , ব্যাথা বা জ্বালা হয়েছে ?	খুব বেশি বেশি অল্প একদম নয়	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
2.	বিগত সপ্তাহে আপনি আপনার স্বকের কারণে কতটা বিরত, আত্মসচেতন , মর্মান্বিত বা দুঃখিত হয়েছেন ?	খুব বেশি বেশি অল্প একদম নয়	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
3.	বিগত এক সপ্তাহে আপনার স্বকের কারণে আপনার নিকট বন্ধু বাস্বব বা আত্মীয়স্বজনের কাছে আপনার কতটা অসুবিধে হয়েছে বা আপনাদের সম্পর্কের ওপর এর কতটা কু প্রভাব পড়েছে ?	খুব বেশি বেশি অল্প একদম নয়	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
4.	বিগত সপ্তাহে আপনার স্বক আপনার পোশাক-আশাকে কতটা বদল এনেছে বা কতটা প্রভাব ফেলেছে ?	খুব বেশি বেশি অল্প একদম নয়	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
5.	বিগত সপ্তাহে আপনার স্বক আপনার খেলাধুলা বা অবসর এর শেখের কাজকর্মে কতটা বাধা দিয়েছে ?	খুব বেশি বেশি অল্প একদম নয়	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
6.	বিগত সপ্তাহে আপনার চর্মরোগের কারণে আপনি সাঁতার বা অন্যান্য বাইরের খেলাধুলা কতটা এড়িয়ে গেছেন ?	খুব বেশি বেশি অল্প একদম নয়	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
7.	বিগত সপ্তাহে : - আপনার কি স্কুল চলছিল - তাহলে বিগত এক সপ্তাহে আপনার স্কুলের কাজে আপনার চর্মরোগ কতটা অসুবিধে সৃষ্টি করেছে ? <u>নাকি</u> - আপনার স্কুলে ছুটি ছিল - তাহলে বিগত এক সপ্তাহে আপনার ছুটিতে আনন্দ করার ক্ষেত্রে আপনার চর্মরোগ কতটা অসুবিধে সৃষ্টি করেছে ?	খুব বেশি বেশি অল্প একদম নয়  খুব বেশি বেশি অল্প একদম নয়	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>  <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>

8.	বিগত সপ্তাহে আপনার কতটা অসুবিধে হয়েছে যেখানে আপনার স্বকের কারণে লোকে আপনাকে উত্যক্ত করেছে বা উল্টোপাল্টা নাম দিয়ে ডেকেছে বা এই নিয়ে আপনাকে প্রশ্ন করেছে বা আপনাকে এই কারণে এড়িয়ে চলেছে ?	খুব বেশি বেশি অল্প একদম নয়	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
9.	বিগত সপ্তাহে আপনার স্বকের কারণে আপনার ঘুমোনার ক্ষেত্রে কতটা ব্যাঘাত পড়েছে ?	খুব বেশি বেশি অল্প একদম নয়	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
10.	বিগত সপ্তাহে আপনার চর্মরোগের চিকিৎসা নিয়ে আপনার কতটা অসুবিধে হয়েছে ?	খুব বেশি বেশি অল্প একদম নয়	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>

অনুগ্রহ করে একটিও বাদ না দিয়ে প্রত্যেকটি প্রশ্নের সঠিক উত্তর দিন। ধন্যবাদ।

**INFANTS' DERMATITIS QUALITY OF LIFE INDEX (IDQOL)**

Name:  
Address:

Date:

IDQOL  
SCORE

**The aim of this chart is to record how your child's dermatitis has been. Each question concerns THE LAST WEEK ONLY. Please could you answer every question.**

**Dermatitis Severity**

Over the last week, **how severe** do you think your child's dermatitis has been?; i.e. how red, scaly, inflamed or widespread.

- Extremely severe
- Severe
- Average
- Fairly good
- None

**Life Quality Index**

1. Over the last week, how much has your child been **itching and scratching**?
  - All the time
  - A lot
  - A little
  - None
  
2. Over the last week, what has your child's **mood** been?
  - Always crying, extremely difficult
  - Very fretful
  - Slightly fretful
  - Happy
  
3. Over the last week approximately how much **time** on average has it taken **to get your child off to sleep** each night?
  - More than 2 hrs
  - 1 - 2 hrs
  - 15mins - 1 hr
  - 0-15mins
  
4. Over the last week, what was the **total time** that your child's **sleep was disturbed** on average each night?
  - 5 hrs or more
  - 3 - 4 hrs
  - 1 - 2 hrs
  - Less than 1 hour
  
5. Over the last week, has your child's eczema interfered with **playing or swimming**?
  - Very much
  - A lot
  - A little
  - Not at all
  
6. Over the last week, has your child's eczema interfered with your child **taking part in or enjoying other family activities**?
  - Very much
  - A lot
  - A little
  - Not at all
  
7. Over the last week, have there been problems with your child at **mealtimes** because of the eczema?
  - Very much
  - A lot
  - A little
  - None
  
8. Over the last week, have there been problems with your child caused by the **treatment**?
  - Very much
  - A lot
  - A little
  - None
  
9. Over the last week, has your child's eczema meant that **dressing and undressing** the child has been **uncomfortable**?
  - Very much
  - A lot
  - A little
  - None
  
10. Over the last week how much has your child having eczema been a problem at **bathtime**?
  - Very much
  - A lot
  - A little
  - None

**Please can you check that you have answered every question.**

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## शिशु त्वचारोग जीवन गुणवत्ता सूची

हॉस्पिटल क्रमांक:

नाम :

रोग निदान:

आईडीक्यूओलएल स्कोर

उम्र:

दिनांक:

पता:

इस प्रश्नोत्तरी का उद्देश्य यह नापना है कि आपके शिशु की त्वचा की परेशानी ने गत सप्ताह में कितना प्रभाव डाला है। कृपया हर प्रश्न के लिए एक बॉक्स पर टिक करें।

### डर्मेटाइटिस की गहनता

- |   |             |                          |
|---|-------------|--------------------------|
| गत सप्ताह आपके अनुसार आपके शिशु की त्वचा की बीमारी कितनी गंभीर थी? जैसे, कितना लालपन, चमड़ा निकलना, सूजन या फैला हुआ? | बहुत ज्यादा | <input type="checkbox"/> |
|   | ज्यादा      | <input type="checkbox"/> |
|   | मध्यम       | <input type="checkbox"/> |
|   | काफ़ी अच्छा | <input type="checkbox"/> |
|   | बिलकुल नहीं | <input type="checkbox"/> |

### जीवन की गुणवत्ता सूचकांक

- गत सप्ताह, आपका शिशु कितनी खुजि कर रहा/रही है?

हर समय	<input type="checkbox"/>
बहुत	<input type="checkbox"/>
थोड़ा	<input type="checkbox"/>
बिलकुल नहीं	<input type="checkbox"/>
- गत सप्ताह, आपका शिशु की मनोदशा कैसी है?

हमेशा रो रहा/रही है,	<input type="checkbox"/>
बहुत ही मुश्किल	<input type="checkbox"/>
बहुत चिड़चिड़ा	<input type="checkbox"/>
थोड़ा चिड़चिड़ा	<input type="checkbox"/>
खुश	<input type="checkbox"/>
- गत सप्ताह, आपका शिशु को सुलाने में लगभग कितना समय लगा?

२ घंटे से ज्यादा	<input type="checkbox"/>
१-२ घंटे	<input type="checkbox"/>
१५ मिनट-१ घंटा	<input type="checkbox"/>
० -१५ मिनट	<input type="checkbox"/>
- गत सप्ताह, हर रात लगभग कितनी देर आपके शिशु की नींद खराब हुई?

५ घंटे या ज्यादा	<input type="checkbox"/>
३-४ घंटे	<input type="checkbox"/>
१-२ घंटे	<input type="checkbox"/>
१ घंटे से कम	<input type="checkbox"/>
- गत सप्ताह, क्या त्वचा की बीमारी के कारण आपके बच्चे के खेलने या तैराकी पर प्रभाव पड़ा?

बहुत ज्यादा	<input type="checkbox"/>
बहुत	<input type="checkbox"/>
थोड़ा	<input type="checkbox"/>
बिलकुल नहीं	<input type="checkbox"/>
- गत सप्ताह, क्या त्वचा की बीमारी के कारण आपके बच्चे के अन्य पारिवारिक कार्यक्रमों में भाग लेने पर प्रभाव पड़ा?

बहुत ज्यादा	<input type="checkbox"/>
बहुत	<input type="checkbox"/>
थोड़ा	<input type="checkbox"/>
बिलकुल नहीं	<input type="checkbox"/>
- गत सप्ताह, क्या त्वचा की बीमारी के कारण आपके बच्चे के भोजन पर प्रभाव पड़ा?

बहुत ज्यादा	<input type="checkbox"/>
बहुत	<input type="checkbox"/>

- |     |  |              |                          |
|-----|--|--------------|--------------------------|
|     |  | थोड़ा        | <input type="checkbox"/> |
|     |  | बिलकुल नहीं  | <input type="checkbox"/> |
| 8.  | गत सप्ताह, क्या त्वचा की बीमारी के उपचार के कारण कुछ मुश्किलें आईं?                        | बहुत ज़्यादा | <input type="checkbox"/> |
|     |  | बहुत         | <input type="checkbox"/> |
|     |  | थोड़ा        | <input type="checkbox"/> |
|     |  | बिलकुल नहीं  | <input type="checkbox"/> |
| 9.  | गत सप्ताह, क्या त्वचा की बीमारी के कारण बच्चे को कपड़े पहनाने या उतारने में मुश्किलें आईं? | बहुत ज़्यादा | <input type="checkbox"/> |
|     |  | बहुत         | <input type="checkbox"/> |
|     |  | थोड़ा        | <input type="checkbox"/> |
|     |  | बिलकुल नहीं  | <input type="checkbox"/> |
| 10. | गत सप्ताह, त्वचा की बीमारी के कारण बच्चे को नहलाने में कितनी मुश्किलें आईं?                | बहुत ज़्यादा | <input type="checkbox"/> |
|     |  | बहुत         | <input type="checkbox"/> |
|     |  | थोड़ा        | <input type="checkbox"/> |
|     |  | बिलकुल नहीं  | <input type="checkbox"/> |

कृपया देख लें कि आपने हर प्रश्न का उत्तर दे दिया है। धन्यवाद।  
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**குழந்தைகள் சரும வாழ்வுத் தரம் அட்டவணை**

மருத்துவமனை எண்:

பெயர்:

வயது:

முகவரி:

தெதி:

நோய்:

**மதிப்பெண்:**

இந்த கேள்வித்தாளின் குறிக்கோள் உங்கள் குழந்தையின் சரும நோய் உங்கள் குழந்தையின் வாழ்க்கையை கடந்த வாரத்தில் எந்த அளவிற்கு பாதித்துள்ளது என்பதை அளவிடுவதாகும். ஒவ்வொரு கேள்விக்கும் ஒவ்வொரு கட்டத்தை கண்டிப்பாகத் தேர்வு செய்யவும்.

**டெர்மடைடிஸ் தீவிரம்:**

கடந்த வாரத்தில் உங்கள் குழந்தையின் டெர்மடைடிஸ்

வெகு தீவிரமாக

எவ்வளவு தீவிரமாக இருந்தது

மிக தீவிரமாக

சாதாரணமாக

குறைவாக

இல்லவே

இல்லை

**வாழ்க்கை தர அட்டவணை:**

கடந்த வாரத்தில் உங்கள் குழந்தை எவ்வளவு

நீண்ட நேரம்

நேரம் அரிப்பாலும் சொறியாலும் வேதனை பட்டான்

குறைந்த நேரம்

அரிக்கவே இல்லை

இல்லவே இல்லை

கடந்த வாரத்தில் உங்கள்

எப்போதும் அழுதுகொண்டே இருந்தான்

குழந்தை எப்படி இருந்தான்

சண்டை போட்டுக்கொண்டே

இருந்தான்

மிகவும் வருந்திக்கொண்டே

இருந்தான்

சிறிது நேரம் வருந்திக்கொண்டு

இருந்தான்

மகிழ்ச்சியாக இருந்தான்

கடந்த வாரத்தில் குழந்தையை தூங்க

மணி நேரத்துக்கு மேல்

வைக்க எவ்வளவு நேரம் ஆனது

மணி நேரங்கள்

நிமிடங்களிலிருந்து மணி

நேரம்

நிமிடங்கள் வரை

கடந்த வாரத்தில் உங்கள் குழந்தையின் தூக்கம்  
எவ்வளவு நேரம் பாதிக்கப்பட்டிருந்தது

மணி நேரம்  
மணி நேரம்  
மணி நேரம்

ஒரு மணி

நேரத்திற்கும் கீழ்  
கடந்த வாரத்தில் உங்கள் குழந்தை விளையாடுவதோ  
அளவில்  
நீந்துவதோ நோயினால் பாதிக்கப்பட்டுள்ளதா

மிகுந்த

ரொம்ப

குறைந்த அளவில்

இல்லவே இல்லை

கடந்த வாரத்தில் உங்கள் குழந்தை குடும்ப நிகழ்வுகளில்  
அளவில் பங்குபெறுதல் பாதிக்கப்பட்டுள்ளதா  
ரொம்ப

மிகுந்த

குறைந்த அளவில்

இல்லவே இல்லை  
மிகுந்த அளவில்  
ரொம்ப

கடந்த வாரத்தில் உங்கள் குழந்தை உணவு உண்பது  
நோயினால் பாதிக்கப்பட்டுள்ளதா

குறைந்த அளவில்

இல்லவே இல்லை

கடந்த வாரத்தில் நோய் சிகிச்சையின் காரணத்தால்  
குழந்தைக்கு ஏதேனும் கஷ்டம் உண்டாகியிருந்ததா  
ரொம்ப

மிகுந்த அளவில்

குறைந்த அளவில்

இல்லவே இல்லை

கடந்த வாரத்தில் குழந்தையின் நோய் காரணமாக மிகுந்த  
அளவில் துணி போடுவதும் களற்றுவதும் சிரமமாக  
இருந்ததா ரொம்ப குறைந்த அளவில்

இல்லவே இல்லை  
கடந்த வாரத்தில் உங்கள் குழந்தையின் நோய் மிகுந்த  
அளவில் குளிப்பதற்கு சிரமம் கொடுத்ததா  
ரொம்ப குறைந்த அளவில்

இல்லை இல்லவே  
மீண்டும் ஒரு முறை அனைத்து கேள்விகளுக்கும் பதில் அளித்துள்ளோமா  
என்பதை சரிபார்த்துக் கொள்ளவும்.

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নবজাতকের / 12 মাসের কম বয়সী বাচ্চার চর্মরোগে সঙ্গতি ও জীবনের মানের সূচক (IDLQOL)

হাসপাতাল নং: \_\_\_\_\_ IDLQOL score \_\_\_\_\_

নাম : \_\_\_\_\_ তারিখ : \_\_\_\_\_

বয়স : \_\_\_\_\_

ঠিকানা : \_\_\_\_\_

এই প্রশ্ন সমূহের উদ্দেশ্য হলো বৃকের সমস্যা বিগত এক সপ্তাহে আপনার শিশুর জীবনকে কতটা প্রভাবিত করেছে তা নির্ণয় করা। প্রত্যেকটি প্রশ্নের যে কোনো একটি অপশনের পাশের বাক্সে টিক - চিহ্ন দিন।

চর্মরোগের বাড়াবাড়ির মাত্রা / প্রকোপ

বিগত এক সপ্তাহে আপনার বাচ্চার বৃকের সমস্যার বাড়াবাড়ি র সম্পর্কে আপনার কি ধারণা - যেমন, কতটা লাল, কতটা আঁশ জাতীয় চামড়া, কতটা ফুলেছে, বা কতটা ছড়িয়েছে?	খুব বেশি বাড়াবাড়ি বেশ বাড়াবাড়ি মাঝামাঝি বা গড়পড়তা অল্প একদম নয়	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
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জীবনের মানের সূচক

1.	বিগত সপ্তাহে আপনার বাচ্চা নিজের বৃক কতটা চুলকিয়েছে বা আঁচড়েছে?	সবসময় ঘনঘন মাঝে-মাঝে একদম নয়	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
2.	বিগত সপ্তাহে আপনার বাচ্চার মেজাজ / শ্ভাব কেমন ছিল?	একনাগাড়ে কাঁদে বা জ্বলাতন করছে সামলানো মুশকিল, মাঝে মাঝেই কাঁদে বেশ খিটেখিটে খানিকটা খিটেখিটে হাসিখুশি	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
3.	বিগত সপ্তাহে আপনার বাচ্চাকে বোজ ঘুম পাড়াতে গড়ে আপনার কতক্ষন সময় লেগেছে?	2 ঘণ্টার বেশি 1 - 2 ঘণ্টা 15 মিনিট - 1 ঘণ্টা 0 - 15 মিনিট	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>

4.	বিগত সপ্তাহে আপনার বাচ্চার প্রত্যেক রাতে মোট কতটা সময় ঘুমে ব্যাঘাত ঘটেছে এই সময়সূচীর ফলে ?	5 ঘণ্টা বা তার বেশি 3 - 4 ঘণ্টা 1 - 2 ঘণ্টা 1 ঘণ্টা র থেকে কম	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
5.	বিগত সপ্তাহে আপনার বাচ্চার খেলায় বা স্নাঁতের এই চর্মরোগ কতটা সমস্যার সৃষ্টি করেছে ?	খুব বেশি সময়ে প্রায় সময়ে অল্পসল্প একদম না	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
6.	বিগত সপ্তাহে পরিবারের অন্যান্য কাজকর্মে অংশগ্রহণ করতে বা আনন্দ করার ক্ষেত্রে আপনার বাচ্চার কোনোরকম সমস্যা হয়েছে ?	খুব বেশি সময়ে প্রায় সময়ে অল্পসল্প একদম না	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
7.	বিগত সপ্তাহে আপনার বাচ্চার খাওয়াদাওয়ার সময়ে কি এই চর্মরোগের ফলে কোনো সমস্যার সৃষ্টি হয়েছে ?	খুব বেশি সময়ে প্রায় সময়ে অল্পসল্প একদম না	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
8.	বিগত সপ্তাহে এই চর্মরোগের চিকিৎসার ওষুধ সংক্রান্ত কোনো পার্শ্বপ্রতিক্রিয়া বা চিকিৎসা সংক্রান্ত অন্যরকম অসুবিধে কি আপনার বাচ্চার হয়েছে ?	খুব বেশি সময়ে প্রায় সময়ে অল্পসল্প একদম না	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
9.	বিগত সপ্তাহে আপনার বাচ্চাকে এই চর্মরোগের কারণে জামাকাপড় পরাতে বা খোলাতে কি আপনার কোনো অসুস্থি বা অস্বাচ্ছন্দ বোধ হয়েছে ?	খুব বেশি সময়ে প্রায় সময়ে অল্পসল্প একদম না	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
10.	বিগত সপ্তাহে আপনার বাচ্চার স্নান করানোর সময়ে এই চর্মরোগের ফলে কতটা সমস্যা হয়েছে ?	খুব বেশি সময়ে প্রায় সময়ে অল্পসল্প একদম না	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>

অনুগ্রহ করে যাঁচাই করে নিন যে আপনি প্রত্যেকটি প্রশ্নের উত্তর দিয়েছেন, একটিও বাদ না দিয়ে। ধন্যবাদ।

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## ANNEXURE-6: IRB APPROVAL



OFFICE OF RESEARCH  
INSTITUTIONAL REVIEW BOARD (IRB)  
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

**Dr. B.J. Prashantham**, M.A., M.A., Dr. Min (Clinical)  
Director, Christian Counseling Center,  
Chairperson, Ethics Committee.

**Dr. Anna Benjamin Pulimood**, M.B.B.S., MD., Ph.D.,  
Chairperson, Research Committee & Principal

**Dr. Biju George**, M.B.B.S., MD., DM.,  
Deputy Chairperson,  
Secretary, Ethics Committee, IRB  
Additional Vice-Principal (Research)

December 08, 2016

Dr. Himadri,  
PG Registrar,  
Department of Dermatology,  
Christian Medical College,  
Vellore - 632 004.

Sub: **Fluid Research Grant NEW PROPOSAL:**

To study the efficacy of thymus and activation-regulated chemokine (TARC) as a diagnostic marker of atopic dermatitis and its association with the severity of the disease in the pediatric age group in the Indian context.

Himadri, Employment number: 29564, Postgraduate registrar, Dermatology, Venereology and Leprosy, Dr. Renu George, Employment Number: 02505, Dermatology, Venereology and Leprosy, Dr. Lydia Mathew, Employment number: 28785, Dermatology, Venereology & Leprosy, Dr. Victoria Job, Employment number: 08517, Clinical biochemistry, Ms. Vanitha S, Employment number: 31528, Clinical Biochemistry, Dr. Visalakshi, Employment number: 31093, Biostatistics.

Ref: IRB Min No: 10320 [DIAGNO] dated 12.10.2016

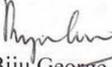
Dear Dr. Himadri,

I enclose the following documents:-

1. Institutional Review Board approval
2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

  
Dr. Biju George  
Secretary (Ethics Committee)  
Institutional Review Board

**Dr. BIJU GEORGE**  
MBBS, MD, DM  
SECRETARY - (ETHICS COMMITTEE)  
Institutional Review Board,  
Christian Medical College, Vellore - 632 002.

Cc: Dr. Renu George, Dept. of Dermatology, CMC, Vellore

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OFFICE OF RESEARCH  
INSTITUTIONAL REVIEW BOARD (IRB)  
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

**Dr. B.J. Prashantham**, M.A., M.A., Dr. Min (Clinical)  
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Chairperson, Ethics Committee.

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Ref: IRB Min No: 10320 [DIAGNO] dated 12.10.2016

Dear Dr. Himadri,  
The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "To study the efficacy of thymus and activation-regulated chemokine (TARC) as a diagnostic marker of atopic dermatitis and its association with the severity of the disease in the pediatric age group in the Indian context" on October 12<sup>th</sup> 2016.

The Committee reviewed the following documents:

1. IRB Application format
2. Patient information sheets and Consent forms (English, Tamil, Hindi, Bengali, Malayalam)
3. Cv's of Drs. Lydia Mathew, renu George, Visalakshi, victoria, Himadri, Vanitha.
4. No. of documents 1 - 3.

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on October 12<sup>th</sup> 2016 in the BRTC Conference Room, Christian Medical College, Bagayam, Vellore 632002.

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**OFFICE OF RESEARCH  
INSTITUTIONAL REVIEW BOARD (IRB)  
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA**

**Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)**  
Director, Christian Counseling Center,  
Chairperson, Ethics Committee.

**Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.**  
Chairperson, Research Committee & Principal

**Dr. Biju George, M.B.B.S., MD., DM.,**  
Deputy Chairperson,  
Secretary, Ethics Committee, IRB  
Additional Vice-Principal (Research)

Name	Qualification	Designation	Affiliation
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician
Dr. B. J. Prashantham	MA(Counseling Psychology), MA (Theology), Dr. Min (Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centre, Vellore	External, Social Scientist
Dr. Ratna Prabha	MBBS, MD (Pharma)	Associate Professor, Clinical Pharmacology, CMC, Vellore	Internal, Pharmacologist
Dr. Rekha Pai	BSc, MSc, PhD	Associate Professor, Pathology, CMC, Vellore	Internal, Basic Medical Scientist
Rev. Joseph Devaraj	BSc, BD	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert
Dr. Santhanam Sridhar	MBBS, DCH, DNB	Professor, Neonatology, CMC, Vellore	Internal, Clinician
Mrs. Sheela Durai	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Ms. Grace Rebekha	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person
Dr. Vivek Mathew	MD (Gen. Med.) DM (Neuro) Dip. NB (Neuro)	Professor, Neurology, CMC, Vellore	Internal, Clinician
Dr. Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Pulmonary Medicine, CMC, Vellore	Internal, Clinician

IRB Min No: 10320 [DIAGNO] dated 12.10.2016

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**OFFICE OF RESEARCH  
INSTITUTIONAL REVIEW BOARD (IRB)  
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA**

**Dr. B.J. Prashantham, M.A., M.A., Dr. MSc (Clinical)**  
Director, Christian Counseling Center,  
Chairperson, Ethics Committee.

**Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,**  
Chairperson, Research Committee & Principal

**Dr. Biju George, M.B.B.S., MD., DM.,**  
Deputy Chairperson,  
Secretary, Ethics Committee, IRB  
Additional Vice-Principal (Research)

Dr. Sneha Varkki	MBBS, DCH, DNB	Professor, Paediatrics, CMC, Vellore	Internal, Clinician
Mrs. Emily Daniel	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Dr. Sathish Kumar	MBBS, MD, DCH	Professor, Child Health, CMC, Vellore	Internal, Clinician
Dr. Inian Samarasam	MS, FRCS, FRACS	Professor, Surgery, CMC, Vellore	Internal, Clinician
Dr. Thomas V Paul	MBBS, MD, DNB, PhD	Professor, Endocrinology, CMC, Vellore	Internal, Clinician

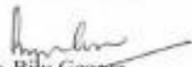
We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "To study the efficacy of thymus and activation-regulated chemokine (TARC) as a diagnostic marker of atopic dermatitis and its association with the severity of the disease in the pediatric age group in the Indian context" on a monthly basis. Please send copies of this to the Research Office ([research@cmcvellore.ac.in](mailto:research@cmcvellore.ac.in)).

Fluid Grant Allocation:

*A sum of 92,670/- INR (Rupees Ninety two thousand six hundred and seventy Only) will be granted for 2 years. 50,000/- INR (Rupees Fifty Thousand only) will be granted for 12 months as an 1st Installment. The rest of the 42,670/- INR (Rupees Forty Two Thousand six hundred and seventy only) will be released at the end of the first year as 2nd installment.*

Yours sincerely,

  
Dr. Biju George  
Secretary (Ethics Committee)  
Institutional Review Board

**Dr. BIJU GEORGE**  
MBBS, MD., DM.  
SECRETARY - (ETHICS COMMITTEE)  
Institutional Review Board,  
Christian Medical College, Vellore - 632 002.

IRB Min No: 10320 [DIAGNO] dated 12.10.2016

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## ANNEXURE-7 : CODES TO MASTER CHART

sno	serial number	<IDNUM>		
name	name			
hospsno	hospital number			
age	age	##.##		
sex	sex	# 1 male 2 female		
add	address	# 1 Tamil Nadu 2 Kerala 3 Karnataka 4 Andhar Pradesh/Telangana 5 West Bengal 6 Bangladesh 7 Bihar 8 Jharkhand 9 Others		
add7	if other places, specify			
diag	diagnosis	# 1 atopic dermatitis 2 seborrheic dermatitis		
3 contact dermatitis	4 candidiasis	5 scabies	6 impetigo	7 psoriasis
AD	atopic dermatitis	# 1 yes 2 no		
delmod	mode of delivery	# 1 vaginal 2 Caesarean		
bo	birth order	#		
ebf	duration of exclusive breastfeeding	##.#		
onsetage	age of onset	###.##		
site of onset				
fc	face	# 1 yes 2 no		
nk	neck	# 1 yes 2 no		
ulf	upperlimb flexor	# 1 yes 2 no		
ule	upperlimb extensor	# 1 yes 2 no		
llf	lowerlimb flexor	# 1 yes 2 no		
lle	lowerlimb extensor	# 1 yes 2 no		
tk	trunk	# 1 yes 2 no		
sp	scalp	# 1 yes 2 no		
muc	mucosa	# 1 yes 2 no		
sites involved				
face	face	# 1 yes 2 no		
neck	neck	# 1 yes 2 no		
ulfl	upperlimb flexor	# 1 yes 2 no		
ulex	upperlimb extensor	# 1 yes 2 no		
LLfl	lowerlimb flexor	# 1 yes 2 no		
LLex	lowerlimb extensor	# 1 yes 2 no		
trunk	trunk	# 1 yes 2 no		
scalp	scalp	# 1 yes 2 no		
mucosa	mucosa	# 1 yes 2 no		
nails	nails	# 1 yes 2 no		
hair	hair	# 1 yes 2 no		
dryskin	dry skin	# 1 yes 2 no		
seasonvar	seasonal variation	# 1 yes 2 no		
win	winter	# 1 yes 2 no		
sum	summer	# 1 yes 2 no		
rain	rainy	# 1 yes 2 no		
aut	autumn	# 1 yes 2 no		
spr	spring	# 1 yes 2 no		
freq	number of exacerbations per year	##		
atopy	personal history of atopy	# 1 yes 2 no		
BA	asthma	# 1 yes 2 no		
AR	allergic rhinitis	# 1 yes 2 no		
AC	allergic conjunctivitis	# 1 yes 2 no		
Triggers				
stress		# 1 yes 2 no		
skininf	skin infections	# 1 yes 2 no		
food	food allergens	# 1 yes 2 no		
air	airborne allergens	# 1 yes 2 no		
sweat	sweating	# 1 yes 2 no		
heat	excessive sweating	# 1 yes 2 no		
winter	winter	# 1 yes 2 no		

wool	wool clothing	# 1	yes	2	no
irritants	irritants	# 1	yes	2	no
scratch	habitual scratching	# 1	yes	2	no
others	miscellaneous	# 1	yes	2	no
ifothers	if others yes	_____			
relief	relieving factors	_____			
expet	exposure to pets	# 1	yes	2	no
dog	exposure to dogs	# 1	yes	2	no
cat	exposure to cats	# 1	yes	2	no
petoth	other pets	# 1	yes	2	no
pettype	if other pets, specify	_____			
sleep	sleep disturbance	# 1	yes	2	no
behave	behavioural changes	# 1	yes	2	no
complications					
inf	skin infection	# 1	yes	2	no
inf_freq	single or recurrent infection	# 1	single	2	recurrent
bact	bacterial	# 1	yes	2	no
pus	documented pus culture	# 1	yes	2	no
pusorg	if pus culture done, organism	_____			
eczher	eczema herpeticum	# 1	yes	2	no
eczvac	eczema vaccinatum	# 1	yes	2	no
sysinf	systemic infections	# 1	yes	2	no
bacteremia	bacteremia	# 1	yes	2	no
respi	respiratory	# 1	yes	2	no
misc	others	# 1	yes	2	no
ifmisc	if others, yes	_____			
Treatment					
nonderm	non dermatological	_____			
derm	dermatological	# 1	yes	2	no
emol	emollients	# 1	yes	2	no
topster	topical steroids	# 1	yes	2	no
topcalinh	topical calcineurin inhibitors	# 1	yes	2	no
antihis	antihistamines used	# 1	yes	2	no
sysster	systemic steroids	# 1	yes	2	no
antibiot	antibiotics used	# 1	yes	2	no
cyclospo	cyclosporine used	# 1	yes	2	no
azathio	azathioprine used	# 1	yes	2	no
mtx	methotrexate used	# 1	yes	2	no
photo	phototherapy used	# 1	yes	2	no
bio	biologicals used	# 1	yes	2	no
oth	other treatment used	# 1	yes	2	no
othwhat	if other therapy used, specify	_____			
famatopy	family history of atopy	# 1	yes	2	no
fam_BA	family history of asthma	# 1	yes	2	no
fam_BAdeg	degree of relative with asthma	#			
fam_AR	family history of allergic rhinitis	# 1	yes	2	no
fam_ARdeg	degree of relative with allergic rhinitis	#			
fam_AC	family history of allergic conjunctivitis	# 1	yes	2	no
fam_ACdeg	degree of relative with allergic conjunctivitis	#			
EXAMINATION					
htcent	height in centile	###.#			
wtcent	weight in centile	###.#			
cerLN	cervical lymphadenopathy	# 1	yes	2	no
axLN	axillary lymphadenopathy	# 1	yes	2	no
ingLN	inguinal lymphadenopathy	# 1	yes	2	no
kerconj	keratoconjunctivitis	# 1	yes	2	no
kerconus	keratoconus	# 1	yes	2	no
cataract	cataract	# 1	yes	2	no
ophmisc	others ophthal findings	_____			
denmor	dennie morgan folds	# 1	yes	2	no
eczema	eczema	# 1	yes	2	no
face_E	eczema on face	# 1	yes	2	no
neck_E	eczema on neck	# 1	yes	2	no
ulflc_E	eczema on cubital fossa	# 1	yes	2	no

ulfla_E	eczema on axilla	# 1	yes	2	no
ulexy_E	eczema on extensor aspect of upper limbs	# 1	yes	2	no
llfly_E	eczema on flexor aspect of lower limbs	# 1	yes	2	no
llex_E	eczema of extensor aspect of lower limbs	# 1	yes	2	no
trunky_E	eczema on trunk	# 1	yes	2	no
lichen	lichenification seen	# 1	yes	2	no
facey	face	# 1	yes	2	no
necky	lichenification on neck	# 1	yes	2	no
ulflc	upperlimb flexor cubital fossa	# 1	yes	2	no
ulfla	upperlimb flexor axillae	# 1	yes	2	no
ULexy	upperlimb extensor	# 1	yes	2	no
LLfly	lowerlimb flexor popliteal fossa	# 1	yes	2	no
LLeXy	lowerlimb extensor	# 1	yes	2	no
trunky	lichenification on trunk	# 1	yes	2	no

other sites involved

scalpy	scalp	# 1	yes	2	no
mucosay	mucosa	# 1	yes	2	no
nailsy	nails	# 1	yes	2	no
hairy	hair	# 1	yes	2	no

prurigo	prurigo	# 1	yes	2	no
pr_site	sites with prurigo lesions	_____			
psor	psoriasiform	# 1	yes	2	no
psor_site	sites with psoriasiform lesions	_____			
excor	excoriation	# 1	yes	2	no
xeros	xerosis	# 1	yes	2	no
secinf	secondary infections	# 1	yes	2	no
pusexam	organism on pus culture	_____			
kp	keratosis pilaris	# 1	yes	2	no
palmhyper	palmar hyperlinearity	# 1	yes	2	no
iv	ichthyosis vulgaris	# 1	yes	2	no
examother	other skin lesions	_____			

SCORobj	Objective SCORAD	##.#
SCORsub	Subjective SCORAD	##.#
TIS	SCORAD index	##.#

Investigations:

TARC	TARC in pg/ml	####.##			
eos	Eosinophils in %	##			
LDH	LDH in units/L	####			
IgE	IgE in units/ml	#####.#			
vitD	Vitamin D in ng/mL	##.#			
ns_cul	Nasal culture done	# 1	yes	2	no
ns_org	Organism on nasal culture	_____			
immunoblot	Atopy immunoblot done	# 1	yes	2	no
food_imm	Positive to food on immunoblot	_____			
foodname	Name of food to which strongly positive	_____			
foodweak	Name of food to which weakly positive	_____			
dustmite	Positive immunoblot to dust mite	# 1	yes	2	no
otherimmuno	Any other agents with positive immunoblot	_____			

IDQOL4	AD child upto 4 years	# 1	yes	2	no
IDQOL	total IDQOL score	##			
dermsever	dermatitis severity score	#			
CDLQI	total CDLQI score	##			

N.A. Not applicable











	EC	ED	EE	EF	EG	EH	EI	EJ	EK	EL	EM	EN	EO	EP	EQ	ER
1	P_sor_spr_site															
2	2.0		EXCOR	XEROS	SECINF	Pse exam	KP	PALM/TYPE	IV	EXAMOTHER	SCOROBJ	SCORSUB	TIS	TARC	EOS	LDT
3	2.0		2.0	2.0	1.0		2.0	1.0	2.0		34.9	7	41.90	519	3	443
4	2.0		2.0	1.0	2.0		2.0	1.0	2.0		7.4	4	11.40	518	7	686
5	2.0		2.0	1.0	2.0		2.0	2.0	2.0	PAPULES: THIGHS, LEGS	16.6	5	21.60	2,155	10	713
6	2.0		1.0	1.0	1.0	MRSA	1.0	1.0	2.0		65.0	18	61.00	1,982	15	795
7	1.0	UL-EXT, LL-EXT	1.0	1.0	2.0		1.0	2.0	2.0	2.0	2.0	17	43.50	894	18	500
8	2.0		2.0	1.0	2.0		2.0	2.0	2.0		14.5	2	16.50	1,061	10	773
9	2.0		2.0	1.0	2.0		2.0	1.0	2.0		10.9	2	12.90	952	5	621
10	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	47.6	13	60.80	2,500	16	1,110
11	2.0		1.0	1.0	1.0	STAPH AUREUS, NFOHB	2.0	2.0	2.0	2.0	66.8	13	79.80	703	23	686
12	2.0		1.0	2.0	2.0		2.0	1.0	2.0		8.8	1	9.80	256	1	442
13	2.0		1.0	2.0	2.0	STAPH, STREP	2.0	2.0	2.0	2.0	75.6	20	85.60	2,500	16	822
14	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	35.5	10	45.50	1,171	20	694
15	2.0		2.0	1.0	2.0		2.0	1.0	2.0	2.0	23.0	12	35.00	695	5	604
16	2.0		2.0	1.0	2.0		2.0	2.0	2.0	2.0	3.9	4	7.90	2,500	9	793
17	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	15.0	8	23.00	940	6	632
18	2.0		1.0	1.0	2.0		2.0	1.0	2.0		58.6	9	67.60	468	28	656
19	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	22.5	6	28.50	2,230	6	468
20	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	34.5	9	43.50	617	6	412
21	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	45.4	6	51.40	625	10	810
22	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	22.6	4	26.60	2,500	16	N.A.
23	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	52.0	10	62.00	354	0	487
24	2.0		2.0	1.0	2.0		2.0	1.0	2.0	2.0	18.3	10	28.30	315	2	445
25	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	45.1	10	55.10	2,500	13	626
26	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	48.5	4	53.50	897	7	819
27	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	15.2	7	22.20	1,148	4	386
28	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	59.5	9	68.50	1,216	13	N.A.
29	2.0		2.0	1.0	2.0		2.0	1.0	2.0	2.0	16.6	3	19.60	145	2	300
30	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	19.5	12	31.50	687	14	N.A.
31	2.0		1.0	1.0	2.0	STAPH, STREP	2.0	2.0	2.0	2.0	69.1	13	82.10	1,164	4	604
32	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	12.1	8	20.10	366	8	N.A.
33	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	19.5	5	23.50	307	3	N.A.
34	2.0		2.0	1.0	2.0		2.0	1.0	2.0	2.0	7.8	3	10.80	262	5	404
35	2.0		2.0	1.0	2.0		2.0	2.0	2.0	2.0	15.2	15	30.20	392	8	704
36	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	23.4	5	28.40	316	10	363
37	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	12.1	7	19.10	1,284	10	669
38	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	13.3	5	18.30	993	4	N.A.
39	1.0	FACE, UL-EXT, LL-EXT	1.0	1.0	2.0		2.0	2.0	2.0	2.0	27.3	4	31.30	214	20	556
40	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	52.3	18	70.30	1,565	13	1,320
41	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	36.5	14	50.50	433	6	994
42	2.0		2.0	1.0	2.0		2.0	1.0	2.0	2.0	3.9	2	5.90	150	4	619
43	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	69.0	18	87.00	2,456	10	818
44	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	59.2	12	71.20	224	6	631
45	2.0		2.0	1.0	2.0		2.0	2.0	2.0	2.0	37.3	14	51.30	1,455	10	725
46	2.0		2.0	1.0	2.0		2.0	1.0	2.0	2.0	8.6	5	13.60	419	4	785
47	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	48.2	16	65.20	2,500	22	1,047
48	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	40.6	12	52.60	553	4	616
49	2.0		2.0	1.0	2.0		2.0	2.0	2.0	2.0	15.2	8	23.20	166	11	477
50	2.0		2.0	1.0	2.0		2.0	2.0	2.0	2.0	14.2	8	22.20	89	7	480
51	2.0		2.0	1.0	2.0		2.0	2.0	2.0	2.0	14.4	1	15.40	672	9	471
52	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	18.9	1	19.90	316	4	359
53	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	61.0	14	75.00	2,503	19	576
54	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	60.3	15	75.30	1,355	17	946
55	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	31.7	11	42.70	751	3	777
56	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	12.3	5	17.30	590	14	382
57	2.0		2.0	1.0	2.0		2.0	1.0	2.0	2.0	20.2	13	33.20	300	8	584
58	2.0		2.0	1.0	2.0		2.0	1.0	2.0	2.0	48.6	16	67.60	390	7	N.A.
59	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	30.7	12	42.70	2,341	10	652
60	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	21.8	11	32.80	2,955	14	445
61	2.0		2.0	1.0	2.0		2.0	2.0	2.0	2.0	3.5	1	4.50	255	3	483
62	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	45.2	5	50.20	234	8	621
63	2.0		2.0	1.0	2.0		2.0	2.0	2.0	2.0	10.9	2	12.90	365	6	N.A.
64	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	18.9	8	26.90	149	3	N.A.
65	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	32.4	19	51.40	187	10	644
66	2.0		1.0	1.0	2.0		2.0	1.0	2.0	2.0	60.6	17	77.60	1,354	5	902
67	2.0		1.0	1.0	2.0		2.0	2.0	2.0	2.0	48.5	12	60.50	968	8	634

	ES	ET	EU	EV	EW	EX	EY	EZ	FA
1	IGE	W/D	NS_Oil	NS_Org	Immuno	FoodImm	Foodname	Foodweak	dustmite
2	2,366.8	12.2	1	Staph	2	N.A.	N.A.	N.A.	N.A.
3	7336	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
4	2,823.6	N.A.	2	N.A.	1	1	SOYBEAN, WHEAT FLOUR, PEANUT, RICE, HAZELNUT	APPLE, POTATO, ALPHA-LACTALBUMIN, CASEIN	2
5	2,995.4	13.4	1	MSSA	2	N.A.	N.A.	N.A.	N.A.
6	15,000.0	8.8	1	MSSA	2	N.A.	N.A.	N.A.	N.A.
7	1,599.5	19.4	1	MSSA	1	1	APPLE	CARROT	1
8	59.6	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
9	22.1	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
10	N.A.	13.3	2	N.A.	1	2	N.A.	N.A.	1
11	82.8	8.8	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
12	984.4	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
13	2,697.3	15.6	2	N.A.	1	1	SOYBEAN, PEANUT, POTATO, EGG WHITE, COW'S MILK, WHEAT FLOUR, EGG YOLK, RICE	CASEIN	2
14	2,995.3	14.8	1	NORMAL	1	1	EGG WHITE, EGG YOLK, WHEAT FLOUR, RICE, PEANUT, HAZELNUT, POTATO	N.A.	1
15	377.2	10.1	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
16	60.1	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
17	1,207.1	16.8	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
18	321.6	26.9	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
19	702.8	25.7	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
20	640.4	12.6	1	STAPH	2	N.A.	N.A.	N.A.	N.A.
21	2,599.6	15.5	1	NORMAL	2	N.A.	N.A.	N.A.	N.A.
22	484.0	N.A.	2	N.A.	1	2	N.A.	N.A.	1
23	3,000.0	12.1	2	N.A.	1	2	N.A.	N.A.	1
24	566.7	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
25	477.1	32.2	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
26	315.7	30.8	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
27	69.5	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
28	15,000.0	22.1	1	MSSA	1	1	COW'S MILK, SOYBEAN, PEANUT, POTATO, ALPHA-LACTALBUMIN, CASEIN, WHEAT FLOUR, HAZELNUT, APPLE	N.A.	1
29	19.5	14.1	2	N.A.	1	1	N.A.	N.A.	N.A.
30	1,750.5	N.A.	2	N.A.	1	2	N.A.	N.A.	1
31	4,010.0	10.1	1	MSSA, BETAHEM STREP	2	N.A.	N.A.	N.A.	N.A.
32	N.A.	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
33	124.6	16.2	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
34	279.9	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
35	1,463.7	29.3	1	HIMFLU-COLOMISER	1	1	N.A.	APPLE-VERY WEAK	N.A.
36	2,230.0	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
37	4,212.0	24.8	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
38	176.2	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
39	14,249.0	18.1	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
40	1,618.8	10.4	1	MSSA	1	1	N.A.	RICE-VERY WEAK	1
41	3,000.0	9	2	N.A.	1	1	1	WHEAT FLOUR, RICE, SOYBEAN, PEANUT, POTATO	2
42	670.8	19.3	2	N.A.	1	2	N.A.	N.A.	1
43	2,163.8	25.8	1	MSSA	1	1	N.A.	EGG WHITE-VERY WEAK	1
44	137.0	25.3	1	MSSA	1	1	N.A.	CODFISH-VERY WEAK	2
45	1,380.2	N.A.	1	Staph	1	1	N.A.	EGG YOLK, HAZELNUT, RICE	1
46	N.A.	22	2	N.A.	1	1	1	N.A.	N.A.
47	15,468.0	9.6	2	NORMAL	2	N.A.	N.A.	N.A.	1
48	1,130.3	12.4	2	N.A.	1	1	HAZELNUT	N.A.	N.A.
49	702.5	10.4	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
50	168.5	N.A.	1	MSSA	2	N.A.	N.A.	N.A.	N.A.
51	1,272.0	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
52	799.3	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
53	N.A.	16.2	2	N.A.	1	1	1	CODFISH, ALPHA & BETA LACTALBUMIN	2
54	2,488.0	17.11	1	STAPH	1	2	N.A.	N.A.	1
55	53.3	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
56	592.0	9	2	N.A.	1	2	N.A.	N.A.	N.A.
57	292.0	6.9	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
58	15,000.0	19.6	1	MSSA	1	1	N.A.	EGG WHITE, CODFISH	1
59	1,175.9	13.8	2	N.A.	1	2	N.A.	N.A.	1
60	7,767.0	16.3	2	N.A.	1	1	1	HAZELNUT	1
61	30.8	N.A.	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
62	2,562.2	15.9	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
63	728.2	12	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
64	37.8	16.6	2	N.A.	2	N.A.	N.A.	N.A.	N.A.
65	3,000.0	18	1	MSSA	1	2	N.A.	N.A.	N.A.
66	840.4	5.7	1	MSSA	1	1	1	WHEAT FLOUR, POTATO	1
67	184.0	18.2	1	NORMAL	1	1	1	EGG WHITE, EGG YOLK, CASEIN, SOYBEAN	2

	FB	FC	FD	FE	FF
	other immuno	IDOOL4	IDOOL	DERMSEVER	CDLQI
1	N.A.	20 N.A.	N.A.	15	
2	N.A.	20 N.A.	N.A.	3	
3	BIRCH, MUGWORT-WEAK	10	3	2 N.A.	26
4	N.A.	20 N.A.	N.A.	27	
5	N.A.	20 N.A.	N.A.	22	
6	MUGWORT, GRASS MIX	10	7	2 N.A.	
7	N.A.	10	2	2 N.A.	
8	N.A.	20 N.A.	N.A.	3 N.A.	17
9	N.A.	10	19	3 N.A.	
10	HORSE, CLADOSPORIUM HERBARUM, A. FUMIGATUS, ALTERNARIA ALTERNATA-WEAK	20 N.A.	N.A.	4 N.A.	16
11	N.A.	10	27	2 N.A.	
12	N.A.	10	14	3 N.A.	
13	CAT, DOG-HIGH POS, GRASS MIX, BIRCH, MUGWORT-WEAK	10	7	3 N.A.	
14	CAT-VERY HIGH, GRASS MIX-HIGH, BIRCH-POS	10	13	3 N.A.	9
15	N.A.	20 N.A.	N.A.	3 N.A.	
16	N.A.	10	11	3 N.A.	8
17	N.A.	20 N.A.	N.A.	22	
18	N.A.	20 N.A.	N.A.	23	
19	N.A.	20 N.A.	N.A.	16	
20	N.A.	20 N.A.	N.A.	20	
21	N.A.	20 N.A.	N.A.	5	
22	N.A.	10	5	3 N.A.	
23	N.A.	10	17	2 N.A.	
24	N.A.	20 N.A.	N.A.	2 N.A.	16
25	N.A.	10	5	2 N.A.	
26	N.A.	20 N.A.	N.A.	2 N.A.	16
27	N.A.	10	13	2 N.A.	
28	GRASS MIX, BIRCH, MUGWORT	20 N.A.	N.A.	4	
29	NEG	20 N.A.	N.A.	17	
30	N.A.	20 N.A.	N.A.	12	
31	N.A.	20 N.A.	N.A.	27	
32	N.A.	20 N.A.	N.A.	5	
33	N.A.	10	10	1 N.A.	
34	N.A.	10	19	1 N.A.	
35	MUGWORT-VERY WEAK	20 N.A.	N.A.	3	
36	N.A.	20 N.A.	N.A.	14	
37	N.A.	20 N.A.	N.A.	6	
38	NEG	10	6	3 N.A.	
39	N.A.	20 N.A.	N.A.	16	
40	N.A.	20 N.A.	N.A.	20	
41	GRASS MIX, BIRCH, MUGWORT	10	12	4 N.A.	
42	N.A.	10	1	1 N.A.	
43	N.A.	20 N.A.	N.A.	25	
44	N.A.	20 N.A.	N.A.	8	
45	GRASS MIX-VERY WEAK	10	19	3 N.A.	
46	NEG	10	11	4 N.A.	
47	N.A.	20 N.A.	N.A.	18	
48	N.A.	20 N.A.	N.A.	21	
49	N.A.	20 N.A.	N.A.	7	
50	N.A.	20 N.A.	N.A.	9	
51	N.A.	20 N.A.	N.A.	6	
52	N.A.	20 N.A.	N.A.	2	
53	N.A.	20 N.A.	N.A.	19	
54	CLADOSPORIUM HERBARUM, ASPERGILLUS FUMIGATUS, ALTERNARIA	20 N.A.	N.A.	17	
55	N.A.	10	7	1 N.A.	
56	NEG	20 N.A.	N.A.	12	
57	N.A.	20 N.A.	N.A.	16	
58	N.A.	20 N.A.	N.A.	15	
59	N.A.	20 N.A.	N.A.	13	
60	N.A.	20 N.A.	N.A.	13	
61	N.A.	20 N.A.	N.A.	0	
62	N.A.	20 N.A.	N.A.	5	
63	N.A.	20 N.A.	N.A.	8	
64	N.A.	20 N.A.	N.A.	7	
65	N.A.	20 N.A.	N.A.	26	
66	N.A.	20 N.A.	N.A.	16	
67	N.A.	10	10	3 N.A.	











	EC	ED	EE	EF	EG	EH	EI	EJ	EK	EL	EM	EN	EO	EP	EQ	ER
68	2.0		1.0	1.0	1.0	1.0	2.0	1.0	2.0		50.3	9 59.30	795	8	919	
69	2.0		1.0	1.0	1.0	2.0	2.0	2.0	2.0		40.1	6 46.10	131	6	542	
70	2.0		1.0	1.0	1.0	2.0	2.0	2.0	2.0		47.8	13 60.80	906	5	833	
71	2.0		1.0	1.0	1.0	2.0	2.0	2.0	2.0	2.0	24.0	10 34.00	466	10	675	
72	2.0		1.0	1.0	1.0	2.0	2.0	2.0	2.0		21.8	8 29.80	369	5	704	
73	2.0		1.0	1.0	1.0	2.0	2.0	2.0	2.0		3.9	5 8.90	60	7	486	
74	2.0		2.0	1.0	2.0	2.0	2.0	1.0	2.0		20.5	5 25.50	299	6	513	
75	2.0		2.0	1.0	2.0	2.0	1.0	1.0	1.0		19.1	1 20.10	155	7	542	
76	2.0		2.0	1.0	2.0	2.0	1.0	1.0	1.0		11.1	6 17.10	225	5	678	
77	2.0		2.0	1.0	2.0	2.0	1.0	1.0	1.0		26.2	12 36.20	14	0	550	
78	2.0		1.0	1.0	1.0	2.0	2.0	2.0	2.0		30.8	11 41.80	1 278	13	738	
79	2.0		2.0	1.0	2.0	2.0	1.0	1.0	1.0		28.5	14 42.50	469	10	N.A.	
80	2.0		1.0	1.0	1.0	2.0	2.0	2.0	2.0		26.8	13 39.80	297	1	709	
81	2.0		1.0	1.0	1.0	2.0	2.0	1.0	1.0		28.4	6 34.40	305	2	555	
82	2.0		1.0	1.0	1.0	2.0	2.0	1.0	1.0		14.6	5 19.60	297	2	601	
83	2.0		2.0	1.0	2.0	2.0	2.0	1.0	1.0		14.7	8 22.70	1 083	9	833	
84	2.0		2.0	1.0	2.0	2.0	2.0	1.0	1.0		12.3	4 16.30	424	7	N.A.	
85	2.0		2.0	1.0	2.0	2.0	2.0	1.0	1.0		25.1	6 31.10	2 083	15	740	
86	2.0		2.0	1.0	2.0	2.0	2.0	1.0	1.0		5.8	2 4.80	553	3	481	
87	2.0		1.0	1.0	1.0	2.0	2.0	1.0	1.0		36.8	7 43.80	441	11	514	
88	2.0		1.0	1.0	1.0	2.0	2.0	1.0	1.0		47.5	6 55.50	2 500	22	1 047	
89	2.0		1.0	1.0	1.0	2.0	2.0	1.0	1.0		15.2	12 27.20	309	4	554	
90	2.0		1.0	1.0	1.0	2.0	2.0	2.0	2.0		15.8	3 18.80	145	8	N.A.	
91	2.0		1.0	1.0	1.0	2.0	2.0	2.0	2.0		35.2	10 45.20	70	3	540	
92	2.0		2.0	1.0	2.0	2.0	1.0	1.0	1.0		4.3	2 6.30	76	4	382	
93	2.0		2.0	1.0	2.0	2.0	1.0	1.0	1.0		26.0	16 42.00	170	12	481	
94	2.0		1.0	1.0	1.0	2.0	2.0	1.0	1.0		3.9	7 10.90	452	3	N.A.	
95	2.0		2.0	1.0	2.0	2.0	2.0	2.0	2.0		14.1	1 15.10	316	1	N.A.	
96	2.0		2.0	1.0	2.0	2.0	2.0	1.0	1.0		18.2	3 21.20	151	4	451	
97	2.0		1.0	1.0	1.0	2.0	2.0	1.0	1.0		38.7	8 47.70	1 415	16	474	
98	2.0		1.0	1.0	1.0	2.0	2.0	1.0	1.0		52.2	18 68.20	2 500	12	1 136	
99	2.0		2.0	1.0	2.0	2.0	2.0	1.0	1.0		41.1	1 42.10	1 660	1	756	
100	2.0		2.0	1.0	2.0	2.0	2.0	1.0	1.0		34.7	0 34.70	222	9	550	
101	2.0		2.0	1.0	2.0	2.0	2.0	1.0	1.0		6.2	1 9.20	372	4	1 077	
102	2.0		2.0	1.0	2.0	2.0	2.0	1.0	1.0		1.6	1 2.60	531	3	677	
103	2.0		2.0	1.0	2.0	2.0	2.0	1.0	1.0		21.8	4 25.80	386	3	955	
104	2.0		2.0	1.0	2.0	2.0	2.0	1.0	1.0		31.9	2 33.90	2 600	4	685	
105	N.A.		N.A.		N.A.	N.A.	N.A.	274	N.A.	N.A.						
106	N.A.		N.A.		N.A.	N.A.	N.A.	1 683	N.A.	N.A.						
107	N.A.		N.A.		N.A.	N.A.	N.A.	149	N.A.	N.A.						
108	N.A.		N.A.		N.A.	N.A.	N.A.	576	N.A.	N.A.						
109	N.A.		N.A.		N.A.	N.A.	N.A.	181	N.A.	N.A.						
110	N.A.		N.A.		N.A.	N.A.	N.A.	107	N.A.	N.A.						
111	N.A.		N.A.		N.A.	N.A.	N.A.	226	N.A.	N.A.						
112	N.A.		N.A.		N.A.	N.A.	N.A.	400	N.A.	N.A.						
113	N.A.		N.A.		N.A.	N.A.	N.A.	1 123	N.A.	N.A.						
114	N.A.		N.A.		N.A.	N.A.	N.A.	2 500	N.A.	N.A.						
115	N.A.		N.A.		N.A.	N.A.	N.A.	846	N.A.	N.A.						
116	N.A.		N.A.		N.A.	N.A.	N.A.	1 112	N.A.	N.A.						
117	N.A.		N.A.		N.A.	N.A.	N.A.	1 136	N.A.	N.A.						
118	N.A.		N.A.		N.A.	N.A.	N.A.	505	N.A.	N.A.						
119	N.A.		N.A.		N.A.	N.A.	N.A.	384	N.A.	N.A.						
120	N.A.		N.A.		N.A.	N.A.	N.A.	251	N.A.	N.A.						
121	N.A.		N.A.		N.A.	N.A.	N.A.	262	N.A.	N.A.						
122	N.A.		N.A.		N.A.	N.A.	N.A.	665	N.A.	N.A.						
123	N.A.		N.A.		N.A.	N.A.	N.A.	1 646	N.A.	N.A.						
124	N.A.		N.A.		N.A.	N.A.	N.A.	277	N.A.	N.A.						
125	N.A.		N.A.		N.A.	N.A.	N.A.	1 399	N.A.	N.A.						
126	N.A.		N.A.		N.A.	N.A.	N.A.	319	N.A.	N.A.						
127	N.A.		N.A.		N.A.	N.A.	N.A.	159	N.A.	N.A.						
128	N.A.		N.A.		N.A.	N.A.	N.A.	117	N.A.	N.A.						
129	N.A.		N.A.		N.A.	N.A.	N.A.	279	N.A.	N.A.						
130	N.A.		N.A.		N.A.	N.A.	N.A.	142	N.A.	N.A.						
131	N.A.		N.A.		N.A.	N.A.	N.A.	270	N.A.	N.A.						
132	N.A.		N.A.		N.A.	N.A.	N.A.	319	N.A.	N.A.						
133	N.A.		N.A.		N.A.	N.A.	N.A.	151	N.A.	N.A.						
134	N.A.		N.A.		N.A.	N.A.	N.A.	N.A.	N.A.	N.A.						

	ES	ET	EU	EV	EW	EX	EY	EZ	FA
68	2761.0	8.5	2 N.A.		2 N.A.			N.A.	N.A.
69	1606.3	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
70	98.5	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
71	4377.0	15.6	1 MSSA		1	1 RICE, POTATO, PEANUT		WHEAT FLOUR, SOYBEAN, HAZELNUT, CARROT	1
72	256.4	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
73	614.5	13.8	2 N.A.		2 N.A.			N.A.	N.A.
74	9215.0	9.2	1 Steeph		1 N.A.			N.A.	N.A.
75	1378.2	10.8	2 N.A.		2 N.A.			N.A.	N.A.
76	183	24.6	2 N.A.		2 N.A.			N.A.	N.A.
77	15000.0	N.A.	2 N.A.		2 N.A.			EGG WHITE, APPLE	1
78	1800.0	49.9	2 N.A.		2 N.A.	1 HAZELNUT, PEANUT, POTATO, EGG WHITE, WHEAT FLOUR, RICE, SOYBEAN, CARROT		N.A.	N.A.
79	1244.6	17.3	2 N.A.		2 N.A.			N.A.	N.A.
80	3000.0	20.2	2 N.A.		2 N.A.			N.A.	N.A.
81	157	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
82	184	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
83	1197.0	42.9	2 N.A.		2 N.A.	1 RICE, PEANUT, POTATO-LOW		N.A.	2
84	335.1	20.7	2 N.A.		2 N.A.			N.A.	1
85	5564.0	30.8	1 NORMAL		2 N.A.			N.A.	N.A.
86	57.1	15.4	2 N.A.		2 N.A.			N.A.	N.A.
87	287.6	29.7	2 N.A.		2 N.A.			N.A.	N.A.
88	656.6	5.2	2 N.A.		2 N.A.			N.A.	N.A.
89	4715.0	21.3	1 MSSA		1	1 POTATO, APPLE, CASEIN, ALPHALACTALBUMIN, PEANUT, HAZELNUT		N.A.	1
90	N.A.	16.8	2 N.A.		1	1 SOYBEAN		N.A.	1
91	1244	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
92	1150	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
93	N.A.	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
94	3160.0	14.5	2 N.A.		2 N.A.	1 SOYBEAN, HAZELNUT, POTATO, EGG WHITE		EGG YOLK, CASEIN, WHEAT FLOUR, RICE, PEANUT	1
95	1.5	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
96	228.8	14.2	2 N.A.		2 N.A.			N.A.	N.A.
97	1693.2	22.4	1 MSSA		1			EGG YOLK	1
98	4021.0	3	2 N.A.		2 N.A.			N.A.	N.A.
99	424.0	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
100	4.9	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
101	41	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
102	158	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
103	40	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
104	N.A.	N.A.	2 N.A.		2 N.A.			N.A.	N.A.
105	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
106	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
107	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
108	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
109	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
110	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
111	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
112	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
113	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
114	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
115	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
116	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
117	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
118	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
119	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
120	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
121	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
122	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
123	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
124	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
125	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
126	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
127	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
128	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
129	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
130	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
131	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
132	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
133	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.
134	N.A.	N.A.	N.A.		N.A.			N.A.	N.A.

	FB	FC	FD	FE	FF
68	N.A.	2.0 N.A.	N.A.		13
69	N.A.	2.0 N.A.	N.A.		4
70	N.A.	1.0	10		3 N.A.
71	GRASS MIX- SIGNIFICANT, BIRCH, MUGWORT, CAT-LOW	2.0 N.A.	N.A.		9
72	N.A.	1.0	9		3 N.A.
73	N.A.	2.0 N.A.	N.A.		13
74	MEG	2.0 N.A.	N.A.		12
75	N.A.	2.0 N.A.	N.A.		6
76	N.A.	2.0 N.A.	N.A.		9
77	N.A.	2.0 N.A.	N.A.		19
78	GRASS MIX, CAT, BIRCH, MUGWORT	2.0 N.A.	N.A.		4 N.A.
79	N.A.	1.0	11		2 N.A.
80	N.A.	1.0	6		
81	N.A.	2.0 N.A.	N.A.		1
82	N.A.	2.0 N.A.	N.A.		16
83	GRASS MIX-LOW	2.0 N.A.	N.A.		4
84	N.A.	1.0	11		2 N.A.
85	N.A.	2.0 N.A.	N.A.		7
86	N.A.	1.0	6		
87	N.A.	2.0 N.A.	N.A.		6
88	GRASS MIX-VERY HIGH, MUGWORT-POS	2.0 N.A.	N.A.		9
89	CAT	2.0 N.A.	N.A.		2
90	N.A.	2.0 N.A.	N.A.		11
91	MEG	2.0 N.A.	N.A.		17
92	N.A.	1.0	13		3 N.A.
93	BIRCH	2.0 N.A.	N.A.		4
94	N.A.	1.0	4		0 N.A.
95	N.A.	2.0 N.A.	N.A.		12
96	BIRCH	2.0 N.A.	N.A.		13
97	N.A.	2.0 N.A.	N.A.		24
98	N.A.	1.0	3		2 N.A.
99	N.A.	1.0	6		0 N.A.
100	N.A.	1.0	3		0 N.A.
101	N.A.	1.0	6		2 N.A.
102	N.A.	1.0	2		3 N.A.
103	N.A.	1.0	6		2 N.A.
104	N.A.	1.0	6		
105	N.A.	N.A.	N.A.	N.A.	N.A.
106	N.A.	N.A.	N.A.	N.A.	N.A.
107	N.A.	N.A.	N.A.	N.A.	N.A.
108	N.A.	N.A.	N.A.	N.A.	N.A.
109	N.A.	N.A.	N.A.	N.A.	N.A.
110	N.A.	N.A.	N.A.	N.A.	N.A.
111	N.A.	N.A.	N.A.	N.A.	N.A.
112	N.A.	N.A.	N.A.	N.A.	N.A.
113	N.A.	N.A.	N.A.	N.A.	N.A.
114	N.A.	N.A.	N.A.	N.A.	N.A.
115	N.A.	N.A.	N.A.	N.A.	N.A.
116	N.A.	N.A.	N.A.	N.A.	N.A.
117	N.A.	N.A.	N.A.	N.A.	N.A.
118	N.A.	N.A.	N.A.	N.A.	N.A.
119	N.A.	N.A.	N.A.	N.A.	N.A.
120	N.A.	N.A.	N.A.	N.A.	N.A.
121	N.A.	N.A.	N.A.	N.A.	N.A.
122	N.A.	N.A.	N.A.	N.A.	N.A.
123	N.A.	N.A.	N.A.	N.A.	N.A.
124	N.A.	N.A.	N.A.	N.A.	N.A.
125	N.A.	N.A.	N.A.	N.A.	N.A.
126	N.A.	N.A.	N.A.	N.A.	N.A.
127	N.A.	N.A.	N.A.	N.A.	N.A.
128	N.A.	N.A.	N.A.	N.A.	N.A.
129	N.A.	N.A.	N.A.	N.A.	N.A.
130	N.A.	N.A.	N.A.	N.A.	N.A.
131	N.A.	N.A.	N.A.	N.A.	N.A.
132	N.A.	N.A.	N.A.	N.A.	N.A.
133	N.A.	N.A.	N.A.	N.A.	N.A.
134	N.A.	N.A.	N.A.	N.A.	N.A.















	FB	FC	FD	FE	FF
135	N.A.	N.A.	N.A.	N.A.	N.A.
136	N.A.	N.A.	N.A.	N.A.	N.A.
137	N.A.	N.A.	N.A.	N.A.	N.A.
138	N.A.	N.A.	N.A.	N.A.	N.A.
139	N.A.	N.A.	N.A.	N.A.	N.A.
140	N.A.	N.A.	N.A.	N.A.	N.A.
141	N.A.	N.A.	N.A.	N.A.	N.A.
142	N.A.	N.A.	N.A.	N.A.	N.A.
143	N.A.	N.A.	N.A.	N.A.	N.A.
144	N.A.	N.A.	N.A.	N.A.	N.A.
145	N.A.	N.A.	N.A.	N.A.	N.A.
146	N.A.	N.A.	N.A.	N.A.	N.A.
147	N.A.	N.A.	N.A.	N.A.	N.A.
148	N.A.	N.A.	N.A.	N.A.	N.A.
149	N.A.	N.A.	N.A.	N.A.	N.A.
150	N.A.	N.A.	N.A.	N.A.	N.A.
151	N.A.	N.A.	N.A.	N.A.	N.A.
152	N.A.	N.A.	N.A.	N.A.	N.A.
153	N.A.	N.A.	N.A.	N.A.	N.A.
154	N.A.	N.A.	N.A.	N.A.	N.A.
155	N.A.	N.A.	N.A.	N.A.	N.A.
156	N.A.	N.A.	N.A.	N.A.	N.A.
157	N.A.	N.A.	N.A.	N.A.	N.A.
158	N.A.	N.A.	N.A.	N.A.	N.A.
159	N.A.	N.A.	N.A.	N.A.	N.A.
160	N.A.	N.A.	N.A.	N.A.	N.A.
161	N.A.	N.A.	N.A.	N.A.	N.A.
162	N.A.	N.A.	N.A.	N.A.	N.A.
163	N.A.	N.A.	N.A.	N.A.	N.A.
164	N.A.	N.A.	N.A.	N.A.	N.A.
165	N.A.	N.A.	N.A.	N.A.	N.A.
166	N.A.	N.A.	N.A.	N.A.	N.A.
167	N.A.	N.A.	N.A.	N.A.	N.A.
168	N.A.	N.A.	N.A.	N.A.	N.A.
169	N.A.	N.A.	N.A.	N.A.	N.A.
170	N.A.	N.A.	N.A.	N.A.	N.A.
171	N.A.	N.A.	N.A.	N.A.	N.A.
172	N.A.	N.A.	N.A.	N.A.	N.A.
173	N.A.	N.A.	N.A.	N.A.	N.A.
174	N.A.	N.A.	N.A.	N.A.	N.A.