

Review Article

Finding the Causes of the Concretion Between Asthma and Urticaria: A Narrative Review

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Abstract

In recent years, asthma and urticaria have become more common globally, imposing a significant economic and health burden on communities everywhere. Th2 cells, mast cells, eosinophil and M2 macrophages are all part of type-2 immune response, which is characteristic of many forms of allergy and asthma. Biomarkers are essential for precision medicine because of the clarity they provide in the identification of disease endotype, clusters, specific diagnoses, therapeutic target selection and the tracking of therapy effectiveness. Accurately measuring the biomarkers requires a variety of tools, including dependable point-of-care systems. It is preferable to collect samples in a way that is both quick and non-intrusive. In recent years, researchers have placed a premium on identifying novel biomarkers of allergic diseases and asthma. There are a number of intriguing markers of urticaria and asthma, including eosinophils, immunoglobulin E (IgE), interleukin and vitamin D insufficiency. The latest findings on the biomarkers associated with asthma and chronic urticaria are summarised in this article.

Keywords: Asthma; Urticaria; Eosinophils; Vitamin-D; IgE

Abbreviation

BAFF: B-cell-Activating Factor; CU = Chronic Urticaria; CSU: Chronic Spontaneous Urticaria; DC: Dendritic Cells; EDN: Eosinophil-Derived Neurotoxin; IL: Interleukin; Ig: Immunoglobulin; LTs: Leukotrienes; ILC2: Type 2 Innate Lymphoid Cells; MBPs: Major Basic Protein; MC: Mast Cell; TSLP: Thymic Stromal Lymphopoietin; TH/Th: T helper Cell

Introduction

Itchy acute and chronic wheals are the hallmark of chronic urticaria, which is a kind of urticaria that lasts for an extended length of time and affects the surface layers of the skin. Mast cells mediate bronchial asthma and urticaria, which are both very common and very severe conditions [1]. Histamine and other inflammatory mediators generated by mast cells are involved in the pathophysiology of both conditions, despite the different triggers for each. Interleukin-4, interleukin-10, interleukin-33 and BAFF are only some of the cytokines and mediators that stimulate various defense cells and the flow of leukocytes to the dermis and airways [2,3]. Anti-IgE medicine is very effective in the treatment of both of these conditions, where elevated IgE levels are

common symptoms [4]. In addition, antihistamines are often used to treat these disorders and respond well to glucocorticosteroids [5]. Due to the similarities between two conditions, doctors have long suspected a link between asthma and urticaria, which often occur together in the same patient. When people suffer from severe urticaria attacks, they often feel respiratory pain, which is not usually the case with asthma sufferers [6]. Wheezing is a frequent symptom of allergy sufferers, but not of asthmatics [7]. Chronic spontaneous urticaria has been linked to asthma, despite the condition being reported extremely rarely in literature (CSU) [8]. Researchers found a concatenation between total serum IgE levels and disease severity in people with chronic spontaneous urticaria [9]. In line with recently published guidelines for chronic spontaneous urticaria, we found that rising IgE levels were unrelated to skin test positivities for aeroallergens. There is no conclusive evidence that urticaria is more frequent in people with asthma [10].

Methodology

Searches of PubMed, BMC Cochrane and Google Scholar were conducted to identify relevant literature on asthma and urticaria. The usage of MeSH terms, including those for: “(Asthma) AND (Vitamin-D)”, “(Urticaria) and (Vitamin-D)”, “(Asthma) and (Urticaria)”, “(Asthma) and (Neutrophil)”, “(Asthma) AND (Eosinophils)”, “(Asthma) and (Interleukin)”, “(Urticaria) and (Neutrophil)”, “(Urticaria) and (Eosinophils)”, “(Urticaria) AND (Interleukin)”. In order to reduce the search, only works published between January 1, 2000 and April 1, 2023 were considered. Each author then reviewed the articles separately and then met to discuss their findings. This search strategy was developed to identify published resources that detailed the relationship between asthma and urticaria and also identified the underlying biomarkers of both conditions.

A Brief Introduction to Biomarkers in Asthma and Urticaria

The term "biomarker" refers to a trait that can be objectively tested and analyzed to identify biologic processes, pathogenic processes, or pharmacologic responses to treatment. [11]. "Asthma, also known as bronchial asthma, is a chronic disorder of the airways that may lead to symptoms such as difficulty breathing, severe constriction in the chest, wheezing, coughing and the production of sputum, as well as activity intolerance. There are many types of asthma and more than three hundred million people worldwide suffer from this respiratory illness [12]. A lack of vitamin D, mast cells, M2 macrophages, Airway Epithelial Cells (AECs), T lymphocytes, fibroblasts, eosinophils and Airway Smooth Muscle (ASM) cells are all factors that contribute to the chronic inflammation that occurs in the airways of asthmatics [13]. Mast cells and basophils have a role in the progression of allergic reactions, inflammatory conditions and blood related disorder. Even though these cells come from different body parts, are located in other parts of the body and have different lifespans, they share many exact activation mechanisms and mediators. Eosinophils, mast cells and basophils produce mediators that are linked to asthma, chronic urticaria and other conditions. Thus, mast cells and basophils activate biomarkers. The ideal biomarker would be consistently identified in blood or other biological fluids, is specific for basophils or mast cells and does not undergo significant metabolic changes. Mast cells and basophil markers are composed of substances expressed on both the surface and the inside of the cell in response to stimulation.

In contrast to basophils, which also produce histamine and lipid mediators, mast cells exclusively display basophil-specific markers like tryptase and other proteases. Mast cells and basophils share several additional characteristics as well. On their cell surfaces, mast cells and basophils present the activation markers CD63 and CD203 [14]. In recent years, an increased risk of severe asthma outcomes and allergic disorders such as chronic urticaria has been linked to a vitamin D deficit [15].

Blood Biomarkers in Asthma and Urticaria

Eosinophils are white blood cells that comprise between 1% and 3% of the total population and are a component of the body's innate immune system. The bone marrow is where these different kinds of cells originate [16]. They are specialized white blood cells called leukocytes that may be found throughout the body, although they are most prevalent in the bronchi, nasal passages and lungs. It is not entirely understood how the eosinophils in the blood link to those in the airways at this time. In addition to the time since the last meal, the level of physical activity and the type of therapy, eosinophil counts in the blood can be easily obtained. Patients with allergic asthma onset and non-allergic asthma onset may have higher eosinophil counts. On the other hand, this is not a diagnostic criterion employed (Fig. 1).

Additionally, blood eosinophils serve as markers for triggering biological therapy and as criteria for the prognosis of asthma. Most authors believe that the precise threshold at which a high blood eosinophil count is deemed to exist ranges between 150

and 300 cells/L, but there is still some controversy about the exact value of this threshold. Exacerbations and acute respiratory episodes occur more often in patients with an eosinophil count greater than 300 cells/L, according to the findings of several studies [17].

In addition to mediators generated by eosinophilic inflammation, the number of inflammatory mediators released by circulating eosinophils promotes bronchoconstriction, T2 cells and airway remodeling [18]. Some of the cytotoxic cationic proteins discovered in eosinophil granules that play a role in mediating inflammation (ROS) include Eosinophil Cationic Protein (ECP), EDN, MBPs and reactive oxygen species [19]. There is evidence that some of these mediators can be measured in the blood, suggesting that they could be used for better asthma clustering or as therapeutic targets. Blood and sputum ECP levels are higher in patients with severe (typically atopic) asthma than those with moderate asthma [20]. ECP levels rise during an asthma exacerbation, but they fall after therapy has begun because they are linked to bronchospasm and airway resistance [21]. Corticosteroid induction and dosage can be guided by ECP; however, this needs to be confirmed. In those with severe asthma, EDN may also be measured in blood, urine and other bodily fluids as an indication of eosinophilic disease and persistent airway limitation. It's a telltale sign of chronic, as opposed to acute pediatric asthma [22].

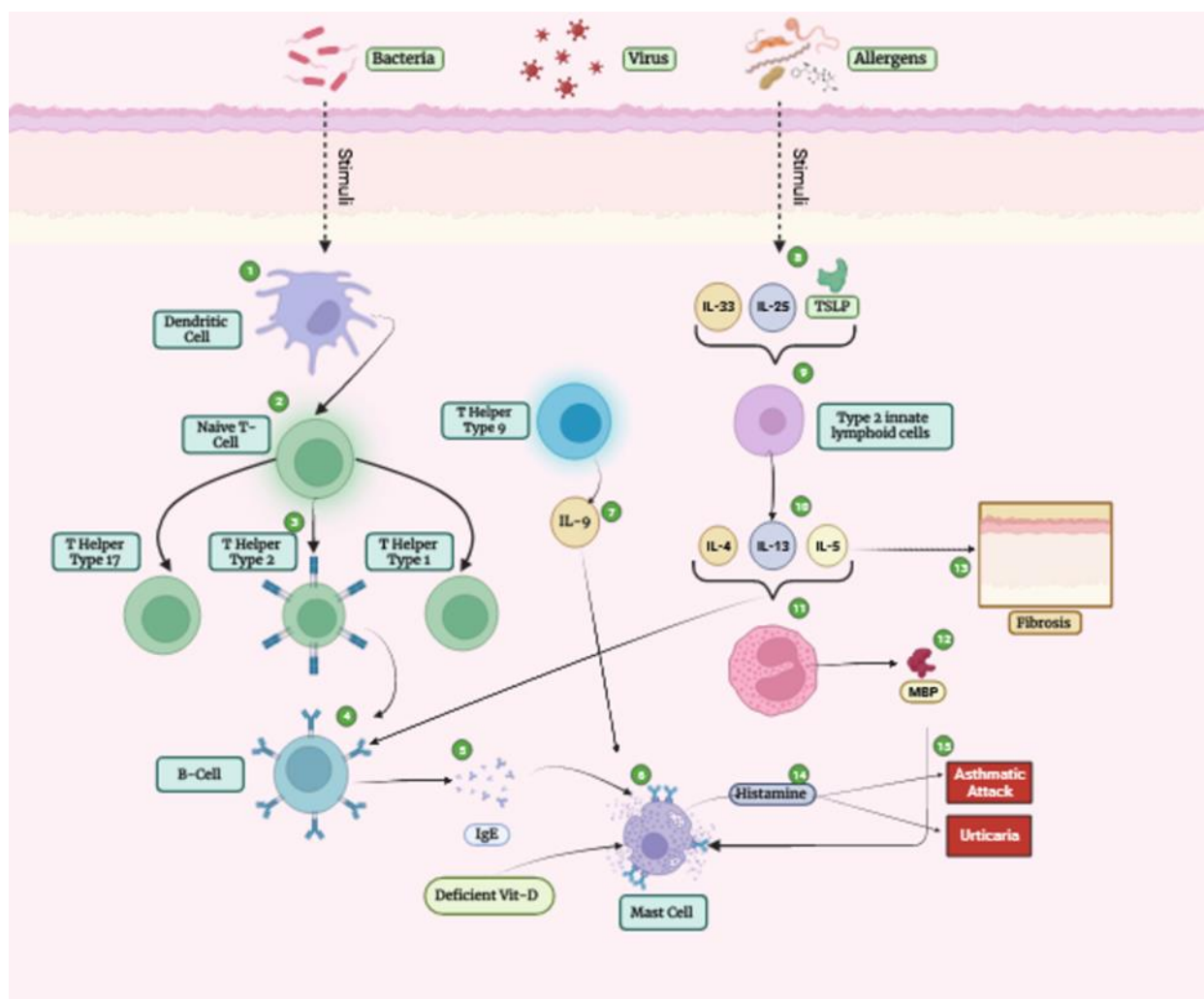


Figure 1: Schematic representation of biomarkers for Chronic Urticaria (CU) and asthma: To activate and differentiate naive T cells into Th2 cells, primed DCs are required. In order to keep type 2 immunity going strong, activated epithelial cells secrete cytokines including IL-25, IL-33 and TSLP, which promote the expansion of ILC2s and Th2 cells. It is the IL-4, IL-5, IL-9 and IL-13 secreted by pro-inflammatory cells that entice eosinophils, activate B cells, stimulate systemic and local IgE synthesis and trigger mast cell degranulation. Asthma and urticaria are both triggered by IgE. Bronchoconstriction and the CU result from the irritation of the smooth muscle lining the airways by these mediators.

Allergies (especially asthma and allergic reactions like urticaria) are associated with eosinophils, recognized effector cells contributing to chronic inflammation and tissue destruction [23]. Together with mast cells, the other primary effector cell during an allergic reaction, they comprise the allergic effector unit [24]. Furthermore, they contribute to the onset of autoimmune diseases, cardiovascular issues and malignancies [25]. Non-lesional skin from people with CU also contains eosinophils. In contrast, lesional skin from those with CU contains eosinophils and mast cells [26]: mast cells, or cutaneous basophils, are degranulated cells in response to the first stimulus. The production of potent vasoactive mediators causes an increase in capillary permeability, leading to the formation of erythema and papules [27]. Other vasoactive mediators such as arachidonic acid metabolites, leukotrienes, prostaglandin D₂, serotonin, acetylcholine, platelet-activating factor, heparin, codeine, anaphylatoxins C3 and C5a, cytokines and neurotransmitters are present and play a role in CU, despite the fact that histamine is the most important factor in the condition. These mediators have a role in the recruitment of more inflammatory cells, such as neutrophils, lymphocytes and mainly eosinophils, all of which contribute to the maintenance of inflammation via the generation of other substances that characterize the cellular infiltrate of the illness [28,29]. Inflammatory infiltrates that are abundant in neutrophils, eosinophils and the progeny of these cell types are a hallmark of pressure urticaria, just as they are of cholinergic CU lesions. Pressure urticaria is similar to cholinergic CU lesions in this regard [30]. Increased eosinophils, neutrophils and vascular indicators in CU-damaged skin lead to tissue edema. Consistent with a role for the innate pathways in the development of CU lesions, increased production of Th2 cytokines in these lesions would contribute to mast cell activation, inflammation and the onset of vascular leakage. In addition, those with CU are more likely to show signs of thrombin generation and their mean levels of D-dimer, a substance involved in the extrinsic route of coagulation and fibrinolysis, are more significant [31].

Deficient of Vitamin-D in Asthma and Urticaria

Chronic urticaria is the medical term for wheals or angioedema that last more than six weeks [32]. Patients with chronic urticaria have a worse quality of life, although it is not lethal. When sickness activity rises, the contour of life declines [33]. CSU is a typical form of chronic urticaria that is triggered by endogenous processes inside the body rather than by external physical stimuli. [34]. In 55% of CSU cases, the underlying etiology is unclear, whereas, in 45%, autoimmunity is the root cause. The D₂ and D₃ forms of vitamin D are fat-soluble [35]. In the skin, the body converts provitamin D₃ into vitamin D₃ (cholecalciferol) through a nonenzymatic mechanism [36,42]. Fatty fish, certain types of mushrooms, fortified milk, egg yolks, cereals and cheese are all good food sources of vitamin D. Deficiency of vit-D is a worldwide disease that affects individuals of all ages [37]. Vitamin D deficiency, however, is universal [38, 43]. Vitamin D is a crucial micronutrient because it promotes the body's innate and adaptive immune responses [39]. It is well known that autoimmune reactions frequently cause CSU [40,44]. The association between vitamin D deficiency and autoimmune and allergic illnesses such as type-2 diabetes, asthma, cancer and cardiovascular disease suggests a link between 25(OH)D levels and CSU [41,45].

A further investigation found that the vitamin D pathway impacted allergic and autoimmune responses. The mast cells' 25-hydroxyvitamin D₃ metabolites counteract the effects of immunoglobulin E on mast cells, preventing their activation [46]. Vitamin D enhances T regulatory cells, which help suppress pro-allergic and autoimmune responses. 1,25-dihydroxy vitamin-D may inhibit cytokine production from T helper (TH) 1 cell, thereby protecting against the development of TH1-mediated autoimmune diseases [47]. 1,25-dihydroxy vitamin D suppresses TH17 cells, which is crucial in initiating autoimmune diseases [48]. Patients with chronic urticaria exhibited a substantially higher incidence of 25-hydroxyvitamin D insufficiency and a significantly lower level of 25-hydroxyvitamin D than those with acute urticaria. Patients' 25-hydroxyvitamin D levels were significantly lower in adults than children [49].

Vitamin D's effects on lung development, immune response modulation and Airway Smooth Muscle remodeling (ASM) may all have a role in asthma pathogenesis. Low vitamin-D levels are related to more severe clinical presentations in patients with asthma, according to studies evaluating this association [50]. However, they have yielded contradictory findings and tenuous links. Research on vitamin D's effects on asthma in children is ongoing owing to its potential as a preventive and therapeutic tool for treating the illness at various severity levels. Coupled with conventional corticosteroid treatment, vitamin-D has also demonstrated positive results in children with asthma [51].

Due to its anti-proliferation properties, vitamin-D may slow the cell cycle in the airways. It prevents the hyperplasia of airway smooth muscle and studies have shown that low levels of 25(OH)D₃ are associated with diminished lung function [52,56]. There

was no connection between these levels and airway inflammation, despite the fact that there was a link between low 25(OH)D3 levels and increased ASM mass. If you don't get enough vitamin D, your blood and platelets will have reduced amounts of the growth hormones calcitriol and calcitriolriol, as well. These chemicals restrict cell proliferation in ASMs without causing the cells to undergo apoptosis. Insufficiency in vitamin D may lead to a number of negative health consequences, including increased bronchial hyperresponsiveness, airway remodeling, decreased lung functions and a more rapid loss in lung function. [53,57]. The metalloproteinases disintegrin and metalloprotease 33 (ADAM-33) help in lung growth and function. Since ASM exhibits functional vitamin-D receptors, 1,25-dihydroxy vitamin-D3 might stimulate 24-hydroxylase/CYP24A1 expression, increasing cell proliferation, differentiation and survival. Vitamin-D may affect airway responsiveness by regulating chemokine synthesis in ASM [54]. Vitamin-D can regulate several genes, including asthma susceptibility and pathogenesis. These genes control glucocorticoid and prostaglandin production, smooth muscle cell contraction and inflammation. Vitamin-D is known to up-regulate multiple genes playing essential roles in cellular mobility, cellular buildup and proliferation and cell death [55,58], all of which may play a role in asthma etiology through alterations to the airway remodeling process.

Conclusion

Diagnosing and treating allergy illnesses is challenging due to the complexity and clinical heterogeneity of their pathogenic molecular pathways. Better disease treatment relies on identifying the phenotypes and endotypes of allergic conditions, requiring well-defined and precise biomarkers. The development of predictive biomarkers is urgently needed to choose appropriate therapy strategies better and monitor treatment results. Despite many years of study, only a few biomarkers for allergic diseases are now available for therapeutic application. Patients with asthma may also be at risk for developing urticaria if they don't get enough vitamin-D. To realize precision medicine-based methods for treating allergic illnesses, it is essential to improve diagnostic biomarkers.

Conflict of Interest

The author has no conflict of interest to declare.

References

1. Papadopoulos J, Karpouzis A, Tentes J, Kouskousis C. Assessment of interleukins IL-4, IL-6, IL-8, IL-10 in acute urticaria. *J Clin MedRes*. 2014;6:133-7.
2. Saluja R, Khan M, Church M, Maurer M. The role of IL-33 and mast cells in allergy and inflammation. *Clinical and Translational Allergy*. 2015;5:33.
3. Kessel A, Yaacoby-Bianu K, Vadasz Z, Peri R, Halasz K, Toubi E. Elevated serum B-cell activating factor in patients with chronic urticaria. *Human Immunol*. 2012;73:620-2.
4. Toubi E, Kessel A, Avshovich N, Bamberger E, Sabo E, Nusem D, et al. Clinical and laboratory parameters in predicting chronic urticaria: a prospective study of 139 patients. *Allergy*. 2004;59:869-73.
5. Ferrer M, Sastre J, Jauregui I, Davila I, Montoro J, del Cuvillo A, et al. Effects of anti-histamine up-dosing in chronic urticaria. *J Invest Allergol Clin Immunol*. 2011;3:34-9.
6. Mizuma H, Tanaka A, Uchida Y, Fujiwara A, Manabe R, Furukawa H, et al. Influence of omalizumab on allergen-specific IgE in patients with adult asthma. *Int Arch Allergy and Immunol*. 2015;168:165-72.
7. Asero R, Madonini E. Bronchial hyperresponsiveness is a common feature in patients with chronic urticaria. *J Invest Allergol Clin Immunol*. 2006;16:19-23.
8. Isik AR, Karakaya G, Celikel S, Demir AU, Kalyoncu AF. Association between asthma, rhinitis, and NSAID hypersensitivity in chronic urticaria patients and prevalence rates. *Int Arch Allergy and Immunol*. 2009;150:299-306.
9. Kessel A, Helou W, Bamberger E, Sabo E, Nusem D, Panassof J, et al. Elevated serum total IgE - a potential marker for severe chronic urticaria. *Int Arch Allergy and Immunol*. 2010;153:288-93.
10. Zuberbier T, Aberer W, Asero R, Bindslev-Jensen C, Brzoza Z, Canonica GW, et al. The EAACI/GA(2) LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. *Allergy*. 2014;69:868-87.
11. Biomarkers Definitions Working Group. Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. *Clinical Pharmacol Therapeutics*. 2001;69(3):89-95.

12. Brusselle GG, Koppelman GH. Biologic therapies for severe asthma. *New England J Med*. 2022;386(2):157-71.
13. Xiao C, Puddicombe SM, Field S. Defective epithelial barrier function in asthma. *J Allergy and Clinical Immunol*. 2011;128(3):549-56.
14. Kabashima K, Nakashima C, Nonomura Y, Otsuka A, Cardamone C, Parente R, et al. Biomarkers for evaluation of mast cell and basophil activation. *Immunological Reviews*. 2018;282(1):114-20.
15. Benetti C, Comberiati P, Capristo C, L Boner A, G Peroni D. Therapeutic effects of vitamin D in asthma and allergy. *Mini Reviews in Medicinal Chemistry*. 2015;15(11):935-43.
16. Uhm TG, Kim BS, Chung IY. Eosinophil development, regulation of eosinophil-specific genes, and role of eosinophils in the pathogenesis of asthma. *Allergy, Asthma Immunology Res*. 2012;4(2):68-79.
17. Kuruvilla ME, Lee FE, Lee GB. Understanding asthma phenotypes, endotypes, and mechanisms of disease. *Clinical Reviews Allergy Immunol*. 2019;56:219-33.
18. Chung KF, Israel E, Gibson PG. Severe asthma. European Respiratory Society. Lausanne, Switzerland. 2019. ERS Monograph.
19. Berry A, Busse WW. Biomarkers in asthmatic patients: has their time come to direct treatment? *J Allergy and Clin Immunol*. 2016;137(5):1317-24.
20. Tiotiu A. Biomarkers in asthma: State of the art. *Asthma Research and Practice*. 2018;4:10.
21. Carr TF, Kraft M. Use of biomarkers to identify phenotypes and endotypes of severe asthma. *Annals of Allergy, Asthma Immunol*. 2018;121:414-20.
22. Minai-Fleminger Y, Levi-Schaffer F. Mast cells and eosinophils: the two key effector cells in allergic inflammation. *Inflammation Research*. 2009;58:631-8.
23. Diny NL, Rose NR, Cihakova D. Eosinophils in autoimmune diseases. *Frontiers in Immunol*. 2017;8:484.
24. Galdiero MR, Varricchi G, Seaf M, Marone G, Levi-Schaffer F, Marone G. Bi-directional mast cell-eosinophil interactions in inflammatory disorders and cancer. *Frontiers in Medicine (Lausanne)*. 2017;4:103.
25. Kay AB, Ying S, Ardelean E, Mlynek A, Kita H, Clark P. Elevations in vascular markers and eosinophils in chronic spontaneous urticarial weals with low-level persistence in uninvolved skin. *British J Dermatol*. 2014;171:505-11.
26. Asero R, Tedeschi A, Riboldi P, Griffini S, Bonanni E, Cugno M. Severe chronic urticaria is associated with elevated plasma levels of D-dimer. *Allergy*. 2008;63:176-80.
27. Criado PR, Antinori LC, Maruta CW, Reis VM. Evaluation of D-dimer serum levels among patients with chronic urticaria, psoriasis and urticarial vasculitis. *Anais Brasileiros de Dermatologia*. 2013;88:355-60.
28. Criado RF, Criado PR, Martins JE, Valente NY, Michalany NS, Vasconcellos C. Urticaria unresponsive to antihistaminic treatment: An open study of therapeutic options based on histopathologic features. *J Derma Treatment*. 2008;19:92-6.
29. Kay AB, Ying S, Ardelean E, Mlynek A, Kita H, Clark P. Elevations in vascular markers and eosinophils in chronic spontaneous urticarial weals with low-level persistence in uninvolved skin. *British J Dermatology*. 2014;171:505-11.
30. Kay AB, Clark P, Maurer M, Ying S. Elevations in T-helper-2-initiating cytokines (interleukin-33, interleukin-25 and thymic stromal lymphopoietin) in lesional skin from chronic spontaneous ('idiopathic') urticaria. *British J Dermatol*. 2015;172:1294-302.
31. Zuberbier T, Asero R, Bindslev-Jensen C, Walter Canonica G, Church MK, Giménez-Arnau A, et al. Dermatology Section of the European Academy of Allergology and Clinical Immunology. Global Allergy and Asthma European Network. European Dermatology Forum. World Allergy Organization EAACI/GA(2)LEN/EDF/WAO guideline: definition, classification and diagnosis of urticaria. *Allergy*. 2009;64:1417-26.
32. Koti I, Weller K, Makris M, Tiligada E, Psaltopoulou T, Papageorgiou C, et al. Disease activity only moderately correlates with quality-of-life impairment in patients with chronic spontaneous urticaria. *Dermatol*. 2013;226:371-9.
33. Kaplan AP, Greaves M. Pathogenesis of chronic urticaria. *Clin Experimental Allergy*. 2009;39:777-87.
34. Rosen CJ. Clinical practice. Vitamin D insufficiency. *The New England J Med*. 2011;364:248-54.
35. Palacios C, Gonzalez L. Is vitamin D deficiency a major global public health problem? *The J Steroid Biochemistry and Molecular Biology*. 2013.
36. Mitchell DM, Henao MP, Finkelstein JS, Burnett-Bowie SA. Prevalence and predictors of vitamin D deficiency in healthy adults. *Endocrine Practice*. 2012;18:914-23.
37. Arabi A, El Rassi R, El-Hajj Fuleihan G. Hypovitaminosis D in developing countries-prevalence, risk factors and outcomes. *Nature Reviews Endocrinol*. 2010;6:550-61.

38. Aranow C. Vitamin D and the immune system. *J Invest Medicine*. 2011;59:881-6.
39. Hewison M. Vitamin D and innate and adaptive immunity. *Vitamins and Hormones*. 2011;86:23-62.
40. Agmon-Levin N, Theodor E, Segal RM, Shoenfeld Y. Vitamin D in systemic and organ-specific autoimmune diseases. *Clinical Reviews in Allergy Immunol*. 2013;45:256-66.
41. Wjst M. The vitamin D slant on allergy. *Pediatric Allergy and Immunol*. 2006;17:477-83.
42. Hossein-nezhad A, Holick MF. Vitamin D for health: a global perspective. *Mayo Clinic Proceedings*. 2013;88:720-55.
43. Pludowski P, Holick MF, Pilz S, Wagner CL, Hollis BW, Grant WB, et al. Vitamin D effects on musculoskeletal health, immunity, autoimmunity, cardiovascular disease, cancer, fertility, pregnancy, dementia and mortality-a review of recent evidence. *Autoimmunity Reviews*. 2013;12:976-89.
44. Song Y, Wang L, Pittas AG, Del Gobbo LC, Zhang C, Manson JE, et al. Blood 25-hydroxy vitamin D levels and incident type 2 diabetes: a meta-analysis of prospective studies. *Diabetes Care*. 2013;36:1422-8.
45. Wang L, Song Y, Manson JE, Pilz S, März W, Michaëlsson K, et al. Circulating 25-hydroxy-vitamin D and risk of cardiovascular disease: a meta-analysis of prospective studies. *Circulation: Cardiovascular Quality and Outcomes*. 2012;5:819-29.
46. Yip KH, Kolesnikoff N, Yu C. Vitamin D (3) represses IgE-dependent mast cell activation via mast cell-CYP27B1 and -vitamin D receptor activity. *The J Allergy and Clinical Immunol*. 2014;133:1356-64.
47. Vassallo MF, Camargo Jr CA. Potential mechanisms for the hypothesized link between sunshine, vitamin D, and food allergy in children. *The J Allergy and Clin Immunol*. 2010;126:217-22.
48. Hewison M. An update on vitamin D and human immunity. *Clinical Endocrinol*. 2012;76:315-25.
49. Tsung-Yui T, Yu-Chen H. Vitamin D deficiency in patients with chronic and acute urticaria: A systematic review and meta-analysis. *J Am Acad Dermatol*. 2018;79(3):573-5.
50. Berraies A, Hamzaoui K, Hamzaoui A. Link between vitamin D and airway remodeling. *J Asthma and Allergy*. 2014;7:23-30.
51. Hall SC, Fischer KD, Agrawal DK. The impact of vitamin D on asthmatic human airway smooth muscle. *Expert Review of Respiratory Medicine*. 2014;10(2):127-35.
52. Gupta A, Sjoukes D, Richards. Relationship between serum vitamin D, disease severity, and airway remodeling in children with asthma. *Am J Respiratory and Critical Care Medicine*. 2011;184(12):1342-9.
53. Banerjee A, Damera G, Bhandare R. Vitamin D and glucocorticoids differentially modulate chemokine expression in human airway smooth muscle cells. *British J Pharmacol*. 2008;155(1):84-92.
54. Britt RD, Faksh A, Vogel ER. Vitamin D attenuates cytokine-induced remodeling in human fetal airway smooth muscle cells. *J Cellular Physiol*. 2015;230(6):1189-98.
55. McKleroy W, Lee TH, and Atabai K. Always cleave up your mess: targeting collagen degradation to treat tissue fibrosis. *Am J Physiology-Lung Cellular and Molecular Physiol*. 2013;304(11):709-21.
56. Visse R and Nagase H. Matrix metalloproteinases and tissue inhibitors of metalloproteinases. *Circulation Res*. 2003;92(8):827-39.
57. Shimanta P, Tausif A, Alok K, Mahedi MRA, Afrin S, Hasan MS, et al. A survey-based study on seasonal diseases and treatment pattern during Winter in Narayanganj City. *Int J Biosci*. 2023;22(1):132-8.

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