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An approach of Urticaria: A review

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Abstract
Urticaria consists of blancheable, erythematous, oedematous papules or 'Weals'. It is estimated that lifetime incidence of urticaria is approximately 20%. It is more common among females than males. Urticaria may be classified on the basis of underlying aetiology or by a clinical classification. Main cause of Urticaria is immunoglobulin E- and non-immunoglobulin E-mediated release of histamine and other inflammatory mediators from mast cells and basophils. Although often self-limited and benign, it can cause significant discomfort, continue for months to years, and uncommonly represent a serious systemic disease or life-threatening allergic reaction. Diagnosis is made by clinically; anaphylaxis must be ruled out if needed. In about 50% of patients urticaria occurs alone where as about 40% of patients urticaria occurs with angioedema and in about 10% of Patients angioedema occurs alone. The mainstay of treatment is avoidance of pollen grains or triggers, if identified. The first-line therapy is second-generation H_1 anti-histamines, which can be titrated to greater than standard doses whereas first-generation H_1 antihistamines, H_2 antihistamines, leukotriene receptor antagonists, high-potency antihistamines, and corticosteroid (pulse therapy) bursts may be used as adjunctive treatment. In case of refractory chronic urticaria, patients can be referred to super specialist for additional treatments approach, like omalizumab or cyclosporine. Using of Unani Medicine is highly effective for the management of urticaria which is based upon multidimensional approach i.e. dietotherapy (avoiding consumption of Ghaleez and Fasid Ghiza), regimes (evacuates morbid/toxins materials from the body with the help of diaphoresis, hijama, fasd, huqna, Idrar etc.) and pharmacotherapy (Islah-e-Jigar, Musaffi Dam and Moaddilat-e-Dam).

Keywords: Urticaria, immunoglobulin E, Triggers, anti-histamines, unani medicine

Introduction
Urticaria consists of a heterogeneous group of diseases [1]. It is also known as "Hives' [2]. It is characterized by the appearance of wheals and/or angioedema, encompassing several subtypes [3].

Prevalence of Urticaria
It is estimated that lifetime incidence of urticaria is approximately 20% [4]. An estimated 15% to 23% of adults have experienced at least 1 episode of acute urticaria at some time in their lives, and the prevalence of chronic urticaria in adults is estimated at 0.5% to 5% [5]. In children, previous studies reported the prevalence of acute urticaria to be 1% to 14.5%, but there is little data on the prevalence of chronic urticaria in children [6] Chronic urticaria is considered less prevalent in children than in adults, and most studies estimating its prevalence are based upon extrapolation from adult data, hospital-based results, or studies of the general adult population [3].

Incidence
It affects 15-20% of the world population. In Europe, the incidence of chronic spontaneous urticaria is 8-10%. Cases of chronic spontaneous urticaria of unknown etiology constitute a further 0.1-3% of diagnoses. It is more common among females than as males, and the peak incidence of chronic spontaneous urticaria falls between 20 and 40 years of age [7].

Classification of Urticaria
Urticaria may be classified on the basis of underlying aetiology or by a clinical classification. In most cases of chronic urticaria it will not be possible to identify the underlying caus [8].

There are various types of Urticaria

1. Physical Urticaria

Physical urticaria is triggered by a physical stimulus. The most common physical Urticaria is Dermatographism in which lesions are created or "written" on the skin by stroking or scratching the skin [9] Cholinergic urticaria is also common and results from a rise in basal body temperature that occurs following physical exertion or exposure to heat [10]. Other physical stimuli which can trigger urticaria include exposure to cold, ultraviolet light (solar urticaria), water and exercise. The lesions produced by these physical stimuli are typically localized to the stimulated area and often resolve within 2 hours [11].

2. Auto-reactive urticaria

Autoreactive urticaria (ArU), a sub-form of chronic urticaria (CU), is caused by circulating histamine-releasing signals. ArU patients are readily identified by the autologous serum skin test, in which they exhibit inflammatory reactions to their serum after intracutaneous injection [12]. CU patients who also exhibit functional autoantibodies against IgE and/or its high affinity receptor Fc (epsilon) RI are thought to suffer from autoimmune urticaria (Aiu). ArU and AiU are pathogenetically and clinically different from other sub-forms of CU [13].

3. Inducible Urticaria

Inducible urticaria is a heterogeneous group of skin disorders characterized by the appearance of wheals, pruritus and/or angioedema, sometimes accompanied by systemic symptoms caused by innocuous stimuli [14]. The signs and symptoms of Chronic Inducible Urticaria may be mild or severe, localized or diffused (and sometimes, extensive), and can vary from one individual to another [15].

4. Cold Urticaria

Cold urticaria is one form of urticaria that may be associated with other forms of physical urticarias. Frequency is generally estimated at two or three per 100 [16]. The triggering effect of cold is found at history taking in most of the cases. The urticaria is usually superficial, and more rarely associated with deep and/or mucosal urticaria. The diagnosis is based on history taking and the ice cube test [17].

5. Heat Contact Urticaria

Localized heat contact urticaria is a cutaneous condition, one of the rarest forms of *urticaria*, where within minutes of *contact* with *heat* from any source, itching and whealing occur at the precise site of *contact*, lasting up to 1 hour. Heat contact urticaria is very rare and it is characterized by the development of wheal limited to the areas of heat contact.[18]

6. Delayed Pressure Urticaria

Delayed pressure urticaria is a type of physical urticaria where erythematous, often painful swellings occur at sites of sustained pressure on the skin, after a delay of several hours [19]. If sought, it is present in up to 40% of patients with ordinary chronic idiopathic urticaria to a varying degree [20].

7. Urticaria Factitia

Urticaria factitia (also known as dermographic urticaria and symptomatic dermographism) is characterized by whealing and itching following a minor stroking pressure, rubbing or scratching of the skin [21]. The majority of patients with urticaria factitia benefits from treatment with nonsedating antihistamines [22].

8. Solar Urticaria

Solar urticaria is a chronic acquired photosensitivity disorder [23]. It consists of recurrent episodes of urticaria rash developed on areas of the skin that are exposed to sunlight [24]. Despite being usually a benign condition, it may be extremely disabling, thus limiting everyday activities and severely altering the quality of life of patients [25].

9. Cholinergic Urticaria

Cholinergic urticaria is a physical type of urticaria caused by an increase in core body temperature after exercise, intake of spicy foods, or exposure to stress. [26] Lesions appear as itchy, numerous, small, 1 to 5 mm papules or wheals that last for a few minutes to a hour [27].

10. Vibratory Urticaria

Vibratory urticaria is a condition in which exposing the skin to vibration, repetitive stretching, or friction results in allergy symptoms such as hives (urticaria), swelling (angioedema), redness (erythema), and itching (pruritus) in the affected area [28]. The reaction can be brought on by towel drying, hand clapping, running, a bumpy ride in a vehicle, or other repetitive stimulation [29].

11. Aquagenic Urticaria

Aquagenic urticaria (AU) is a rare inducible form of physical urticaria, which occurs in response to cutaneous exposure to water, including sweat and tears [30]. Patients present with characteristic 1-3 mm folliculocentric wheals with surrounding 1-3 cm erythematous flares within 20-30 minutes following skin contact with water [31].

12. Contact Urticaria

Contact urticaria is defined as the development of a wheal-and-flare reaction at a site where an external agent contacts the skin or mucosa. Symptoms of contact urticaria range from pruritic, localized wheal-and-flare reactions to generalized urticaria and anaphylaxis [32]. Contact urticaria has been reported following skin contact with a multitude of substances ranging from simple chemicals to macromolecules [33]

13. Acute Urticaria

Acute urticaria is a common condition, which presents in all age groups and to multiple specialties. It may be a presenting symptom of anaphylaxis [34].

14. Chronic Urticaria

Chronic urticaria (CU) is defined by recurrent episodes occurring at least twice a week for 6 weeks [2]. Females are more commonly affected than males [10]. Establishing the cause of CU is difficult and at times almost impossible [35]. This renders cause specific management difficult and frustration on part of the patient and the treating physician. Also, CU is associated with lower quality of life (QoL) levels [36]. Recent advances of its pathogenesis include the finding of autoantibodies to mast cell receptors in nearly half of patients [37]. This possibility of an autoimmune basis to chronic idiopathic urticaria (CIU) is now widely explored [38]. Chronic urticaria may arise due to both external and internal causes of urticaria [2].

15. Physical factors

The physical urticarias are a heterogeneous subgroup of chronic urticarias in which wheals can be reproducibly induced by different specific physical stimuli such as cold, heat, pressure, vibration, or sunlight [9, 28]

16. Infections

Urticaria has been reported to be associated with a number of infections; however, these associations are not strong and may be spurious [39]. Infectious agents reported to cause urticaria include hepatitis-B virus, *Streptococcus* and *Mycoplasma* species, Helicobacter *pylori, Mycobacterium tuberculosis*, and herpes simplex virus [40].

17. Idiopathic/others

Most cases of CU are considered idiopathic [41]. It has recently been accepted that autoimmunity plays a critical role in its pathogenesis in some of these patients. A few others are medications, contactants, neurological factors, stress, vasculitic, pseudoallegens etc [42]

18. Pathophysiology of Chronic urticaria

The mast cell is believed to be the major effector cell in most forms of urticaria, though other cell types may be involved [43]. Degranulation of mast cells with release of histamine is central to the development of wheals and angioedema. Urticaria is due to a local increase in permeability of capillaries and venules [44]. These changes are dependent on activation of the cutaneous mast cells, which contain a range of mediators predominantly histamine. The mast cells respond with a lowered threshold of releasability [45]. Vascular permeability in skin is produced by the interaction of both H_1 and H_2 histamine receptors [46]. Activation of H_1receptors in the skin induces itching, flare, erythema, whealing and contraction of smooth muscle in respiratory and gastro-intestinal tract. Activation of H_2 receptors contributes to erythema and whealing in the skin [47]. Chronic autoimmune urticaria is caused by anti-FcåRI and less frequently, by anti-IgE autoantibodies that lead to mast cell and basophil activation [2]. The postulated effector mechanisms for immunological and non-immunological activation of mast cells. A few preclinical investigations have demonstrated an upregulation of TNF-α in patients with CIU [48].

19. Clinical Features of Chronic Urticaria

Chronic Urticaria is associated with diverse clinical presentations. It is chiefly characterized by the rapid appearance of wheals and/or angioedema.[49] A wheal consists of three typical features: (i) a central swelling of variable size; (ii) an associated itching or sometimes burning; and (iii) a fleeting duration of usually 1-24 h. [2] Angioedema is defined as a sudden, pronounced swelling of the lower dermis and subcutis. It is sometimes painful and resolution is slower than for wheals (up to 72 h). In 40-50% of cases, urticaria is associated with angioedema [50]. Lesions may appear anywhere on the body including scalp, palms and soles.[2] Urticaria wheals are very itchy and patients tend to rub rather than scratch, hence excoriation marks are not seen.[51] Headache, dizziness, hoarseness of voice, shortness of breath, nausea, vomiting and abdominal pain may occur as concomitant systemic manifestations of severe episodes of urticaria [52].

Although patients with autoimmune antibodies have no distinctive diagnostic clinical features, the diagnosis of chronic autoimmune urticaria often can be suspected from a past or family history of autoimmune diseases, especially thyroiditis [53].

20. Investigations for Chronic Urticaria

In spite of extensive laboratory investigations, 50% cases of chronic urticaria remain idiopathic [54]. An elevated ESR suggests the possibility of an underlying systemic disease and eosinophilia should prompt a search for parasitic diseases.[55] Screening test for thyroid function and antithyroid peroxidase and antithyroglobulin antibodies may be carried out in candidate patients [56] Positive autologous serum skin test (ASST). Suggests an underlying autoimmune mechanism [57, 58].

21. Management of Chronic Urticaria

The treatment regimen should be tailored to the individual patient General measures include removal of any identifiable cause, explanation, information and reassurance [2]. Avoidance of aspirin and other NSAIDs is recommended because these drugs aggravate chronic urticaria in about 30% of patients [59] Treatment of underlying diseases, i.e. Hashimoto's thyroiditis, cryoglobulinemia and Helicobacter pylori when present is indicated [60] Ingestion of high quantities of salicylate in diet and its relation to urticaria has long been a matter of debate, although the same has been refuted by others [2] In one study, only 19% of patients reacted severely to challenge capsules containing food additives and salicylic acid [3]

22. Pharmacotherapy

Primary Line of treatment for Urticaria

The newer generation H1 antihistamines with less sedating and less cholinergic effects are preferred over the older generation H1 antihistamines as the initial choice of therapy [61]. In pregnancy, chlorpheniramine and diphenhydramine are the antihistaminics of choice for oral and parenteral route respectively [62] Certain antihistamines have been proposed as preferred for particular subtypes of chronic urticaria, such as hydroxyzine for cholinergic urticaria and cyproheptadine for cold induced urticaria [63] Second generation non-sedating (or less sedating) antihistamines like cetirizine, loratidine, fexofenadine, desloratadine, mizolastine, etc. also can be used [64]

23. Second line treatments for Urticaria:

Short courses of systemic steroids (for example prednisone 0.3-0-5 mg/kg daily or methylprednisolone 16 mg daily to be tapered and stopped within 3-4 weeks) can be given in resistant cases of chronic urticaria, but long term therapy cannot be proposed because of known adverse effects [65] Prolonged treatment of chronic urticaria with oral corticosteroids may be required in urticaria vasculitis [66]. If urticaria relapses after a short course of steroid therapy, and symptoms are not adequately controlled by H1 antihistamines, leukotriene-receptor antagonists could be tried [67].

24. Unani Treatment

Unani treatment is based upon multidimensional approach i.e. dietotherapy (avoiding consumption of Ghaleez and Fasid Ghiza), regimes (evacuates morbid/toxins materials from the body with the help of diaphoresis, hijama, fasd, huqna, idrar etc) and pharmacotherapy [68]

Pharmacotherapy consists of single and compound drugs which act as Islah-e-Jigar, Imala-e-Mavad, tanqiya-e-Mavad, Musaffi Dam, Tadil-e-Dam. These drugs are used in the form of decoction, safoof, jawarish, majoon, sharbat, arque and tila. [69, 70]

Conclusion

Avoiding consumption of Fasid and Ghaleez Ghiza and use of those drugs which acts as Islah-e-Jigar, tanqiya-e-Mavad,

Musaffi Dam, Tadil-e-Dam, are highly effective for the management of Urticaria.

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References

1. Amar SM, Dreskin SC. Urticaria Prim Care. 2008; 35(1):141-57.
2. Sachdeva S, Gupta V, Amin SS, Tahseen M. Chronic UrticariaIndian J Dermatol. 2011; 56(6):622-628.
3. Zuberbier T. Classification of Urticaria. Indian J Dermatol. 2013; 58(3):208-210.
4. Schaefer P. Acute and Chronic Urticaria: Evaluation and Treatment. Am Fam Physician. 2017; 95(11):717-724.
5. Lee SJ *et al*. Prevalence and Risk Factors of Urticaria with a Focus on Chronic Urticaria in Children. Allergy Asthma Immunol Res. 2017; 9(3):212-219.
6. Khakoo G, Sofianou-Katsoulis A, Perkin MR, Lack G. Clinical features and natural history of physical urticaria in children. Pediatr Allergy Immunol. 2008; 19(4):363-6.
7. Raciborski F *et al*. Epidemiology of urticaria in Poland - nationally representative survey results. Postepy Dermatol Alergol. 2018; 35(1):67-73.
8. Choi SH *et al*. Approaches to the diagnosis and management of chronic urticaria in children Korean J Pediatr. 2015; 58(5):159-164.
9. Abajian M, Młynek A, Maurer M. Physical urticaria. Curr Allergy Asthma Rep. 2012; 12(4):281-7.
10. Deacock SJ. An approach to the patient with urticaria.Clin Exp Immunol. 2008; 153(2):151-161.
11. Dice JP. Physical urticaria. Immunol Allergy Clin North Am. 2004; 24(2):225-46.
12. Auyeung P. Autoreactive T cells in chronic spontaneous urticaria target the IgE Fc receptor Iα subunit. 2016; 138(3):761-768.e4
13. Maurer M, Metz M, Magerl M, Siebenhaar F, Staubach P. Autoreactive urticaria and autoimmune urticaria. Hautarzt. 2004; 55(4):350-6.
14. Amaya D, Sánchez A, Sánchez J. Inducible urticaria: Case series and literature review. Biomedica. 2016; 36(1):10-21
15. Maurer M, Fluhr JW, Khan DA. How to Approach Chronic Inducible Urticaria. J Allergy Clin Immunol Pract. 2018; 6(4):1119-1130.
16. Claudy A. Cold urticaria. J Investig Dermatol Symp Proc. 2001; 6(2):141-2.
17. Singleton R, Halverstam CP. Diagnosis and management of cold urticaria. Cutis. 2016; 97(1):59-62.
18. Chung HS, Lee KH, Ro JY. Heat contact urticaria--a case report. Yonsei Med J. 1996; 37(3):230-5.
19. Kobza-Black A. Delayed pressure urticaria. J Investig Dermatol Symp Proc. 2001; 6(2):148-9.
20. Lawlor F, Black AK. Delayed pressure urticaria. Immunol Allergy Clin North Am. 2004; 24(2):247-58,
21. Bauer A. Urticaria factitia. Dtsch Med Wochenschr. 2000; 125(11):337.
22. Krause K, Ardelean E, Kessler B, Magerl M, Metz M, Siebenhaar F *et al*. Antihistamine-resistant urticaria factitia successfully treated with anti-immunoglobulin E therapy. Allergy. 2010; 65(11):1494-5.
23. Badri T, Schlessinger J. Solar Urticaria. Stat Pearls Publishing, 2018.
24. Goetze S, Elsner P. Solar urticaria. J Dtsch Dermatol Ges. 2015; 13(12):1250-3.
25. Roelandts R. Diagnosis and treatment of solar urticaria. Dermatol Ther. 2003; 16(1):52-6.
26. Godse K, Farooqui S, Nadkarni N, Patil S. Prevalence of cholinergic urticaria in Indian adults. Indian Dermatol Online J. 2013; 4(1):62-63.
27. Altrichter S, Wosny K, Maurer M. Successful treatment of cholinergic urticaria with methantheliniumbromide. J Dermatol. 2015; 42(4):422-4.
28. Kaplan AP, Greenberger PA, Geller M. Vibratory Urticaria and ADGRE2. N Engl J Med. 20167; 375(1):94-5.
29. Boyden SE *et al*. Vibratory Urticaria Associated with a Missense Variant in ADGRE2. N Engl J Med. 2016; 374(7):656-63.
30. Park H *et al*. Aquagenic Urticaria: A Report of Two Cases. Ann Dermatol. 2011; 23(Suppl 3):S371-S374.
31. Rothbaum R, McGee JS. Aquagenic urticaria: diagnostic and management challenges. J Asthma Allergy. 2016; 9:209-213.
32. Bhatia R, Alikhan A, Maibach H. Contact Urticaria: Present Scenario Indian J Dermatol. 2009; 54(3):264-268.
33. Williams JD, Lee AY, Matheson MC, Frowen KE, Noonan AM, Nixon RL. Occupational contact urticaria: Australian data. Br J Dermatol. 2008; 159:125-31.
34. Sabroe RA. Acute urticaria. Immunol Allergy Clin North Am. 2014; 34(1):11-21.
35. Uguz F, Engin B, Yilmaz E. Quality of life in patients with chronic idiopathic urticaria: The impact of Axis I and Axis II psychiatric disorders. Gen Hosp Psychiatry. 2008; 30:453-7.
36. Reeves GE, Boyle MJ, Bonfield J, Dobson P, Loewenthal M. Impact of hydroxychloroquine therapy on chronic urticaria: Chronic autoimmune urticaria study and evaluation. Intern Med J. 2004; 34:182-6.
37. Sharma VK, Gera V, Tiwari VD. Chronic urticaria: Expanding the autoimmune kaleidoscope. Med J Armed Force India. 2004; 60:372-8
38. Fraser K, Robertson L. Chronic urticaria and autoimmunity. Skin Therapy Lett. 2013; 18(7):5-9.
39. Wedi B, Raap U, Wieczorek D, Kapp A. Urticaria and infections. Allergy Asthma Clin Immunol. 2009; 5(1):10.
40. Wedi B, Raap U, Kapp A. Chronic urticaria and infections. Curr Opin Allergy Clin Immunol. 2004; 4(5):387-96
41. Tonacci A, Billeci L, Pioggia G, Navarra M, Gangemi S. Omalizumab for the Treatment of Chronic Idiopathic Urticaria: Systematic Review of the Literature. Pharmacotherapy. 2017; 37(4):464-480.
42. Magerl M, Pisarevskaja D, Scheufele R, Zuberbier T, Maurer M. Effects of a pseudo allergen-free diet on chronic spontaneous urticaria: a prospective trial. Allergy. 2010; 65(1):78-83.
43. Church MK, Kolkhir P, Metz M, Maurer M. The role and relevance of mast cells in urticaria. Immunol Rev. 2018; 282(1):232-247.
44. Ono S, Egawa G, Kabashima K. Regulation of blood vascular permeability in the skin. Inflamm Regen. 2017; 37:11.
45. Khalaf AT, Li W, Jinquan T. Current advances in the management of urticaria. Arch Immunol Ther Exp (Warsz). 2008; 56(2):103-14.
46. Criado PR, Criado RF, Takakura CF, Pagliari C, de Carvalho JF, Sotto MN *et al*. Ultrastructure of vascular permeability in urticaria. Isr Med Assoc J. 2013; 15(4):173-7.

47. Popov TA. Challenges in the Management of hronic Urticaria. World Allergy Organ J. 2011; 4(Suppl 3):S28-S31.
48. Sand FL, Thomsen SF.TNF-Alpha Inhibitors for Chronic Urticaria: Experience in 20 Patients. J Allergy (Cairo). 2013; 2013:130905.
49. Ban YG *et al*. Clinical features of elderly chronic urticaria. Korean J Intern Med. 2014; 29(6):800-806.
50. Misra L *et al*. Angioedema: Classification, management and emerging therapies for the perioperative physician Indian J Anaesth. 2016; 60(8):534-541.
51. Deza G, Giménez-Arnau AM.Itch in Urticaria Management. Curr Probl Dermatol. 2016; 50:77-85.
52. Perkowska J *et al*. Occurrence of sleep-related breathing disorders in patients with chronic urticaria at its asymptomatic or oligosymptomatic stages Postepy Dermatol Alergol. 2016; 33(1):63-67.
53. Ivan Cherrez-Ojeda *et al*. Checklist for a complete chronic urticaria medical history: an easy tool. World Allergy Organ J. 2017; 10(1):34.
54. Khalaf AT, Li W, Jinquan T. Current advances in the management of urticaria. Arch Immunol Ther Exp (Warsz). 2008; 56(2):103-14.
55. Schoepke N, Doumoulakis G, Maurer M. Diagnosis of urticaria. Indian J Dermatol. 2013; 58(3):211-218.
56. Nuzzo V *et al*. Idiopathic chronic urticaria and thyroid autoimmunity Experience of a single center Dermatoendocrinol. 2011; 3(4):255-258.
57. Ghosh SK, Ghosh S. Autologous Serum Skin Test. Indian J Dermatol. 2009; 54(1):86-87.
58. Pajno GB. Through the Looking Glass: Chronic Urticaria Treated with Anti-IgE Therapy. Pediatr Allergy Immunol Pulmonol. 2016; 29(1):56-57.
59. Chaudhry T, Hissaria P, Wiese M, Heddle R, Kette F, Smith WB. Oral drug challenges in non-steroidal anti-inflammatory drug-induced urticaria, angioedema and anaphylaxis. Intern Med J. 2012; 42(6):665-71.
60. Kozel MM, Sabroe RA. Chronic urticaria: aetiology, management and current and future treatment options. Drugs. 2004; 64(22):2515-36.
61. Sharma M, Bennett C, Cohen SN, Carter B. H1-antihistamines for chronic spontaneous urticaria. Cochrane Database Syst Rev. 2014; (11):CD006137.
62. Hasala H, Moilanen E, Janka-Junttila M, Giembycz MA, Kankaanranta H. First-generation antihistamines diphenhydramine and chlorpheniramine reverse cytokine-afforded eosinophil survival by enhancing apoptosis. Allergy Asthma Proc. 2007; 28(1):79-86.
63. Hong-Woo Cheon. A Case of Combined Cholinergic and Cold Urticaria. Korean J Intern Med. 2012; 27(4):478-479.
64. Ortonne JP. Urticaria and its subtypes: the role of second-generation antihistamines. Eur. J Intern Med. 2012; 23(1):26-30.
65. Jongen PJ *et al*. Patient-reported adverse effects of high-dose intravenous methylprednisolone treatment: a prospective web-based multi-center study in multiple sclerosis patients with a relapse. J Neurol. 2016; 263:1641-1651.
66. Alberto Tedeschi A, Girolomoni G, Asero R. Chronic urticaria: Diagnostic workup and treatment. Eur Ann Allergy Clin Immunol. 2006; 39:221-4
67. Di Lorenzo G, D'Alcamo A, Rizzo M, Leto-Barone MS, Bianco CL, Ditta V *et al*. Leukotriene receptor antagonists in monotherapy or in combination with antihistamines in the treatment of chronic urticaria: a systematic review. J Asthma Allergy. 2008; 2:9-16.
68. Samarqandi N, Shareh Asbab. Part-II. Idara Kitab Us Shifa New Delhi, 2007, 198-199.
69. Ahmed AK, Mobeen A, Alam MA, Quamri MA. Clinical efficacy and safety of unani formulation for the management of Sharaa (Urticaria) - A case series study. The Pharma Innovation. 2019; 8(2):454-455.
70. Khan HA, Haziq Jaseem. Book Depo. New Delhi, 1987.