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Ayurvedic clinical decision-making methods to predict, prevent and manage childhood allergic disorders

K.P. Karthik [a,*], Aparna Dileep [a], S. Rajagopala [b], Mahapatra Arun Kumar [b], Prasanth Dharmarajan [c], Jessica Vellela [d]

[a] All India Institute of Ayurveda, India
[b] Department of Kaumarabhritya, All Institute of Ayurveda, India
[c] Department of Panchakarma, All Institute of Ayurveda, India
[d] AYU Academy, Plano, TX, United States

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ABSTRACT

Allergy is a conundrum lacking satisfactory answers despite its global prevalence. Traditional systems of medicine may contain sustainable and effective solutions for the same. For mainstreaming them, an evaluation based on the system's own methods is inevitable rather than symptom-based correlations. Atopy is a novel entity in Ayurveda, but the methods of tripartite delineation (disease pattern, disease targets and influencing factors) of novel diseases and multifactorial approach to diagnosis and management in Ayurveda can bring about comprehensiveness in collection and categorization of data regarding the entity. This in turn can make the prediction, prevention and management of the same more precise, effective and sustainable. The article provides a template for the application of Ayurvedic biological framework in the diagnosis and management of novel diseases, with special reference to childhood allergic disorders.

1. Introduction

Allergy is a state of altered reactivity to stimuli, especially certain antigens. Stimuli that do not elicit any clinical presentation in normal subjects create clinical symptoms by triggering pathogenic pathways in allergic individuals. Globally, the most prevalent forms of allergies are allergic rhinitis (approximately 400 million people) and asthma (approximately 300 million). According to epidemiological studies, the worldwide prevalence of allergic disorders is on the rise. The number of premature deaths resulting from asthma worldwide is 250,000, despite many being avoidable. Anaphylaxis varies from 1 to 761 in 100,000 person-years globally [1]. Urticaria is prevalent in 1832 among 1,00,000 children globally [2].

The conventional pharmacotherapeutic approach to allergic disease has been able to provide symptomatic relief, but they rarely address the root cause or arrest the pathological progression. Allergy immunotherapy, a novel approach that is considered relatively more effective, is also not free from limitations, as systemic allergic reactions, occasional anaphylaxis, and even fatalities have been reported as adverse effects. The relative contraindication of immunotherapy in multiple groups like pregnant women, children below 5 years, subjects with existing medical or immunological disease, subjects receiving beta-blockers, etc. has also hindered its universal applicability. It is at this crossroads that effective, safe and sustainable solutions become the goals of medical intervention. These goals are inherent in Ayurvedic Medical management, however they may be perceived to be attainable only at the expense of convenience of the patient [3].

Ayurveda is a stream of knowledge in which there exists a theoretical, systematic, and scientific framework that facilitates effective diagnosis and management of existing and new diseases. The modus operandi for approaching new conditions has been laid down in classical literature. A novel disease must be analyzed based on three essential components: Disease patterns (*vikaara prakrti*), disease targets in the body (*adhishthana*), and factors influencing the disease (especially etiological ones, *hetu*) [4]. These components connect across eleven domains namely, *dushya* (body tissue), *desha* (habitat), *bala* (strength-of patient and disease), *kaala* (period), *agni* (digestive power), *prakrti* (Baseline constitution), *vaya* (age), *satva* (mind), *saatmya* (conducive

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* Corresponding author.
E-mail address: kpkarthik131@gmail.com (K.P. Karthik).

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factors), *ahara* (diet), *avastha* (stage) [5], requiring the analysis throughout the larger framework. This exercise allows a precise and complete understanding of any disease for effective management. Drawing parallels between a novel disease and a similar Ayurvedic description based on comparison of symptomatology alone is not a valid approach in scientific Ayurvedic methodology. This article endeavors to analyze the full spectrum of allergic disorders in terms of the components mentioned above to yield a clinical decision-making tool that can predict, prevent, and give precision intervention at appropriate times.

2. Review of literature

The knowledge available in the Ayurvedic texts are in the form of a "tree inside a seed". The seed contains all parts of a tree, but in a miniscule form. To help a seed grow into tree, inputs like sunlight, water and soil are required. Similarly, the wisdom in Ayurvedic literature also must be augmented using current observations and experiences.

Concepts and observations were collected and documented from multiple sources through observational studies, interventional studies, and review articles, primarily from the databases PubMed, ScienceDirect, Scopus and Google Scholar from 1960 to 2022. Articles from both Western biomedicine and Ayurveda were considered. Ayurvedic texts, especially the greater triad were researched and analyzed for symptoms, targets, and pathological processes like that of allergic disorders. Concepts and opinions of experienced Ayurvedic clinicians were gathered from various seminars, group discussions and conferences and practitioners regarding the possible pathogenic processes involved in allergic disorders. The keywords used for searching were "childhood allergy", "childhood allergic disorders", "immunology", "allergic rhinitis", "asthma", "pediatric eczema", "childhood onset asthma", "pediatric atopic dermatitis", "pediatric urticaria", and "anaphylaxis". The terms were coupled (AND command) with "pediatric" and "childhood" for relevant results. Subdomains of interest like tissue, organ, system, genetical make-up, gut, bowel, etc. were also added to the keywords during search. The manuscripts received were filtered based on relevance to the topic, availability of the full text, and timeline of the manuscript.

The data collected were categorized under three main domains (targets, patterns, and influencing factors) and their subdomains. The subdomains are constituted by the extrapolations of the eleven factors mentioned by *Vagbhata* (classical author) for the assessment of *dosha* (bioregulator) and *aushadha* (medicine without side effect) (Fig. 1).

3. Observations

3.1. Patterns

An individual's external stimuli, diet, and habits are classified according to their wholesomeness (*pathyatva*) and the individual's ability to habituate to it (*satmyatva*). Diets and habits which are regularly wholesome and habituated lead to better individual health. Those which are not initially wholesome but are gradually and judiciously habituated can become harmless to the body. Certain stimuli are unwholesome and cannot be habituated. These promote pathogenesis unless the individual's immunity is strong enough to overcome it. In certain individuals, stimuli that are generally tolerated, initiate an immune response, indicating an inability in them to habituate to these stimuli. These stimuli are considered allergenic as they provoke an immune response and subtle yet clinically detectable symptoms. An individual's impairment in habituation can be attributed to genetic and epigenetic mechanisms.

Unhabituated stimuli lead to a weakening of the digestive and metabolic mechanisms of the body (*agni*) which renders the person vulnerable to illnesses from further exposure to the same or other stimuli. In parallel, the impairment of metabolism leads to the genesis of ill-formed metabolites (*ama*). The persistence of these metabolites gradually confers them a toxic nature (*amavisha*) [5], bifurcating into two possibilities: one similar to a mild, slow-acting toxin (*dushivisha*), and the other, similar to severe acute acting one (*ashukari visha*). The former shows a biphasic nature. There is a latent phase wherein it

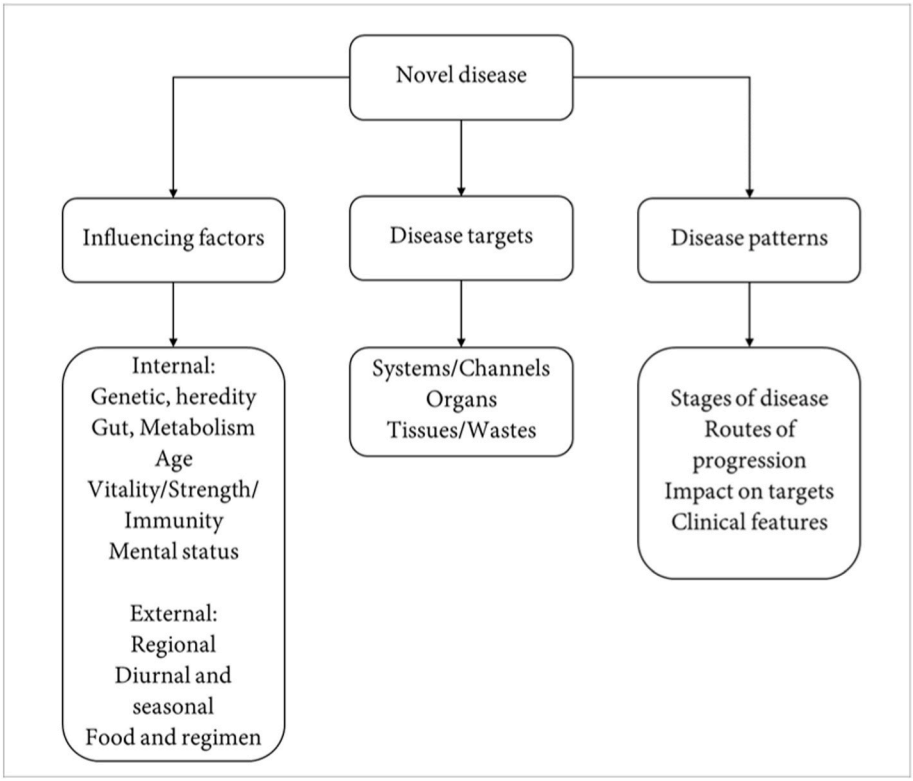

Fig. 1. Ayurveda's approach to novel disease.

remains silent or latent through diet, regimen, season, and immunological factors (*leena avastha*). When conditions shift to favor the pathology, it expresses its features [6] which may lead to the severe acute condition mentioned above. The clinical features and sites of manifestation present by favoring vulnerable sites of the body first (*kha-vaigunya*) [5]. These weak sites develop over time from cumulative damage of previously encountered stimuli (Fig. 2).

Many of variegated manifestations of allergy can be observed in the mentioning of *dushivisha* and localized *visha* in Ayurveda. Urticaria (*kotha*), anaphylactic reactions (swelling of mucosa (*aasyashopha*), unconsciousness/dizziness (*moha/murccha*), obstruction of throat (*galagraha*)), discoloration (*vaivarnya*)) [7], features of atopic dermatitis (erythema (*mandala*), pruritis (*kandu*), signs of blood vitiation (*rakta-dushti*)) [8] asthma (dyspnea (*śvaasa*), cough (*kaasa*)) [9] are examples [5,6].

3.2. Targets (Dushya)

Targets of allergic disorders were identified at three levels: exudative networks of channels (*srotas*), formed organs (*avayava*), and tissue pools (*dhatu*).

On examining the āyurvedic literature for the symptoms and pathological processes resembling allergic disorders, it was seen that this disease pattern displays specific affinity to the first and second tissue systems (*rasa* and *rakta dhatus)*, the organs of the skin , lungs , and structures above the clavicles (*jatrurdhva avayava*), and the waste products, stool (*purisha*), urine (*mutra*) and sweat (*sveda*).

Components of the body that are primarily liquid are often implicated in allergic disorders when they are aggravated by causative stimuli. Subsequently, these further degrade the integrity of fluid compartments in the body (*kleda*). Two common examples can be seen in the urine which is responsible for eliminating moisture from consumed food and sweat which checks moisture loss [5].

The exudative networks of channels (*srotases*) involved in allergic disorders include vital force *(praana),* food nutrient (*anna),* feces (*purisha),* aqueous component of body (*udaka),* sweat (*sveda),* urine (*mutra),* body component with nutrients and essence (*rasa*), and blood tissue (*rakta)*. The deeper *dhaatus* (bio-element), their *srotasas*, and the pathways of disease (*rogamarga*) including vital points (*marmas*) are seldom affected, except in life-threatening conditions like anaphylaxis (Table 1).

The identification of the skin-gut-lung model in conditions like atopic dermatitis also demonstrates the validity of this model. The impaired epidermal epithelial barrier acts as sites of allergen sensitization and also triggers a systemic TH2 response leading to epithelial dysfunction in the intestinal and respiratory tract epithelia. This leads to the manifestation of atopic march [17]. The relationship between the skin, respiratory system, cardiovascular system and gut are evident in conditions like anaphylaxis.

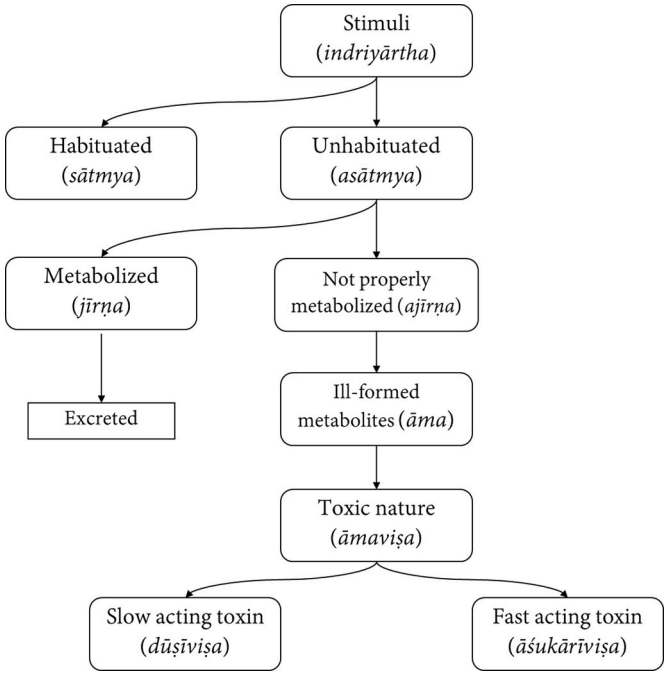

Fig. 2. Disease pattern and pathogenesis of allergy according to Ayurveda.

3.3. Influencing factors

3.3.1. Baseline constitution (Prakriti)

3.3.1.1. Genetics. *Prakriti* is the innate, inherent level and proportion of *doshas* and their presentations in an individual. Even though this baseline state of *doshas* indicates some level of inherent derangement, it does not directly produce disease [5]. Understanding the role of *Prakriti* in health and disease has improved in the light of recent advances like Ayurgenomics [18]. *Prakriti* influences inter-individual variations on several levels:

- Genetic material constitution
- Genetic expression characterized by anatomical and physiological peculiarities
- Physiological processes characterized by response to stimuli, biochemical markers
- Susceptibility to disease
- Severity, prognosis, and response to treatment

The three single-predominant *dosha prakritis* are *vata*, *pitta*, and *kapha, which* vary on several bases, especially in terms of their digestion and metabolism (*agni*) and strength (*bala*).

In studies involving comparison of *prakritis* for immunological aspects, each *prakriti* exhibited varying functions. The genes involving innate immunity were expressed more in *pitta prakriti*, whereas those pertaining to adaptive immunity were more expressed in *kapha prakriti*, likely due to their corresponding baseline levels for digestion, metabolism and strength. In pitta *prakriti* individuals, their naturally strong

Table 1
Disease targets in allergy with supporting evidence

Exudative networks of channels	Formed organs	Tissue pools, Metabolic wastes	Correlating evidence
Praana	Lungs, organs above clavicle	–	Directly involved in asthma, allergic rhinitis, allergic conjunctivitis
Rasa	Heart	*Rasa*	Whole body involvement (Rasa), Anaphylaxis (*Hrdaya*)
Rakta	Skin	*Rakta*	Dermatitis
Anna, Purisha	Gut	*Purisha*	Constipation and increased risk of asthma [10], atopic dermatitis [11] and atopy [12] in children. Association of functional gastrointestinal disorders and atopy [13].
Mutra	–	*Mutra*	Overactive bladder associated with allergy in children [14]. Urine Metabolomic analysis in allergic rhinitis patients differentiating between pre-challenge post-challenge values, severity [15].
Sveda	–	*Sveda*	Sweat allergy in patients of eczema, cholinergic urticaria [16]
Udaka		*Kleda, Lasika*	Thirst – Histamine cycle

digestion and metabolism (*tikshna agni*) can overcome infectious agents. In *kapha prakriti*, their high level of baseline strength (*uttama bala*) allows them to retain a high level of resilience even after consuming foods that are bitter, spicy, and astringent which would normally reduce strength. This lays the foundation of the hypotheses that *prakriti* can help delineate the inter-individual variations in disease susceptibility, especially in infections, atopy, and allergic reactions.

In addition, some evidence suggests variations in clinical manifestations of the same allergic pathogenesis between individuals of various *prakriti*. For example, *pitta prakriti* individuals are more likely to develop reddish discoloration of the sclera [5]. *Vaata prakriti* individuals are more susceptible to epidermal and intestinal epithelial barrier dysfunction due to their inherent dryness (*ruksha guna*) which likely predisposes to the initiation and progression of atopic march. *Prakriti* also plays a considerable role in determining the prognosis and response of a disease to therapeutic intervention.

The predisposition to atopy and asthma and their expression involves polygenic interactions and multiple polymorphisms. About 100 genes have been understood to be involved in their pathogeneses [19]. A deeper and detailed understanding of their *prakriti*-wide distribution can facilitate prediction of allergic diseases and their likely course in the clinical setting. The following examples of genes have been extensively studied for association with allergic diseases and may be further studied within the Ayurvedic framework (Table 2).

3.3.1.2. Inheritance. Ayurveda considers the soft tissues and organs are to be inherited predominantly from the maternal side [5]. As allergic disorders primarily pertain to soft tissues, presence of allergy on the maternal side is more likely to affect the child than that on the paternal side. This is substantiated by contemporary research [22].

3.3.2. Geographic region (Desha

The impact of one's geographic region on individual health is assessed in three levels.

1. The seasonal variations of the region
2. The diet and regimen appropriate for the region
3. The diseases prevalent in the region [23].

On examining the studies conducted on the distribution of prevalence (per 1 lakh of population, or 100,000) of allergic diseases in India on a geographical basis, it has been observed that the states Kerala, West Bengal Tripura, and Mizoram had 3000-4000, while the states of Andhra Pradesh, Orissa and Arunachal Pradesh had a prevalence ranging from 2000 to 3000. The remaining states had the prevalence of allergic diseases below 2000. The species and genus of potential allergens (and in cases where they could not be specified, families) commonly seen in the North, East, West and South zones of India have also been identified. In the North zone, Asteraceae, Arecaceae, Amaranthaceae and Poaceae were the reported families producing pollens. The species reported were *Putranjiva roxburghii* Wall., *Holoptelea integrifolia* Planch., *Ricinus communis* L., *Cedrus deodara* G. Don, *varieties of Cassia*(*Cassia fistula* L., *Cassia occidentalis* L., and *Cassia tora* L), *Quercus, Eucalyptus,* etc. In the other zones, the families observed were almost same, except that in South and Central zones, Cyperaceae was seen in addition. The species seen in East zone were *Madhuca indica* J.F.Gmel, *Areca catechu* L., *Cocos nucifera* L., *Pongamia pinnata* (L.)Pierre, *Borassus flabellifer* L., *Azadirachta indica* A. Juss, *Phoenix sylvestris* (L) Roxb., etc. In South, *Cocos nucifera* L., *Casuarina equisetifolia* L., *Parthenium hysterophorus* L., *Spathodia campanulata* Beauv., varieties of *Eucalyptus*, etc. were seen. *Moringa oleifera* Lam., *Azadirachta indica* A.Juss, *Parthenium hysterophorus* L., *Prosopis julifera* (Sw.) DC., *Casuarina equisetifolia* L., *varieties of Eucalyptus and Sizygium,* etc. were noted in West zone. *Argemone mexicana* L., *Cocos nucifera* L., *Ricinus communis* L., *Ailanthus excelsa* Roxb., *Holoptelea integrifolia* Planch., *Cicer aurietinum* L., Hibiscus and Rosa varieties, etc. [24].

Table 2
Genetic basis of allergy; SNP- single nucleotide polymorphism, IL4- Interleukin 4, IL13- Interleukin 13, Th2-T helper 2, ORMDL3- Orosomucoid like 3

Chromosome	Gene	Allele/SNP	Role
1q21	Filaggrin	R501X/ 2282del4/ Combined	Atopic dermatitis/ Atopic dermatitis, Asthma, Atopy/ Peanut allergy [19]
5q31-33	IL4 and IL13 production by Th2 lymphocytes	IL13 Arg130Gln and IL4 C-589 T	Atopic dermatitis and atopy at 24 months [20]
5q31.3	IL13	arg130-to-gln (R130Q)	Susceptibility to Allergic rhinitis [19]
17q21	ORMDL3 (Endoplasmic reticulum protein, Sphingolipid homeostasis)	rs7216389	Pediatric age onset childhood asthma [21]

3.3.3. Strength, vitality, immunity, resilience (Bala)

Bala is a term that has been explored in Ayurveda in various dimensions. It is often used in the meaning the ability to carry out physical activities, vitality, immunity, etc. It is considered to be three-fold. One is the manifestation of genetic make-up. The *bala* imparted by the genetic make-up can partially be explained by the *prakrti* of the individual. Another aspect of *bala* is that which is imparted by the season, which is due to the factor of time *(kaala)*. The last and most influential factor is the total of one's diet and regimen. A person interacts with the surrounding season, stimuli, and actions through food, sleep and other physical activities. These components fall under *aahaara* and *saatmya* [5].

3.3.4. Time, transformation and season (Kala)

Seasons and their region-specific patterns were found to exert influence on total and differential incidences of allergic disorders. Unified seasonal profiles of allergies are unavailable in children. Childhood asthma had its peak in winter and spring and nadir in summer irrespective of their subtype [25]. AD primarily exhibits bimodal exacerbations throughout the year, i.e., in the winter and summer. Infantile AD: 67.14% (W), 23.36% (S). Childhood AD: 58% (W), 32.92% (S). In an Indian study where 505 adults were sensitized to allergy, 94 were sensitized in the months of November to December 2017, 54 in January to February 2018, 86 in March to April 2018, 93 in May to June, 80 in July to August, and 98 in September to October. Common allergens occur during specific times, including dust mites (20.82%) and dust (12.49%) in November to February (winter season), pollen (17.49%) in March to June (summer season), and fungi (4.9%) and insects (5.83%) in July to October (rainy season) [26]. The predominance of tree pollen in dry winter and grass and weed pollen in the summer in Mexico demonstrates regional variations in the seasonal allergen prevalence and necessitates region-specific research and documentation. Species-wise data on seasonal pollination or spore shedding patterns of potential aeroallergens are also available [27].

3.3.5. Digestion and metabolism, and the GIT (Agni and Koshtha)

The structural and functional integrity of the gut is a significant yet often overlooked component in allergic disorders. Children suffering from constipation were 2.36 times more likely to develop asthma and 2.31 times more likely to develop atopic dermatitis compared to the general population [10,11]. The presence of constipation doubled the risk of allergic rhinitis in adults [28]. The study postulates mechanism of constipation inducing allergy as a fall in the gut population of *Bifidobacteria* and *Lactobacilli* and altered gut permeability leading to hypersecretion of inflammation-promoting biomarkers such as chemokines and cytokines [28]. Additionally, the co-existence of diabetes, hypertension, IBS, and several other disorders were found to increase the risk

of allergic rhinitis in constipation patients. The alleviation of constipation was found to restore the impaired gut flora and hence, reverse the pathogenesis [29]. General atopy in children did not associate with constipation, though conflicting evidence is seen in this aspect [12].

The relation of allergic disorders to the gut is not confined to constipation alone. Early life exposure to laxatives was associated with the development of allergic disorders. A study cross-sectional study conducted among 23,471 subjects in the UK demonstrated a statistically significant overlap between functional gastrointestinal disorders (irritable bowel syndrome, functional dyspepsia and constipation) and atopy (especially characterized by four diseases, asthma, eczema, allergic rhinitis and conjunctivitis) and it was partially explained by their common connection with mood disorders [13].

3.3.6. *Age (vaya)*

Within the childhood age group, there are variations in causes, triggers, and manifestations of allergic conditions. The age of the patient is an important consideration in identifying possible etiological factors. Previous studies have proven a decline in physical activities in early adolescence. The age group 6–12 years are proven to be more sensitized to allergens and exhibits symptoms in increased grade. Thus, the factors: increased locomotor activities and age make the 6 to 12 age group susceptible to higher risk of exposure towards the inhaled allergens [30,31]. Childhood asthma was most prevalent in 10–12 years [25]. Atopic dermatitis showed no age-group specific clustering (12.1% in 6 months to 6 years, 13.0% in 6–12 years, and 14.8% in 12 years–18 years) [32]. Hen's egg white allergy and cow's milk allergy express their onset in the first year of life, and among them, 75% of the former resolve by seven years, and the latter by five years. Peanut and tree nut allergies were often seen in children in the second year, but they were persistent with 25% or fewer cases resolving. The onset of wheat and soybean allergies usually occur during weaning, 6 months to 2 years. The soybean allergy usually subsides by 2 years and the wheat allergy usually takes more time, subsiding by around five years. Hypersensitivity to fish, shellfish and fruits like apple, carrot, kiwi, etc. have their onset in late childhood and adulthood, with unknown resolution period [33]. In India, the third phase of the International Study of Asthma and Allergy in Children (ISAAC) states that 7% among Indian children within the age groups 6–7 and 13–14 years currently experience wheezing. The prevalence of eczema in these groups is 2.7% and 3.6% respectively. Food allergies were found to be comparatively lower, seen in 0.14% of children ranging from 6 to 11 years. Allergic rhinitis, as recorded by another study, was prevalent in 11. 3% of the children aged 6–7 years, and 24.4% of the children aged 13–14 years [34]. Acute urticaria was more prevalent in the 1–5 years age group [35]. The age wise prevalence of allergic disorders have been given in Table 3.

3.3.7. *Determination, Mental state, and temperament (Satva)*

The mental state of an individual, both congenital and acquired, plays an important role in the incidence as well as exacerbation of allergic diseases. This is the reason why the mind-body issues in allergic disorders have been a genre subjected to extensive research. Stressful stimuli in both prenatal and postnatal life are potential influencers of immune responses in childhood and adulthood. Maternal stress in the prenatal period was found to be associated with increased production of IL-8 and TNF-α on exposure to microbial stimuli, and increased IL-13 production on stimulation using dust mite and reduced phytohemagglutinin-induced gamma interferon, denoting impairment at both the levels of innate and adaptive immunity. Atopic immune profile in children who had a positive family history of atopy was found to be more incident in those exposed to early childhood stress [36].

In Puerto Rico, where violence and asthma are highly prevalent, a case-control study conducted among 516 children from 6 to 14 years revealed that violence led to the methylation of a CpG site in the promoter (cg11218385) of adenylate-cyclase activating polypeptide 1 receptor (ADCYAP1R1) which in turn led to asthma in children [37]. In the Indian scenario, food allergy was found to coexist with attention deficit hyperactive disorder (ADHD), anorexia nervosa, and generalized anxiety disorder [38,39]. Chronic urticaria with hypocortisolism in adults had a significant positive correlation with stress scores Presumptive Stressful Life Events (PSLE) and Daily Hassles and Uplifts Scale-Revised (DHUS-R) [40].

Table 3
Agewise prevalence distribution of different allergies in children.

Allergic condition	Prevalence: 6–7 years	Prevalence: 13–14 years
Allergic rhinitis	11.3%	24.4%
Asthma	7%	7%
Eczema	2.7%	3.6%
Food allergy	Prevalence: 6–11 years → 0.14%	

Source: Mahesh, PA, Moitra, S, Mabalirajan, U et al. Allergic diseases in India – Prevalence, risk factors and current challenges. *Clin* Exp *Allergy*. 2023; 53: 276–294. doi: 10.1111/cea.14239

3.3.8. *Habituation, adaptation (Satmya)*

Ayurveda describes the practice of habituation wherein a subject is administered an allergenic stimulus in harmless doses repeatedly to develop tolerance. There is a similar hypothesis in Western biomedicine that is not universally accepted but is widely valid, called the hygiene hypothesis. Some infectious agents that have evolved with mankind protect against allergy and auto-immune mechanisms. Hence, the current rise of allergic disorders in developed and developing countries is likely attributable to microbial deprivation [41].

3.3.9. *Dietary factors (Aahara)*

Ayurvedic texts describe the properties and actions of many prevalent substances of the period. The attributes described are assumed to exist under ideal circumstances to produce efficacy. When applied in a real-life situation, multiple factors complicate their use and expected outcomes, including dosage, timing, preparation, administration, geographical area, bodily constitution, state of *doshas* and other related factors [4]. Ayurveda acknowledges dynamic life mechanisms and establishes that dietary recommendations are required to optimize therapeutic outcomes. These recommendations must be personalized to account for many factors described previously.

The primary guideline for a healthy diet is diversity in flavors and digestible constituents. Meals should include all six flavors with a predominance of sweet (*madhura rasa*) [5]. Additional factors including eating speed, frequency, surroundings, status of mind, manners, etc. also directly determine the resultant effect of food on the individual's health or disease [4]. Derangement in these factors hampers metabolism thus furthering the pathogenesis.

In the context of allergic disorders, contemporary research has also recognized the relevance of diet and dietary habits. Research conducted among 5257 parents in the UK reported lower risk of wheezing or shortness of breath associated with wheezing in children who consumed fruits, tomatoes, and cooked vegetables. At the same time, consumption of bread, butter and margarine caused an increased risk of these symptoms [42]. A study conducted with 856 children to understand the relationship between feeding practices and allergic disorders showed that a high food diversity in the first year of life had a protective effect against asthma, food allergies and food sensitization [43]. It was also found to be associated with an increased regulatory T cell marker. The Guidelines for Atopic Disease Prevention (GLAD-p) currently acknowledges prebiotics as dietary supplements for infants due to their potential preventive effect against asthma and food allergies, and probiotics as preventive and therapeutic components in allergy management. This again signifies the importance of diet and its role in preventing and managing allergic conditions [44]. Dietary habits like meal frequency have been found to have significant impacts on metabolism [45]. These should be analyzed in the context of allergic disorders.

4. Discussion

The review analyzes the nuances in allergic disorders through the lens of Ayurvedic parameters used for understanding novel diseases. Some of them like *desha, kaala, vaya, agni, koshtha,* etc. have well established relation to the diseases whereas those like the research works exploring the parameters *prakrti, saatmya*, etc. are in their infantile stage.

The soft tissues, i.e., the initial *dhatus* are more vulnerable to atopic manifestations. The identification of target involved streamlines the etiology and risk factors (specific to the vitiation of the substratum). *Prakrti* has predictive potential in disorders including allergy but needs further research to be of better translational value. Caraka's delineation of *prakrti*-specific response to *viṣas* may throw light on this aspect. Ayurvedic literature describes the features of moist, damp regions (*anupa desha)* as situated near oceans or water bodies, possessing plants coming under the families of Arecaceae and Poaceae. These regions are generally not conducive to health [4]. This observation holds well in the case of allergic disorders as well. Poaceae consists of the globally leading aeroallergens [46]. Winters, springs, and rainy seasons are the exacerbators of *dushivisha*, which correlates with the seasonal peak of asthma and atopic dermatitis. Rainy seasons promote proliferation and winds promote the circulation of aeroallergens [47]. Season of birth was also observed to influence allergic predisposition. Children in Boston born in the fall or winter presented with higher food allergies [48], denoting the role of birth time in determining the *bala* of an individual [4]. Constipated gut (*krura koshtha*) is positively associated with allergy. This is probably due to the hampering of the body's self-cleansing mechanism. The body expels the impaired metabolites. If this process is interrupted, it is to be corrected with digestive (*pachana*) or eliminative (*shodhana*) drugs [5].

Age division among pediatric groups is broad in Ayurveda attributable to the dynamic physiology in children. The divisions in the later texts like *Arogyakalpadruma* (11 age groups from *jatamatra*) are more posology-oriented and have scarce descriptions, hence of limited utility in drawing clinical assumptions. But the age factor remains a strong predictive component in pediatric allergies.

The utility of each of these concepts in prediction, prevention, and precision management approach towards allergic disorders are as follows. Most parameters have multiple utilities, but predominant targets in each utility (prevention level) have been mentioned along with stagewise interventional strategies (Fig. 3).

4.1. Prediction

Parameters like *prakrti, koshtha, agni,* and *vaya* are predictive of vulnerability and course of the disease and resultant manifestations in an individual. Prediction at every stage facilitates corresponding intervention.

4.2. Prevention

4.2.1. Primordial

Diet, and habits related to diet and regimen are critical in the prevention of risk factors. Current dietetics focus primarily on the food content, but Ayurveda lays down guidelines regarding its method of intake as well. Early life sensitization to various stimuli are also part of Ayurvedic primordial prevention. The *samskaaras* (rites at various stages of life) mentioned in Ayurvedic pediatric treatises probably encompass this component. The administration of honey in ghee is advised in

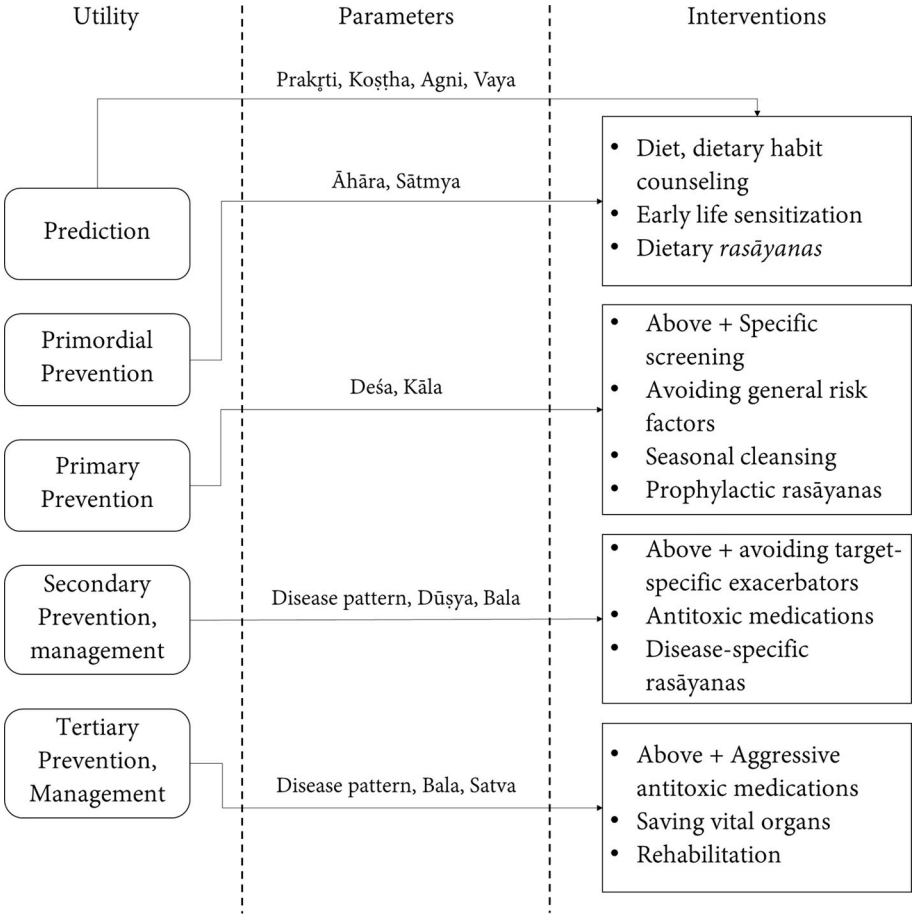

Fig. 3. Utilities of Ayurvedic parameters and corresponding interventional strategies. Source: Original.

subtherapeutic doses in neonates at Indian birth rites (*jatakarma)*. Honey is a source of pollen, and a potent immunostimulant [49]. It's immunostimulant action is coupled with its addition of ghee (which is incompatible in equal amounts with honey: *matraviruddha*) [4]. The consumption of dietary rejuvenative formulations (*ajasrika rasayanas*) are also part of primordial prevention measures.

4.2.2. Primary

In subjects who have encountered risk factors, the geographic region and season are tools that help prevention. In them, early screening based on identified risk factors and prophylactic measures to counter the effects of *desha* and *kala* are to be taken (cleaning of dust, removal of indoor moisture, etc.). Prophylactic body cleansing (*rtu shodhana*) suitable to the age group, a major step in this phase, has multiple documented benefits [50].

4.2.3. Secondary

Once symptoms have manifested, interventions become a major priority and here, the disease pattern, target involved, and the resilience of the body are important tools.

The understanding of '*visha*' disease pattern as a basis for allergic pathogenesis increases the management options like *Vilvadi Gutikaa, Patolakaturohinyadi kwatha, Dushivishri agada,* etc. in the management of these conditions, which would otherwise be symptomatic. These formulations have been used in management of allergic and autoimmune diseases with the same principle [51,52]. This knowledge coupled with that of the targets help in choosing antitoxic drugs (*vishahara*) specific to the substratum involved. E.g.: *Hemidesmus indicus* Hook.f. in disorders of blood (*rakta*), *Curcuma longa* L. in diseases of adipose tissue (*medas*). The strength of the body and disease also influence drug choice. The therapeutic regimen also varies according to the target involved. Exacerbators (like exposure to substrate-specific risk factors, seasonal triggers, etc.) are to be avoided in this stage.

4.2.4. Tertiary

Rehabilitation, prevention of damage to vital organs, sustaining the vital functions, aggressive symptomatic and antitoxic management are the priority of the same. The evidence pertaining to the same is modest in Ayurveda.

4.3. Precision management

Āyurveda lays emphasis on precision than protocols. Even patients suffering from the same disease exhibit different constellations of symptoms due to difference in the above factors [53]. This perspective recognizes unique domains that must be considered in therapeutic intervention. Antitoxic drugs and substances (*visha-hara*) shall be of special interest considering the pathogenesis explained. Understanding the site of origin and disease progression aids precise management. For example, in atopic march triggered from an impaired skin epithelial barrier, medicated oil may be used externally with drugs enhancing epithelial integrity administered internally.

The Ayurveda concept that disorders are generated by inappropriate habituation (*saatmya-asaatmya janya*) explains not only allergies, but also several other disorders, namely auto-immune diseases. The model also provides directions and possible guidance for future diseases. The inter-*prakrti* variations based on predisposition and clinical presentation are examples. In spite of these strong foundations, there are limitations in understanding and explaining the complex variations in presentation without detailed knowledge of genetic and epigenetic mechanisms. Epigenetic mechanisms that modify gene expression may be protective or pathogenic. Differentiating these mechanisms is a challenge in predicting an individual's predisposition or pathological progression. Additional variations in disease presentations vary from region to region and time to time. Hence, a universal protocol for diagnosing and managing all allergic disorders is not possible.

4.4. Limitations

The review only considers the most prevalent allergic disorders. Rare allergies have been omitted from the review due to extensiveness of the domain. Lack of data specific to children has been a significant challenge. This article depends on research works considered outside Ayurvedic fraternity, hence there is often lack of coincidence between study outcomes and Ayurvedic parameters (for example, lack of direct correlate of *agni* as a parameter). Review does not consider two of the three minor pillars of life (*trayopastambhas*, i.e., sleep and physical activity despite their probable role in atopy. Divergent views are compiled in the work, and consolidating them into questionnaires, proformas, and addressing the research gaps has been deferred, which is a scope for future works. Specific considerations in Ayurvedic view with regards to pediatric allergy is an area of multiple possibilities.

5. Conclusion

Ayurvedic parameters for approach to novel diseases can aid predictive, preventive, and interventional strategies against childhood allergic disorders. Predictive tools, novel screening criteria, unique therapeutic considerations, and personalized prevention and management are the strongholds in the approach that can contribute to the emerging vision of P4 medicine [54]. The approach comprehensively collates data on the disease and can be extrapolated to other pathologies as well. The information exchange can be mutual, i.e., Ayurvedic principles like age can also be fortified by taking inputs and insights from biomedical research. The evidence gaps identified in the review put forward potential areas for research in the future.

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Author contributions

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Ethical considerations

None of the steps involved participants or animal models, hence ethical considerations not applicable.

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Declaration of competing interest

None.

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