" EFFECT OF VITAMIN D THERAPY IN ALLERGIC RHINITIS, A ONE YEAR INTERVENTIONAL STUDY IN KLES DR PRABHAKAR KORE HOSPITAL, BELGAUM"

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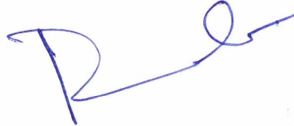

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LIST OF ABBREVIATIONS

GLOSSARY	ABBREVIATIONS
AR	Allergic rhinitis
ARIA	Allergic rhinitis and its impact on asthma
IAR	Intermittent allergic rhinitis
IgE	Immunoglobulin E
IgG	Immunoglobulin G
AEC	Absolute eosinophil count
TNSS	Total nasal symptom score
WHO	World health organisation
GDP	Gross domestic product
HLA	Human leucocyte antigen
NAR	Non allergic rhinitis
NARES	Non allergic rhinitis with eosinophilia syndrome
DC	Dendritic cells
IL -2	Interleukin - 2
IL - 10	Interleukin -10
TH 1	T helper cell 1
TH 2	T helper cell 2
TH 17	T helper cell 17

VDR	Vitamin D receptor
VDRE	Vitamin D receptor element
25 OHD	25 hydroxy vitamin D3
VAS	Visual analogue scale
RQLQ	Rhinoconjunctivitis quality of life questionnaire
tregs	T regulatory cells
INCS	Intranasal corticosteroids
LTRA	Leukotriene receptor anatagonists
DNA	Deoxy ribonucleic acid

ABSTRACT:

AIM:

The purpose of this study is to know the impact of vitamin D on absolute eosinophil count and IgE levels in allergic rhinitis and to evaluate the clinical improvement following vitamin D administration using the allergy symptom score.

METHODS:

A one year interventional study was conducted in KLES Dr Prabhakar Kore hospital with 50 study participants of allergic rhinitis.

RESULTS:

Among the 50 participants, 50% were female participants and 50% were male with a mean age of patients is 27.98 ± 7.27. The mean IgE and AEC levels before intervention was (472.38) and (0.70) respectively, which was significantly reduced after supplementation with vitamin D (243.60) and (0.40).Further the mean TNSS score before intervention is 7.08 which was significantly reduced (3.22) after supplementation with vitamin D, thus supporting the immunomodulatory role of vitamin D in allergic rhinitis.

CONCLUSION:

This study revealed that intervention with vitamin D led to a significant improvement in serum IgE levels and AEC count, as well as a symptomatic improvement in the total nasal symptom score. Furthermore, a inversely proportional relationship between vitamin D, IgE and AEC is observed, suggesting that vitamin D has immunomodulatory function and its deficiency is associated with severity and recurrence of Allergic rhinitis.

Keywords: Allergic rhinitis, Vitamin D, Immunoglobulin E (IgE), Absolute eosinophil count (AEC)

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INTRODUCTION:

AR is one of the prevalent forms of chronic rhinitis facilitated by IgE, on exposure to various allergens.[1] The presenting complaints are nasal block, discharge from nose, sneezing and itching. In India, AR is seen in nearly 10% - 30% of adults. It is an immune-driven process that happens when the allergen comes in contact with the nasal mucosa, triggering an inflammatory response that is mediated by IgE. Although the precise reason of AR is not known, environmental and genetic variables are known to be significant in the disease's development.[2]

Common allergens implicated in AR are dust mites, pollen, molds, allergens specific to occupations and pet dander. The prevalence differs amid countries, perhaps owing to geographic and aeroallergen differences. Significant decline in sleep, work performance, and quality of life have all been linked to severe AR. Effective therapies are obtainable, such as steroid nasal sprays and antihistamines. However, novel therapeutic approaches are required, especially those that focus on newer targets and have minimal side effects.[3]

In addition to its role in maintaining calcium equilibrium, vitamin D is a hormone with other biological functions. Prevalence of vitamin D deficit and the revelation that many cells express VDR have led to the awareness of its immunomodulatory role. This has sparked interest in the possible function of vitamin D in nonskeletal conditions, such as the regulation of both the innate and adaptive immune systems.[4] These are the actions that vitamin D does:

1. It activates Macrophages, Dendritic cells and lymphocytes with the receptors these cells possess
2. It inhibits the growth of T cells, causes an alteration in T cell phenotype from Th1 to Th2, and triggers the production of T regulatory cells, all of which are critical immunological responses during allergic rhinorrhea.
3. It has been shown to inhibit Th1-associated pro-inflammatory cytokines as well as inhibits the production of IL-17 on Th17 cells.
4. It causes activated B cells to undergo apoptosis, and it also prevents the proliferation of plasma cells and the release of immunoglobulins, including IgE.[4,5,6]

Since Vitamin D has the above mentioned actions on the immune system, it is seen to act in the Late phase of Allergic Rhinitis.

There is an affiliation between vitamin D deficiency and allergic diseases, according to recent research. In India, vitamin D insufficiency is highly common, affecting 70% to 80% of people of all ages and genders. Insufficient consumption of calcium and vitamin D due to shifting dietary choices, genetic reasons, sedantry lifestyle with less exposure to sun, and cultural clothing customs shielding women from the sun are the foremost cause of vitamin D deficit in India. Foods like milk and yogurt aren't vitamin D-fortified in our country. As a result, latent vitamin D deficit is extremely prevalent among all socioeconomic backgrounds, in both urban and rural areas.[4]

The invent of VDR has sparked interest to explore the vitamin and its role in immunomodulation. Research states that vitamin D is involved in process of differentiation of cells, inhibition of cell growth , immunomodulation and regulation

of hormones. By influencing the mechanism that suppresses the allergic response, it is said to have an immune-modulator reaction.[4]

There is vitamin D deficit noted in both sun-deprived and sufficiently sunexposed countries. Additionally, it is the nation's most overlooked and neglected nutritional deficiency. It has been discovered that adding vitamin D along with standard topical steroid spray significantly improved the postintervention score.[5]

IgE is believed to play a significant part in the pathophysiology of atopy. On mast cells IgE-specific Fc receptors exist. IgE-mediated antigen cross-bridging causes mast cells to produce mediators, which is a typical of allergic reactions. Along with initiating hypersensitivity reactions, IgE facilitates antibody-mediated cell cytotoxicity.[7] Serum IgE levels is used in the diagnosis as well as in prognosis of AR[8]

It's been proposed that elevated IgE levels are linked to vitamin D deficiency. Research indicates that VDR are found in cells associated with immunity, indicating the significance of vitamin D in immunity and disorders related to it. Vitamin D deficiency is linked with a twenty-fourfold greater risk of chronic AR in patients than those with normal vitamin D levels. This data justifies the addition of vitamin D supplements in conventional management of AR.[8]

It is proven that eosinophils has an important part to play in the etiology of allergic disorders. Eosinophils are known to heighten the allergic reaction by prompting the enrolment of TH2 cells and medling with DC.[9]

Lately, it is testified that the active and infective form of eosinophil, are unswervingly involved in the emergence of eosinophilic illnesses such as allergic esophagitis and bronchial asthma. But, it is not known if they correspond to the severity in allergic rhinitis.[9] Serum IgE levels is used in the diagnosis as well as in prognosis of AR. It is said that lack of vitamin D is linked with elevated IgE levels.

This study's primary goals are to evaluate the impact of vitamin D on IgE and AEC count in AR and to look for symptomatic relief using TNSS score.

OBJECTIVE OF STUDY:

1. To study the effect of vitamin D on IgE levels and eosinophil count in allergic rhinitis.
2. To assess the symptomatic improvement with allergy symptom score after vitamin d supplementation.

REVIEW OF LITERATURE:

AR:

The hallmarks of AR include inflammatory alterations in the nasal mucosa brought on by allergen exposure by inhalation. The patient has already been exposed to an allergen, resulting in an inflammatory reaction. The person's aberrant reaction involves the making of IgE, which assigns itself to mast cell receptors. Mast cell degranulation is triggered by this receptor/IgE complex upon subsequent allergen exposure. Nations with a lesser prevalence of asthma (<5%) namely the Indonesia, Rome and Greece is found to have lesser prevalence of AR. On the contrary, nations like UK, Australia and New Zealand is found to have a high occurrence of rhinitis (15–20%).[10]

These inflammatory mediators produce the characteristic symptoms, which include sneezing, nasal obstruction, anterior or posterior rhinorrhea, and/or nose itching for more than an hour on most days, for two or more days in a row. There are two types of allergic rhinitis: mild or persistent (moderate to severe).[10]

AR is categorized by ARIA as persistent and intermittent.

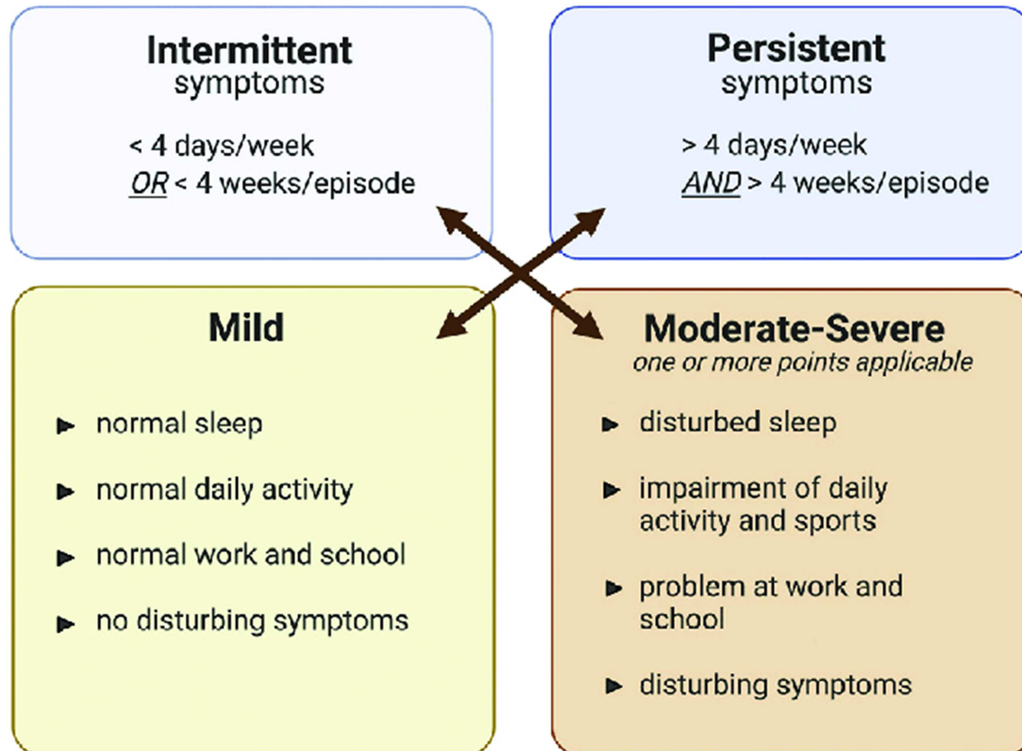


Fig 1 ARIA Classification[10]

ARIA is a non-governmental association that works in partnership with WHO.[10] Depending on how long and how severe the symptoms are, ARIA categorizes AR as "Intermittent AR" wherein the symptoms persist for four weeks straight or for a minimum of four days every week., whereas in " "Persistent AR" refers to symptoms that persist for longer than four weeks or more than four days each week. According to Quentin Gardner et al. in Scott Brown, 8th edition, patients with impairment of sleep who are able to carry out their daily activities are classified as having "mild" symptoms; those with impairment of sleep who have bothersome symptoms that interfere with routine activities are classified as having "moderate-severe" symptoms.[10]

NATURAL HISTORY

Passàli D et al in their study 'Natural history of allergic rhinitis a review' highlighted the interaction between the atopic person and allergenic substances in the early stages of the allergy, resulting in pale nasal mucosa, edema of the middle and lower turbinates, increased watery secretion, itching and sneezing, rhinorrhea, and nasal congestion as the natural course of allergic rhinitis. Suffering such as sinusitis, otitis media with effusion, or asthma ensues after this. Furthermore, nose problems may make it difficult to focus throughout the day and sleep at night. In order to prevent numerous recurrences of the condition, it is crucial to interfere with the normal course of allergic rhinitis by adhering to certain instructions, such as avoiding contact with the underlying allergen, receiving preventative therapy in the case of seasonal rhinitis, and continuous care in the case of chronic nasal allergy.[11]

RELEVANT ANATOMY AND PHYSIOLOGY

The respiratory tract's most cephalic portion is the nose. It uses its anterior apertures, called nares, and its posterior aperture, called choanae, to connect with the outside world. This cavity is divided into two by the septum, and each cavity is supported by a cartilaginous and bony framework.[12]

Its purpose is to make the air that is inspired warmer and more humid.. Before the air reaches the lower airways, it is cleared of small airborne particles and other debris as it travels through the nasal cavity. Columnar epithelium lines the inside of the nasal cavity. In addition to coating the lining, this type of epithelial lining secretes mucus, which helps the mucociliary system remove small aerosolized particles that get stuck in the nasal mucosa. The air-containing mucosal-lined sinuses that

encompass the frontal, paired maxillary, sphenoid, and ethmoid sinuses make up the nasal cavity (fig. 2). The nasal cavity and these cavities have direct communication. These sinuses empty into the nasal cavity through their thin-walled ostia. Mucus is secreted by the sinus wall lining as well as the nasal cavity. Mucus is swept by the surface cilia in a manner akin to a carpet, and then it is directed toward the nasal ostia. The sinus ducts that drain into the ostia and the turbinates are covered by spiral-shaped mucosal folds that make up the lateral walls. Turbinates are designed in a spiral pattern to maximize the surface area of inspired air.[12]

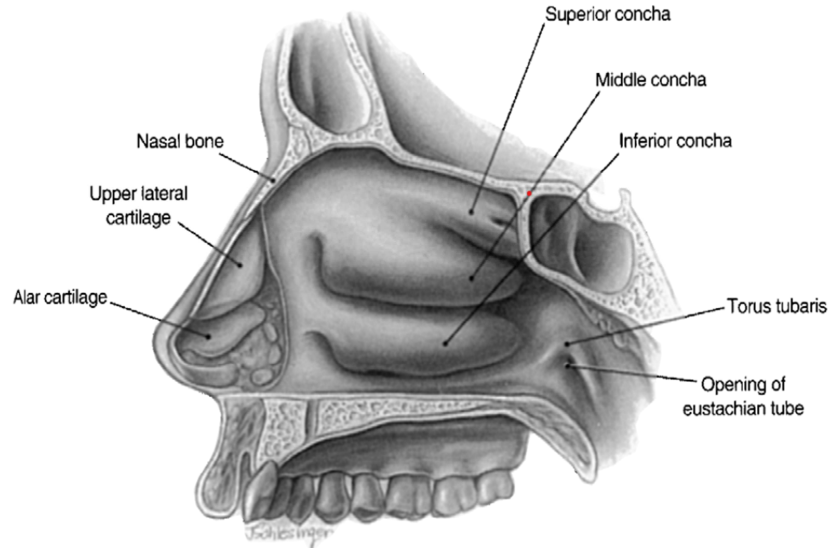


Fig 2 Anatomy of lateral wall of nose [13]

PARANASAL SINUS AND ITS FUNCTION:

Dustin M Dalgorf et al in scott brown 8th edition describes that the paranasal sinuses' functions, through a network of well-defined routes, wherein the cilia beat in unison to transfer the mucous layer that captures particles from the sinus into the nose. Based on these drainage channels, the anterior, posterior, and sphenoid

compartments of the paranasal sinuses function as functional units. The maxillary, anterior ethmoid, and frontal sinuses make up the anterior functional unit. The middle meatus osteomatal complex allows these sinuses to empty into the nose. The superior meatus of the nose allows the posterior ethmoid sinus to empty into the nasal cavity. The sphenoid sinus, which makes up the sphenoid functional unit, empties into the sphenoethmoidal recess.[10]

IMMUNOPATHOLOGY

Antibodies are used to fight viruses or bacterial agents in the prevention of infections; cell-mediated immunity is used to fight viral, fungal, infections. Immune responses are incredibly effective at killing organisms and can quickly destroy organisms if directed correctly; however, these same immune responses can cause diseases. This damaging effect of immune responses is referred to as allergy or hypersensitivity, and is known to be immunopathological disorder.[7]

The reactions can be divided as four groups (i.e.) Type I – IV. The atopic and allergic diseases fall into Type I or mast cell mediated reactions.

Type I reactions, or mast cell-mediated reactions:

Release of mast cell or basophil mediators result in reactions to sensitizing allergens. These reactions can be IgE independent (sensitivity to iodide contrast media) or IgE dependent (anaphylaxis).[7]

RISK FACTORS:

Skoner D P et al in their study, mentioned that positive SPT are a major risk factor for the onset of complaints, and AR rises with age. Individuals who are born during the pollen-laden season, those from higher economic strata, non-White persons, and those with a family history of allergies are more likely to experience it. Additionally, there is a higher chance of AR among firstborn children. Early food or formula introduction, maternal smoking, indoor exposure to allergens (like pet dander), were associated with a higher likelihood of AR in young children.[14]

AETIOLOGY:

Genetics:

Daniel R Cox et al in Cummings 7th edition mentioned AR has a well-known familial component, with some studies estimating its heritability at least 80 percent. The genetic causes of AR are thought to be complex and involve a variety of genes. Several single nucleotide polymorphisms have been identified in genes that are thought to be associated with AR, such as those that encode human leukocyte antigen (HLA) subtypes, and cytokines, including interleukins. In addition to genetic mutations, epigenetic variations may contribute to the inherited patterns observed in AR. DNA methylation can be affected by environmental conditions such as maternal smoking and air pollution, and methylation profiles have been shown to be crucial in AR.[7]

HYGIENE OR BIODIVERSITY HYPOTHESIS:

Daniel R Cox et al in Cummings 7th edition said that in developed countries, epidemiological studies show a increase in the occurrence of allergic disorders. As a result of antibiotics, vaccination, and improved sanitation, the incidence of many infectious diseases in developed countries has decreased. This so-called "hygiene hypothesis" has been attributed to a rise in the incidence of allergic disease, implying the potential protective effect of mucosa colonization with environmental microflora.[7]

The study of variations in the human microbiome and the effect that these changes may have on allergy development is also linked to the hygiene/biodiversity hypothesis. The human body interacts with trillions of microbes within the skin and digestive tract. The microbiome is the group of microbes that colonize a given organism, and the relationship between the microbiome and human disease has been steadily established since 2007. As the host begins to be colonized, the human host and the microbiome interact in the first days of life. A correlation has been found between early life microbiome structure and allergy development.[7]

SOCIOECONOMIC FACTORS

Asthma and atopy are seen to be more common in industrialized and developed nations than in less developed and wealthy nations. In Europe, there is a positive correlation between the GDP and the prevalence of non-communicable diseases including diabetes and bronchial asthma. Research targeting migrants has shown that environmental and lifestyle variables contribute to the emergence of allergy-related disorders.[7]

GEOGRAPHY:

Daniel R Cox et al in Cummings 7th edition mentioned that low socioeconomic status and high temperatures—two traits common to southern countries—can increase the risk of infections in a number of ways, including laxer monitoring of food and water contamination by microorganisms, a higher risk of bacterial proliferation at higher ambient temperatures, and substandard housing conditions. Geographic variance in allergy diseases may be influenced by climate.[7]

In the endocrine system, vitamin D has an integral role in reducing the risk of various chronic illnesses, like the cancer, autoimmune diseases, inflammation, and cardiovascular disease. Vitamin D levels and sun exposure have been related to this phenomena. It may influence chronic inflammation through T cells, DC, and macrophages, in addition to its capacity to encourage tregs to produce IL-10.[7]

PATHOPHYSIOLOGY

L bjermer et al in their study the claimed that there are two phases in AR. Exposure to allergens, like the house dust mites, pet dander, which are recognized by receptors in IgE, sets off the response in presensitized individuals.(15) The early-phase reaction is characterized by mast cell degranulation, which causes severe nasal symptoms (such as congestion and rhinorrhea) to appear quickly (often within minutes) and ocular symptoms (such as irritation, redness, and watering of eyes) to develop. Release of histamine is the cause of these symptoms. Together with additional strong pro-inflammatory cytokines (leukotrienes) and eicosanoids (prostaglandins and kinins), this early-phase histamine release raises the blood as seen in fig 3.[15]

The late-phase reaction happens several hours after an allergen is first encountered. It is defined by the production of several mediators,as shown in fig 3[15]

This late-phase inflammatory response is linked to tissue remodeling, increased tissue oedema, and the development and maintenance of nasal congestion—one of the symptoms of AR that patients find most annoying. Due to mucosal inflammation, tissues get sensitized and react more powerfully when exposed to allergens. These late-phase reactions and changes in tissue responsiveness, as shown in fig. 3, lead to bronchial hyperresponsiveness. [15]

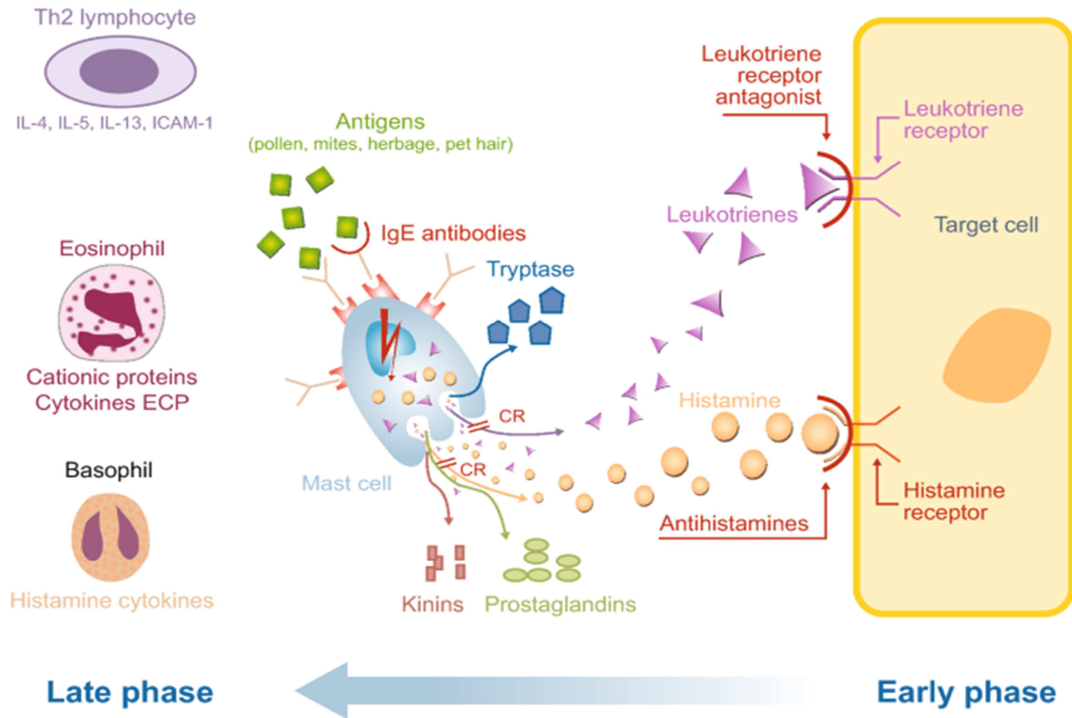


Fig 3 Early and late stages, as reported by L. Bjermer et al., illustrating the pathophysiological mechanisms and triggers of allergic rhinitis as well as the possible locations for pharmaceutical intervention.[15]

EVALUATION AND DIAGNOSIS

HISTORY

Shruthi Gowthami et al in their study stated that patients with chronic AR presented with postnasal drip, persistent nasal congestion, and obstruction, while patients with AR exhibited watery eyes, rhinorrhea, and sneezing. These patients will have a familial or personal history of allergic rhinitis or asthma. People who experience intermittent rhinorrhea may be able to identify triggers such as pollens, tobacco smoke, pet dander, carpets and upholstery, mold, dampness, and/or perfumes.[16]

PHYSICAL EXAMINATION:

Akhouri S et al in threir study, mentioned the physical examination findings of AR as,

- Dark circles beneath the eyes (allergic shiners);
- Frequent sniffing and/or throat clearing;
- A transverse supra-tip nasal crease.

In children, the nasal supratip crease is more prevalent. Thin, transparent secretions and nasal mucosal edema are visible on an anterior rhinoscopy. The nasal mucosa may seem cobblestone-like, and the inferior turbinates may have a blue hue. To rule out nasal polyps, a diagnostic nasal endoscopy must be done. Patients who have prolonged symptoms may become painful when their sinuses are palpated. In addition, these patients must to be examined for indications of dermatitis or asthma and questioned about their aspirin sensitivity.[17]

DIAGNOSIS:

Patients are often given a course of empiric medical treatment, which may include an INCS spray or an oral antihistamine. If empiric therapy fails, allergy testing is performed to confirm diagnosis.[7]

Skin prick tests and checking for serum IgE levels are the two most commonly used methods to confirm the diagnosis of AR.[7]

SKIN PRICK TEST

Using lancets that restrict skin penetration to a depth of 1 mm, antigen extracts are applied epicutaneously to the skin during skin prick testing. Producing the allergen extract's diluent, which acts as a negative control , and a positive control consisting of the mast cell degranulating agent codeine or histamine, comes after the testing. A patient may experience a wheal and flare reaction if they are sensitive to a certain antigen. After 15 to 20 minutes, the wheal size is measured at its largest diameter. A wheal is deemed positive if it is 3 mm bigger than the negative control.[7]

IN VITRO TESTING

SERUM TOTAL IgE

Akanksha agarwal et al in their study the diagnostic utility of serum IgE and AEC count in cases of AR stated that the ability to detect patients with atopic disorders is the primary benefit of serum total IgE levels, especially when these levels are markedly increased. Furthermore, it has been proposed that the efficacy of immunotherapy may be predicted by the ratio of total to specific IgE. A blood test termed an absolute eosinophil count counts the quantity of eosinophils, a particular

type of white blood cell.(8) IgE levels in healthy, non-allergic people are less than 120 IU/ml.[18]

The ability to detect patients with atopic disorders is the primary benefit of serum total IgE levels, especially when these levels are markedly increased. Furthermore, it has been proposed that the efficacy of immunotherapy may be predicted by the ratio of total to specific IgE.[18]

AEC

Eosinophil is a pro-inflammatory granulocyte that helps in the defense against parasitic infections and is implicated in allergic disorders. They also promote inflammation by secreting lipid mediators, oxygen metabolites, and cytokines, resulting in a decrease in arterial permeability. The normal range of eosinophils is between 0–6%, but it can be different in different laboratories.[(17)] . The normal AEC is 40-450 cells/mm^3 [19]

NASAL BIOPSY

The traditional method for examining the nasal tissues of patients with AR was the histological examination of nasal biopsy specimens, but this has been largely replaced by other testing techniques. It also has no value, mainly when alternative diagnoses such as granulomatous nasal disorders are considered.[7]

NASAL CYTOLOGY

Nasal cytology refers to the collection and sampling of surface cells in the nasal mucosa. Although nasal cytology findings are often not necessary in the

diagnosis of AR, they can help distinguish between many types, like AR, NAR, NARES.[7]

TREATMENT

A study by P Small et al stated that avoidance tactics, saline irrigation, oral antihistamines, INCS, sprays combining INCS and antihistamines, LTRAs, and allergen immunotherapy are among the treatments for AR. Referral to an allergist must be considered if the symptoms do not recover after receiving therapy.[20]

AVOIDANCE OF ALLERGEN:

The first line of treatment for allergic rhinitis is to stay away from allergens (including mold, pets, pollens, and home dust mites) and irritants (like tobacco smoke). Individuals with dust mite allergies in the home should be encouraged to use

Use bedding made of allergen-impermeable materials and maintain a minimum relative humidity of 50% in the home to prevent the growth of mites. By minimizing outside exposure, using screen filters to windows, and minimizing period expended outside, one can lessen their exposure to pollen. Removing animal dander from the home is advised for individuals who are allergic to it; symptoms typically significantly improve in 4-6 months. [20]

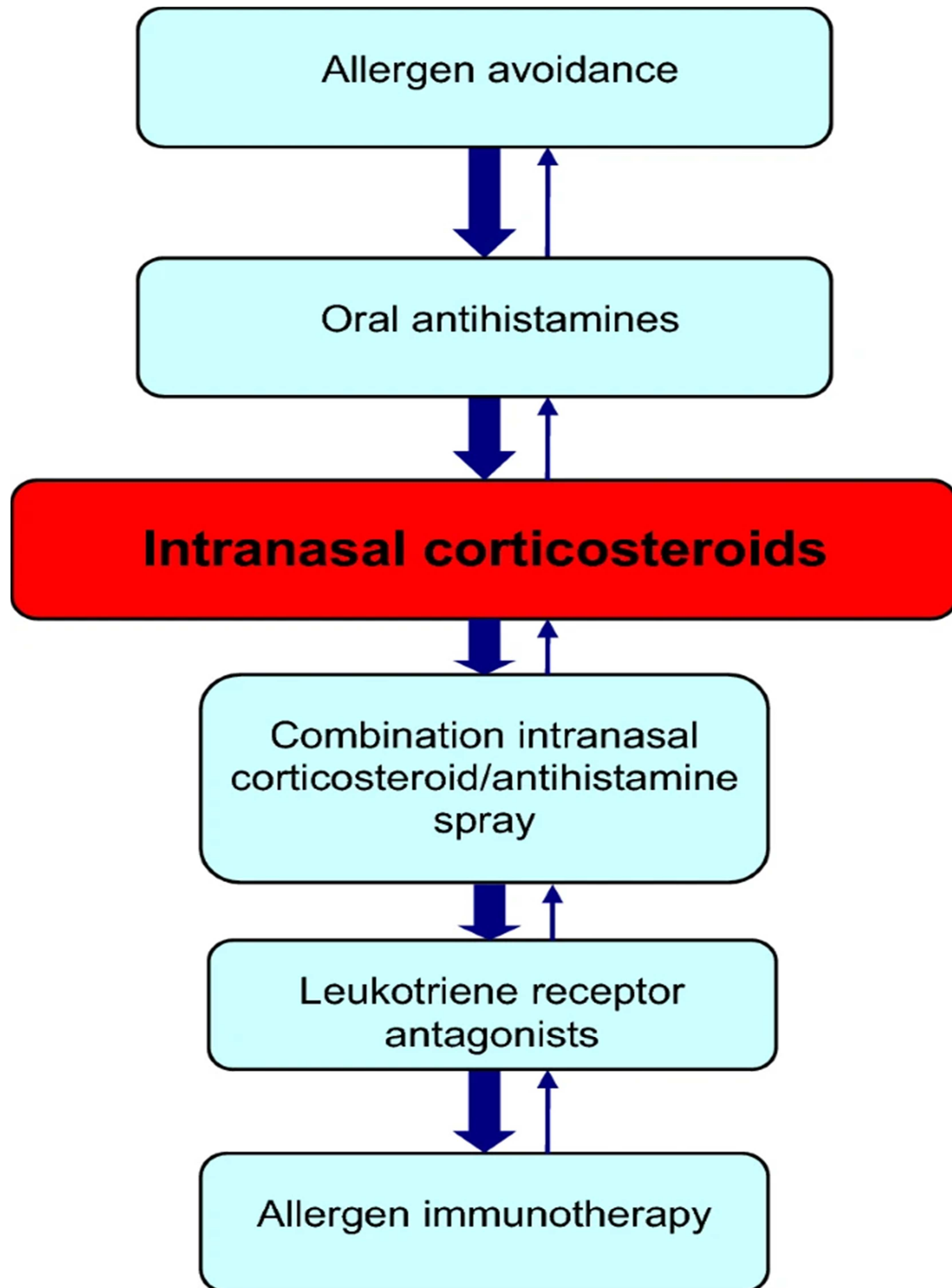


Fig 4 Treatment Algorithm for AR.[20]

Antihistamines:

All patients with allergic rhinitis are advised to start with second-generation oral anti-histamines, such as cetirizine, fexofenadine, loratadine, and desloratadine. Bilastine and rupatadine are two novel second-generation antihistamines that were just brought on the market.[20]

The second-generation oral antihistamines have demonstrated an effective reduction in coughing, inflammation, and discharge from nose when taken during the onset of symptoms or before allergen exposure. While 1st-generation antihistamines are also useful for symptom relief, research has indicated that their effects on cognition and functioning are negative.[20]

INCS:

INCS are either used alone or in conjunction with oral antihistamines as first-line treatment alternatives. When administered appropriately, intranasal corticosteroids greatly reduce nasal mucosal inflammation and improve mucosal pathology. It has been demonstrated that INCS are more effective than antihistamines and LTRAs in treating symptoms of AR, such as rhinorrhea and nasal congestion. It is also known to lessen symptoms related to the lower airways and improve ocular symptoms in people with co-occurring asthma and allergic rhinitis.[20]

Table 1 Overview of Pharmacological management of AR [20]

Usual adult dose	Usual paediatric dose
Oral antihistamines (second generation)	
Bilastine (Blexten)	1 tablet (20 mg) once daily
Cetirizine (Reactine)	1–2 tablets (5 mg) once daily 1 tablet (10 mg) once daily
Desloratadine (Aerius)	1 tablet (5 mg) once daily
Fexofenadine (Allegra)	1 tablet (60 mg) every 12 h (12-h formulation) 1 tablet (120 mg), once daily (24-h formulation)
Loratadine (Claritin)	1 tablet (10 mg), once daily
Rupatadine (Rupall)	1 tablet (10 mg) once daily
Intranasal corticosteroids	
Beclomethasone (Beconase)	1–2 sprays (50 µg/spray) EN, twice daily
Budesonide (Rhinocort)	2 sprays (64 µg/spray) EN, once daily or 1 spray EN, twice daily
Ciclesonide (Omnaris)	2 sprays (50 µg/spray) EN, once daily
Fluticasone furoate (Avamys)	2 sprays (27.5 µg/spray) EN, once daily
Fluticasone propionate (Flonase)	2 sprays (50 µg/spray) EN, once daily or every 12 h (for severe rhinitis)
Mometasone furoate (Nasonex)	2 sprays (50 µg/spray) EN, once daily
Combination intranasal corticosteroid/antihistamine nasal spray	2 sprays (55 µg/spray) EN, once daily
Fluticasone propionate/azelastine hydrochloride (Dymista)	1 spray EN, twice daily
Leukotriene receptor antagonists	
Montelukast	1 tablet (10 mg), once daily

In table 1, It should be instructed to patients on how to use the devices correctly since correct administration of the nasal spray is essential to a successful clinical response. The commonly used INCS with their dosage are shown in fig 1.[20]

Combination of INCS and antihistamine nasal spray

Sprays that combine corticosteroids and antihistamines can be utilized if INCS prove ineffective. It has been discovered that this combination spray is more efficient than the individual parts, and it has a safety profile that is comparable to INCS.[20]

LTRAs:

While LTRAs such as zafirlukast and montelukast are useful in preventing allergic rhinitis, their efficacy does not seem to match that of INCS. If INCS, antihistamines, or combination of these are not tolerated well, they ought to be taken into consideration.[20]

Immunotherapy:

In allergy-specific immunotherapy, the patient's allergens are administered in progressively larger doses until a concentration is attained that effectively triggers the development of immunologic tolerance to the allergen. Treating AR with immunotherapy is effective, especially for patients with IAR brought on by allergens from grass, trees. Additionally,it has been established to be successful in treating AR brought on by cockroaches, alternaria, home dust mites, and dog and cat dander. Allergy immunotherapy ought to be saved for patients for whom the best avoidance techniques combined with medication are either intolerable or inadequate in symptom relief. Only medical professionals who are experienced in this type of therapy should prescribe it because it can cause anaphylactic shock.[20]

VITAMIN D AND AR:

Dehydrocholesterol in the skin is changed to pre-vitamin D3 following Ultra violet B exposure, and this isomerization is thermally driven and results in the conversion of pre-vitamin D3 to vitamin D3 (cholecalciferol). You can get vitamin D3 from your meals, supplements, or your gut. Following hydroxylation in the liver, vitamin D3 in circulation becomes 25 OHD, which is subsequently hydroxylates once more in the kidney to produce 1,25-dihydroxyvitamin D3, the physiologically active form (calcitriol).[6]

Since a predisposition to allergies can be acquired in utero or during immune system development, many studies have also investigated the potential that a mother's level of vitamin D influences her child's risk of allergies. There has also been a lot of interest in vitamin D's ability to treat inflammatory diseases by changing the morphology of cells that are frequently associated with adaptive immunity.[21]

The potential of vitamin D to alleviate inflammatory illnesses by modifying the behavior of cells commonly linked to adaptive immunity has garnered interest. It is claimed that vitamin D inhibits DC activation, lowers immune receptor expression on monocyte DCs, and diminishes the functionality of these cells. By reducing TH1 cytokine release, it prevents T-cell proliferation. It was not discovered that vitamin D supplementation influenced TH2 responses in vivo. In contrast, vitamin D administration was found to suppress TH17 responses. Additionally, it increases the levels of IL-10 and decreases the levels IL-2 from regulatory T (Treg) cells, which promotes hyporesponsiveness.[21]

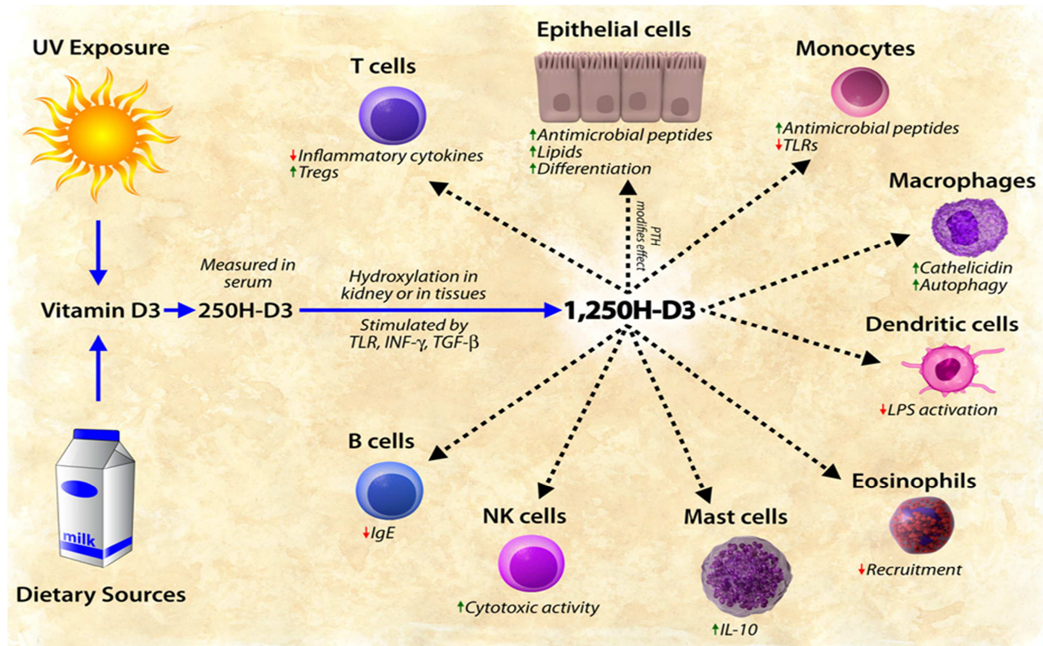


Fig 5 An overview of vitamin D and how it interacts with immune system cells.[21]

METHODOLOGY:

Our study was done in the department of ENT and HNS from October 2022 to September 2023 to study the effect of vitamin D on IgE levels and AEC in AR. A total of 50 participants were included for the study.

STUDY DESIGN: Interventional study

STUDY PERIOD : 1 Year

STUDY POPULATION: Patients between 18 - 55 years of age presenting with symptoms of AR to the outpatient department of ENT & HNS at KLES Dr Prabhakar Kore charitable hospital were chosen.

SAMPLE SIZE: 50

$$n = \frac{z_\alpha^2 P(1-P)}{d^2}$$

where P is the prevalence rate and d is the percentage likely difference in the prevalence. z_α is linked with the level of significance. For 5% level of the significance $z_\alpha = 1.96$.

Ref:

Sachdeva P, Joshi S, Anand S. Serum vitamin D and immunoglobulin E levels in children of allergic rhinitis: a case-control study from Central India. International Journal of Contemporary Pediatrics. 2021;8(6):1038.[2]

The parameter considered in the calculation is the prevalence rate of deficit of vitamin D3 in AR which is above 50% With P = 55% and d = 25% of P = 13.75%, the sample size is 50.

ETHICAL CLEARANCE: Attained from instituitional ethical committee.

INCLUSION CRITERIA: Patients with Allergic rhinits attending outpatient department in KLES Dr Prabhakar Kore Hospital aged between 18-55 years of age.

EXCLUSION CRITERIA:

- Patients with immunological / Inflammatory conditions like Rheumatoid Arthritis, Nasal Polyposis
- Patients with Chronic illnesses like Diabetes mellitus, Renal insufficiency and Abnormal Vitamin D metabolism.
- Patients on Vitamin D Supplementation in the last 2 years.

METHODOLOGY:

- The patients coming to the otolaryngology clinic with complaints of AR were evaluated for AR using a allergic rhinitis history questionnaire.
- Diagnosis of AR is made based on ARIA classification, following which the serum vitamin D levels was measured in all patients.
- Informed consent is taken before the intervention is given.
- The patients received 60,000 IU cholecalciferol weekly along with inhalational corticosteroids (fluticasone propionate with each spray delivering 50mcg) for 6 weeks and subsequently followed up.

- The IgE (normal - <150 IU/Ml) and AEC levels (normal – 0.02 -0.5 x $10^{3/\mu L}$) were tested before and after intervention with Vitamin D.
- TNSS score was used before and after intervention with vitamin D.
- The pre and post intervention values were assessed which was recorded by maintaining a log book.

1. Please rate how your **nasal congestion** has been over the past:	12 hours	Last 2 weeks
None	0 ○	0 ○
Mild (symptom clearly present but easily tolerated)	1 ○	1 ○
Moderate (symptom bothersome but tolerable)	2 ○	2 ○
Severe (symptom difficult to tolerate – interferes with activities)	3 ○	3 ○

2. Please rate how your **runny nose** has been over the past:	12 hours	Last 2 weeks
None	0 ○	0 ○
Mild (symptom clearly present but easily tolerated)	1 ○	1 ○
Moderate (symptom bothersome but tolerable)	2 ○	2 ○
Severe (symptom difficult to tolerate – interferes with activities)	3 ○	3 ○

3. Please rate how your **nasal itching** has been over the past:	12 hours	Last 2 weeks
None	0 ○	0 ○
Mild (symptom clearly present but easily tolerated)	1 ○	1 ○
Moderate (symptom bothersome but tolerable)	2 ○	2 ○
Severe (symptom difficult to tolerate – interferes with activities)	3 ○	3 ○

4. Please rate how your **sneezing** has been over the past:	12 hours	Last 2 weeks
None	0 ○	0 ○
Mild (symptom clearly present but easily tolerated)	1 ○	1 ○
Moderate (symptom bothersome but tolerable)	2 ○	2 ○
Severe (symptom difficult to tolerate – interferes with activities)	3 ○	3 ○

5. Please rate how **difficult sleep** has been with nasal symptoms:	Last night	Last 2 weeks
None	0 ○	0 ○
Mild (symptom clearly present but easily tolerated)	1 ○	1 ○
Moderate (symptom bothersome but tolerable)	2 ○	2 ○
Severe (symptom difficult to tolerate – interferes with activities)	3 ○	3 ○

TOTAL SCORE: 0 / 0

Fig 6 TNSS Questionnaire [22]

STATISTICAL ANALYSIS:

For the continuous quantitative variables mean and standard deviation will be calculated. The continuous variables will be compared using suitable tools of statistics like student's unpaired t test. The pre and post treatment measures will be compared using student's paired t test

Discrete variables will be represented by median.

The categorical data will be expressed in terms of rates, ratios and percentages. The association between the outcome, clinical and demographic characteristics will be tested using Chi-square test, test of proportion or Fisher's exact test.

For discrete variables nonparametric tests will be used.

Apart from the above suitable tools like ANOVA, correlation, regression etc., will be used according to the need.

For all the tests the value of p less than 5% (0.05) is be considered significant.

Special Investigation:

Vitamin D supplementation and serum vitamin D levels were needed to be specifically investigated in this study.

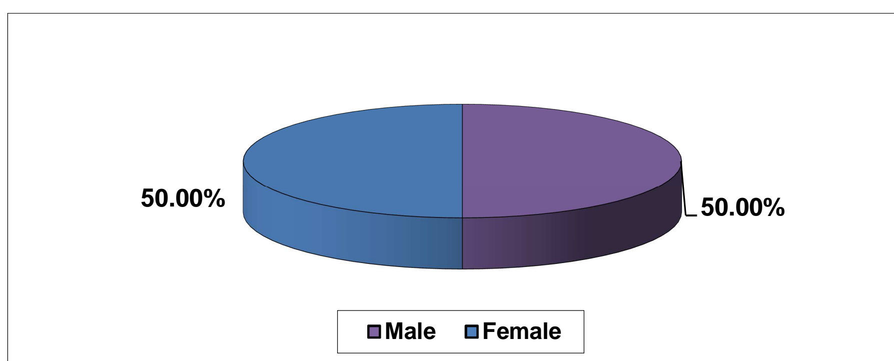
RESULTS:

50 patients in total are included in the study after giving their informed consent. The mean age of patients is 27.98 ± 7.27, with 50% female participants and 50% were male participants.

Table 2 Distribution of participants according to the age

Age group (Years)	Distribution (n=50)	
	No	%
18 to 30	35	70.00
31 to 40	13	26.00
41 to 50	2	4.00
Total	**50**	**100.00**

Their mean age was 27.98 ± 7.27 years, with (70%) of patients in the age group 18 to 30 years, followed by (26%) 31- 40 years and 41- 50 years (4%) which is shown in (Table 2).



Graph 1 Distribution of participants according to the gender

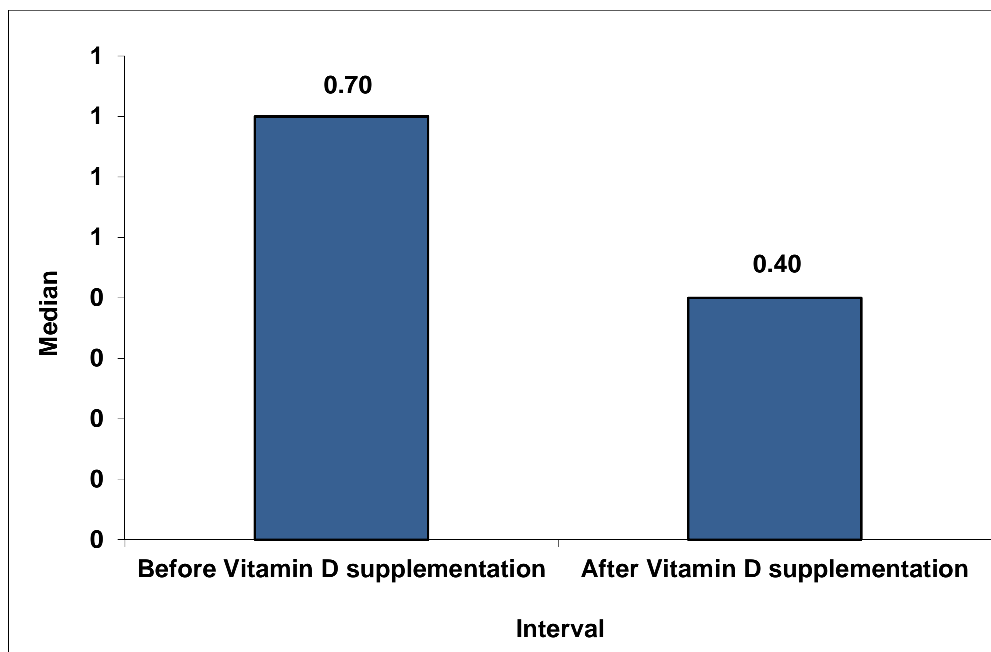
Graph 1 shows gender wise distribution of patients wherein there are 25 male patients (50%) and 25 female patients (50%) with no gender preponderance.

Table 3 Distribution of participants according to the TNSS score before supplementation		
TNSS score before supplementation	**Distribution**	
	No	**%**
6	9	18.00
7	31	62.00
8	7	14.00
9	3	6.00
Total	**50**	**100.00**

Table 4 Distribution of participants according to the TNSS score after supplementation		
TNSS score after supplementation	**Distribution**	
	No	**%**
2	3	6.00
3	33	66.00
4	14	28.00
Total	**50**	**100.00**

In table 3, the TNSS score before supplementation is shown which showed 31 patients with score of 7 (62%), followed by 9 patients with a score of 6 (18%) comprising the majority respectively.

In table 4 the distribution of participants according to the TNSS score after supplementation is shown where, 33 patients (66%) had total nasal symptom score of three after intervention, followed by 14 patients (28%) with score of 4 and 3 patients with a score of 2 (6%), thus implicating the sympotomatic improvement after vitamin D supplementation.

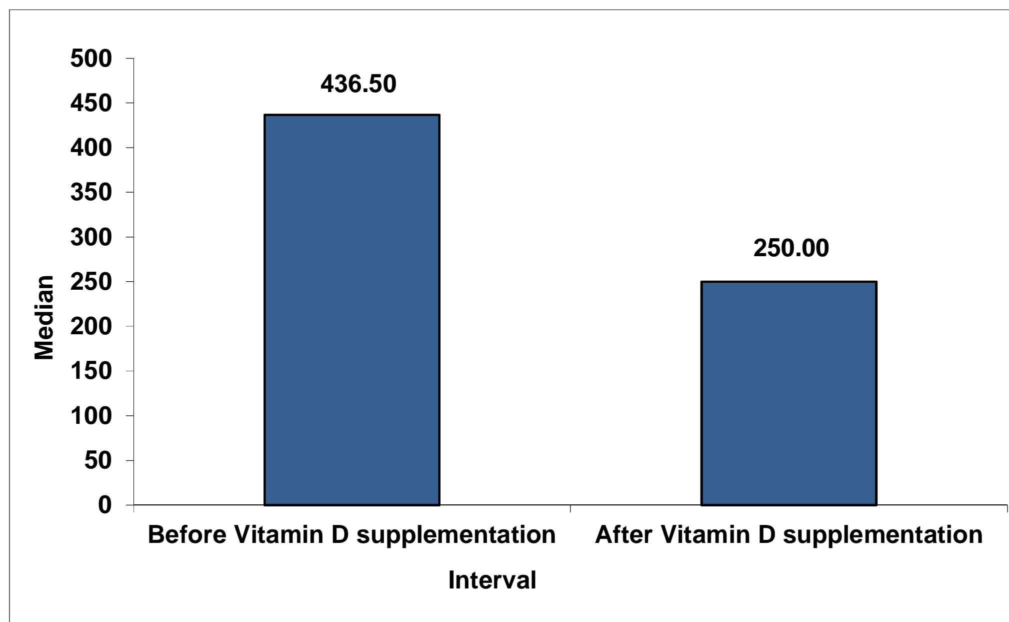


Graph 2 Comparison of AEC levels

Graph 2 represents the comparison Of AEC levels before and after supplementation with vitamin D. The median AEC level before intervention was (0.70) and and after intervention was (0.40) which showed statistically significant difference. **($p < 0.001$)**

Table 5 Comparison of IgE levels.

Interval	IgE levels (n=50)			
	Mean	**SD**	**Median**	**IQR**
Before Vitamin D supplementation	472.38	153.09	436.5	192.5
After Vitamin D supplementation	243.6	55.62	250	95.25
p value (Wilcoxon signed Rank Test)	**<0.001**			

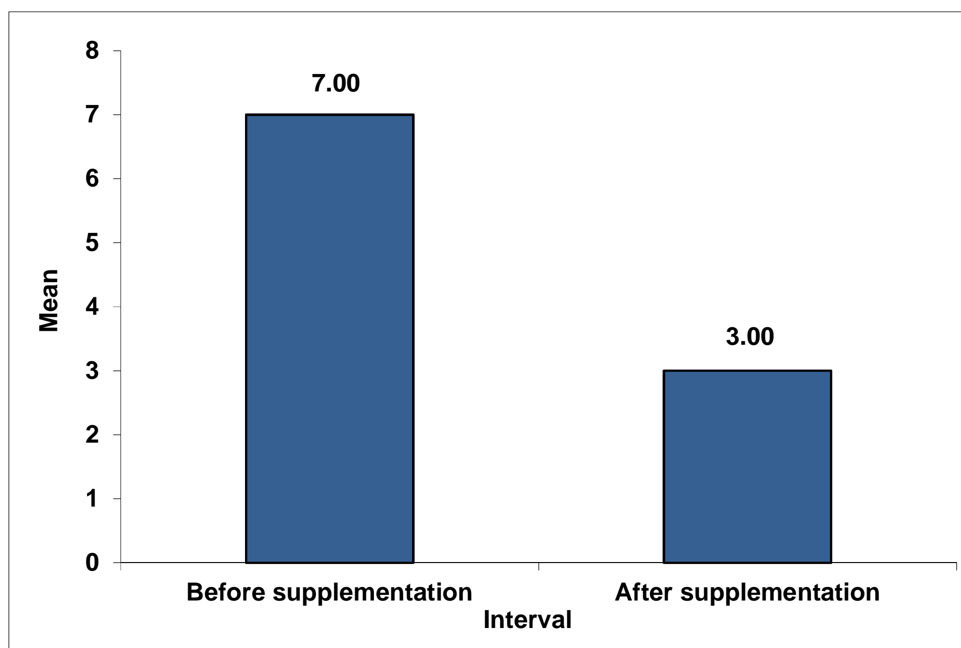


Graph 3. Comparison of IgE levels

Table 5 and Graph 3 shows the comparison of IgE levels before and after intervention with vitamin D is shown. The median IgE levels before intervention was (436.5) and after intervention was (250), which showed statistically significant difference (**p <0.001**)

Table 6 Comparison of TNSS score before and after supplementation

Interval	AEC levels (n=50)			
	Mean	SD	Median	IQR
Before supplementation	7.08	0.75	7	0
After supplementation	3.22	0.55	3	1
p value (Wilcoxon signed Rank Test)	**<0.001**			



Graph 4. Comparison of TNSS score before and after supplementation

Table 6 and graph 4 shows comparison of TNSS score before and after supplementation with vitamin D. Here, the TNSS score before supplementation was 7 and after supplementation was 3, which showed statistically significant difference **(p <0.001).**

Table 7 Descriptive data of the study population

Parameters	Mean (n=50)		Median		Range		*p value
	Mean	SD	Median	IQR	Minimum	Maximum	
Age (Years)	27.98	7.27	28	13	18	46	**0.035**
Total nasal symptom score before intervention	7.08	0.75	7	0	6	9	**<0.001**
AEC levels before Vitamin D supplementation	0.68	0.09	0.7	0.1	0.5	0.9	**<0.001**
Serum IgE levels before Vitamin D Supplementation	472.38	153.09	436.5	192.5	258	1110	**<0.001**
Serum Vitamin D3 levels before Vitamin D supplementation	17.95	4.28	18	7.25	10.8	27	0.241
AEC levels after Vitamin D supplementation	0.39	0.07	0.4	0.1	0.2	0.5	**<0.001**
Serum IgE levels after Vitamin D supplementation	243.6	55.62	250	95.25	127	350	**0.023**
Total nasal symptom score after supplementation.	3.22	0.55	3	1	2	4	**<0.001**

**Shapiro Wilk test for normality*

Table 7 represents descriptive data of the study population. As described in the above tables and graphs a statistically significant difference was noted in mean and median values of IgE, AEC and TNSS score before and after intervention with vitamin D.

DISCUSSION:

More than 1/3rd of the inhabitants of the world are affected by allergic disorders, regardless of age group or geographical location. Various substances can cause allergic disorders, including respiratory allergens, food allergens, skin allergens, and medications. In the development, progression, and management of allergies, many factors have been implicated. These include genetic predisposition, environmental influences, nutritional status, and a variety of biochemical variables. IgE is one such factor that has a well-established role in allergic disorders.[23]

Following cytokine stimulation by interleukin-4 and interleukin-13, the B lymphocytes produce IgE. In allergic situations, IgE is mainly thought to be involved in allergy and anaphylaxis, but it can also be involved in the immune system's functional activation of TH2 cells and wound healing.[24] In allergic conditions, B cells upregulate IgE production, which then leads to class switching of immunoglobulins, i.e., from normal IgG to IgE, when exposed to any foreign particles in mucosa and mucosal secretions which makes them more prone to allergic reactions.[25]

Vitamin D is not synthesized by skin in most cases, due to inadequate sun exposure, hence supplementation is necessary. Along with calcium homeostasis vitamin D is also involved in the regulating the neuromuscular function, cell differentiation, insulin secretion, and blood pressure. Studies reveal vitamin D has immunomodulatory as well as antioxidant benefits. VDR, which are located in the nucleus that control transcription, combine with vitamin D, which in turn controls cell function. Further, the VDR acts on VDRE, which eventually take over transcriptional control of genes [26]

Our study aims to evaluate the influence of vitamin D on IgE levels and AEC count in AR and to assess the symptomatic improvement with TNSS score after vitamin D supplementation. The study was conducted at the Department of ENT and HNS Surgery at jawaharlal nehru medical college, Belgaum. 50 participants were included in the study who were aged between 18 – 55 years. In our study, subjects received 60,000 IU Cholecalciferol weekly along with inhalational corticosteroids for 6 weeks.

In our study, subjects had a mean age of 27.98 ±7.27 years with 70% of patients in the age group 18 to 30 years, 26% in 31- 40 years followed by 4% in 41-50 years. A similar study by Agarwal et al documented that , AR is mostly seen in early adulthood and children while the incidence declines in old age.[18] Halonen et al in their prospective study stated that the decline in serum IgE as time passes probably explains in part the decrease in skin-test reactivity after age 25.[27]

In our study, 25 patients were male (50%) and 25 patients were female (50%) study partcipants with no gender preponderance. In contrary, Agarwal et al in their study mentioned that males were affected with allergic rhinitis as compared to females.[18] A study by Seung-No Hong et al., with 2883 participants stated that the proportion of allergen sensitivity was more in males compared to females (48.7% and 44.1%, respectively; P = .046).[28] Whereas, Kumar N et al in their study showed that the allergic disorders was predominant in, males (62%) than females (38%) with a female : male ratio 1:1.6.[29.]

On assessment of the IgE and AEC levels before and after supplementation with Vitamin D we found a substantial change in the mean scores. (**p<0.001**) The IgE levels before supplementation with Vitamin D was found to be significantly higher

(0.68) compared to that after supplementation (0.39), with significant p value of **p<0.001**. The AEC levels before supplementation with Vitamin D was found to be higher (472.38) compared to that after supplementation (243.6), with significant p value of **p<0.001.** The Total nasal symptom score was found to be significantly higher before supplementation with Vitamin D (7.08) compared to after treatment (3.22), with a significant p value of **p<0.001**, The average serum vitamin D levels were (17.95) in the patients.

Here in our study, the serum IgE levels were found to significantly reduce after supplementation with vitamin D, thus proving their relationship to be inverse. In a similar study by Nukhbat and sohail et al with 224 study participants it was concluded that there is a statistically significant rise in IgE levels in moderate-severe AR when compared to mild AR, and that a vitamin D deficiency is associated with a higher severity of AR symptoms.[(8)] Hence, it is important to measure the levels of vitamin D in AR patients.

In a prospective study done by Halonen et al, it was proved that with increasing IgE, the frequency of eosinophilia increased, and concluded that there was a strong relationship between peripheral eosinophils and serum IgE. They also stated that IgE is an effective diagnostic as well as a promising indicator.[27]

The TNSS score is higher prior to supplementation with Vitamin D (7.08) compared to after supplementation (3.22), with a significant p value of **p<0.001**. In a similar study conducted by P Xiong et al with 59 study participants documented a positive association between interferon and Vitamin D, but a negative connection between total IgE, VAS, and RQLQ scores in the AR group , which shows that the lower the vitamin D level, higher the VAS and RQLQ scores, and hence more severe

the symptoms in AR group.[30] In a similar study done by Gary N at al, with 1176 study participants stated that, significant improvements were seen in the morning and evening TNSS scores thus suggesting daily improvement.[31]

Hence, in this study we have evaluated the impact of serum vitamin D on IgE and AEC levels in patients with AR and assessment of their symptomatic improvement with TNSS score, wherein an inverse relationship between vitamin D levels IgE and AEC is noted, thus indicating its role in immunomodulation, severity and recurrence in AR.

The limitations of the study - were the high cost of vitamin D estimation and the follow up.

CONCLUSION

Despite the recovery of Allergic rhinitis with conventional treatment there is chances of recurrence , recurrence rates varying from 12% to 50%[32]. So in such cases the prevention of recurrence can be obtained by treating the predisposing vitamin D deficiency. The severity and recurrence of AR are correlated with low vitamin D levels [33]. From this study, we found that, significant improvement in serum IgE levels and AEC count were noted after intervention with vitamin D along with symptomatic improvement in total nasal symptom score, thus indicating the immunoregulatory function of vitamin D in AR. Also, a contrasting relationship was noted between vitamin D, IgE and AEC signifying the function of vitamin D in severity and recurrence of AR along with its immunomodulatory role. Thus, vitamin D has a important part in treatment of AR along with INCS and routine testing of serum vitamin D levels must be performed. Correcting the vitamin D levels leads to lower recurrence and severity of AR and its associated symptoms. Further studies with larger sample size can help to determine if vitamin D supplementation can be added to routine treatment regime of allergic rhinitis.

SUMMARY:

This study was conducted in "KLES Dr Prabhakar Kore Hospital, Belagavi during a study period of one year on patients aged between 18 and 55 years with AR attending ENT & HNS outpatient department".

A questionnaire on the history of allergic rhinitis was used to assess individuals presenting to the otolaryngology clinic with complaints of AR. The ARIA classification is used to make the diagnosis, and serum vitamin D levels were assessed in all patients. Prior to the intervention, informed consent is obtained.

For six weeks, the patients were given 60,000 IU of cholecalciferol per week in addition to inhalational corticosteroids (fluticasone propionate, each spray providing 50 mg), and they were then monitored further. TNSS score was used before and after intervention with vitamin D.

The following results were noted:

- The study found no gender preponderance, with a notable increase particularly in the 18–35 age group.
- AEC and IgE levels compared before and after the intervention showed a significant improvement along with improved TNSS score.
- An inverse relationship was noted between Vitamin D, IgE and AEC levels, indicating the function of vitamin D in severity and recurrence of AR along with its immunomodulatory role

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ANNEXURES

ANNEXURE I – CONSENT FORM

EFFECT OF VITAMIN D THERAPY IN ALLERGIC RHINITIS, A ONE YEAR INTERVENTIONAL STUDY IN KLES DR PRABHAKAR KORE HOSPITAL, BELGAUM

Name of Student/Principal Investigator: REG NO: BE0121007

Name of Guide/ Co Investigators:

INTRODUCTION AND PURPOSE:

The present study is conducted among patients who are confirmed cases of allergic rhinitis in ENT & HNS department in KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi to evaluate the impact of vitamin D on IgE and AEC count in allergic rhinitis and to look for symptomatic relief based on TNSS score.

PROCEDURE:

If you agree to participate in this study, the relevant data will be collected as per the proforma and the final diagnosis will be confirmed.

After getting enrolled in the study, you will be evaluated for Serum Vitamin D level.

BENEFITS:

This study may help to benefit in improving the line of treatment of the patients coming with complaints of allergic rhinitis.

RISKS:

Methods applied and the drugs used in the study are safe.

COST OF PARTICIPATION:

The cost of the Investigation will be borne by the researcher.

PRIVACY AND CONFIDENTIALITY:

The results of the study may be published in journals for scientific purposes. However, your identity will not be revealed. All information collected will be coded so that no one other than the investigator will know your identity.

WITHDRAWAL FROM THE STUDY:

You can withdraw from the study at any time if you wish to do so.

AUTHORIZATION TO PUBLISH THE RESULTS:

The researcher may use the information gathered from this study for presentation in scientific meetings.

However your identity will not be revealed.

QUERIES AND CONTACT:

Questions:

If you have any question or complaints with regard to your right as study participant you may contact **Dr Harsha Hegde,** Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

Legal rights: By signing this consent form, we are not waving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision to participate in the study "**EFFECT OF VITAMIN D THERAPY IN ALLERGIC RHINITIS, A ONE YEAR INTERVENTIONAL STUDY IN KLES DR PRABHAKAR KORE HOSPITAL, BELGAUM**". My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name and Signature/ left thumb impression of the participant:

Name and Signature of the interviewer:

Name and Signature/ left thumb impression of the eyewitness (Relative):

Signature of the guide:

Date:

ANNEXURE II – PROFORMA

EFFECT OF VITAMIN D THERAPY IN ALLERGIC RHINITIS, A ONE YEAR INTERVENTIONAL STUDY IN KLES DR PRABHAKAR KORE HOSPITAL, BELGAUM

Date:

O.P. No:

Name:	Age:
Sex:	Occupation:
Address:	Phone No:

CLINICAL PROFILE:

Chief Complaint :

History of Present Illness :

Past History :

Personal History :

Family History :

General Physical Examination -

Built:

Nourishment:

Blood Pressure:

Pulse:

Respiratory Rate:

Pallor/ Icterus/Cyanosis/ Clubbing/Lymphadenopathy/Edema.

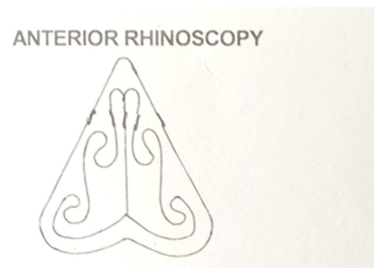
NOSE EXAMINATION

External appearance:

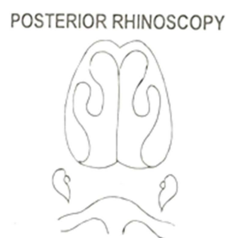
- Root
- Bridge
- Dorsum
- Alae
- Tip
- Columella

Cold spatula test :

Anterior Rhinoscopy :



Posterior Rhinoscopy :



Paranasal Sinus Examination :

2. EAR EXAMINATION:

Right **Left**

Pinna

Pre auricular area

Post auricular area

External auditory canal Tympanic membrane

TUNING FORK TESTS:

Rinne's test 256 Hz

512 Hz

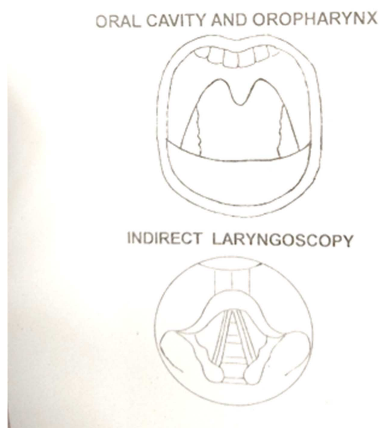
1024 Hz

Weber's test:

Absolute Bone Conduction test:

FACIAL NERVE EXAMINATION:

THROAT EXAMINATION:



ORAL CAVITY:

OROPHARYNX:

4. NECK EXAMINATION :

INVESTIGATIONS BEFORE VITAMIN D3 THERAPY

VITAMIN D3

IgE

ABSOLUTE EOSINOPHIL COUNT

INVESTIGATIONS AFTER VITAMIN D3 THERAPY

IgE

ABSOLUTE EOSINOPHIL COUNT

DIAGNOSIS:

AR History Questionnaire:[34]

1	Do you have parents/relatives suffering from rhinitis and/or asthma?
2	Do you suffer from itchy/red/watery eyes during the year?
3	Do you experience runny nose/nasal obstruction/nasal itching for many consecutive days?
4	Your nasal/ocular complaints do usually start or worsen during the spring?
5	Have you ever heard wheezing breath?
6	Did you ever had cough or shortness of breath, even during exercise?
7	Do you have nocturnal awakenings due to shortness of breath or cough?
8	Do you use nasal sprays frequently?
9	Do you feel that your nasal symptoms worsen in dusty environments?

Y/N answers allowed.

ANNEXURE III – MASTER CHART

SL NO	NAME	AGE	GENDER	IP NUMBER	AEC levels before Vitamin D supplementation	Serum IgE levels before Vitamin D Supplementation	Serum Vitamin D3 levels before Vitamin D supplementation	TNSS before Vitamin D supplementation	Serum IgE levels after Vitamin D supplementation	AEC levels after Vitamin D supplementation	Total nasal symptom score after supplementation.
1	Raju	35	Male	1156343	0.8	448	18	7	305	0.5	3
2	Manjula	36	Female	1156547	0.7	350	19	8	250	0.4	4
3	Suresh	34	Male	1157456	0.9	1110	13.47	9	350	0.4	4
4	Laxmi	30	Female	1157890	0.8	600	19.22	7	280	0.4	4
5	Kamatchi	27	Female	1157836	0.7	700	14	6	300	0.3	3
6	Hridya	29	Female	1161548	0.6	400	15	6	225	0.5	2
7	Suresh	34	Male	1161193	0.6	450	12.47	7	287	0.3	3
8	Sakshi	20	Female	1161511	0.7	800	16	8	310	0.4	4
9	Rasul	28	Female	1162432	0.7	600	18	7	283	0.4	4
10	Rekha	29	Female	1163423	0.8	650	22	7	312	0.5	3
11	Umar	29	Male	1163208	0.6	524	19	7	293	0.4	4
12	Mohammad Iliyas	25	Male	1163199	0.7	450	12	6	243	0.3	3
13	Prema	21	Female	1163401	0.7	500	11	7	300	0.4	4
14	Shankar	33	Male	1164398	0.6	537	15.6	7	197	0.3	3
15	Abhinav	18	Male	6794846	0.8	645	19.8	7	205	0.3	4
16	Megha	22	Female	1157332	0.7	547	14.7	8	267	0.2	3
17	Shwetha	20	Female	6584428	0.8	400	17.6	7	205	0.4	3
18	Najeer	28	Male	1875125	0.7	325	12.7	7	248	0.3	4
19	Farzana Begum	23	Female	1150399	0.6	458	13.5	6	211	0.4	3
20	Sitamma	30	Female	1151202	0.8	360	14.7	7	250	0.5	3
21	Renuka	37	Female	1152304	0.5	650	15.8	7	267	0.3	4
22	Edna	27	Female	1152450	0.6	500	10.8	7	251	0.4	3
23	Sabah	27	Female	1154678	0.7	379	11.38	8	169	0.4	3
24	Kriti	27	Female	1152133	0.8	397	13.2	7	289	0.4	3
25	Isha	28	Female	1151238	0.7	600	14.8	6	291	0.5	3

SL NO	NAME	AGE	GENDER	IP NUMBER	AEC levels before Vitamin D supplementation	Serum IgE levels before Vitamin D Supplementation	Serum Vitamin D3 levels before Vitamin D supplementation	TNSS before Vitamin D supplementation	Serum IgE levels after Vitamin D supplementation	AEC levels after Vitamin D supplementation	Total nasal symptom score after supplementation.
26	Parvati	36	Female	1152676	0.9	633	12.9	7	312	0.5	3
27	Muralidhar	38	Male	1154576	0.6	542	27	7	289	0.4	4
28	Yogita	36	Female	1154657	0.7	600	18.4	7	301	0.5	3
29	Praveen	39	Male	1156980	0.6	550	21.2	7	273	0.4	3
30	Prakash	40	Male	1156431	0.7	421	12.7	6	247	0.3	3
31	Appasaheb	26	Male	1157332	0.6	358	22	7	278	0.4	3
32	Ajay	29	Male	1157412	0.6	422	23	7	194	0.3	3
33	Om	24	Male	1158321	0.7	350	22	7	205	0.4	3
34	Harshitha	38	Female	1005632	0.6	258	26	6	190	0.5	4
35	Sunil	30	Male	10022845	0.8	550	17.7	7	294	0.4	3
36	Subhangi	30	Female	1156786	0.7	322	18.3	8	155	0.4	4
37	Mahesh	41	Male	1159453	0.8	466	24	9	298	0.5	3
38	Rahul	23	Male	10019382	0.7	500	19.2	7	174	0.4	3
39	Siddapa	33	Male	10020345	0.6	322	22	7	153	0.3	3
40	Shivanand	19	Male	1154323	0.6	300	20	6	127	0.4	2
41	Kavya	21	Female	1157654	0.7	356	17	9	245	0.4	3
42	Pooja	20	Female	1156789	0.6	385	19	8	182	0.4	3
43	Sampat	19	Male	10012365	0.6	259	18	7	144	0.3	2
44	Srinivas	18	Male	10010944	0.6	355	23	7	137	0.4	3
45	Jyothi	18	Female	10009013	0.7	370	25	6	242	0.4	3
46	Kamala	46	Female	10008419	0.6	417	21.7	7	294	0.3	3
47	Aditya	16	Male	10008276	0.6	400	23.2	7	279	0.4	3
48	Muralidhar	22	Male	10001171	0.6	336	25.2	7	187	0.4	4
49	Nagadarshan	19	Male	10002724	0.6	342	16	8	214	0.4	3
50	Abhinandhan	19	Male	10002646	0.6	425	19.3	7	178	0.3	3