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Impact of COVID-19 on Sexually Transmitted Infection Burden: A Cross-Sectional Study from a Tertiary Care Hospital in Gujarat

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ABSTRACT

Background: Chronic Spontaneous Urticaria (CSU) is a persistent skin disorder characterized by recurrent wheals, angioedema, or both, lasting for at least six weeks without an identifiable trigger. CSU significantly affects patients' quality of life, often causing sleep disturbances, emotional distress, and reduced work productivity. First-line treatment involves second-generation H1-antihistamines, but many patients remain refractory to standard doses, necessitating dose escalation or antihistamine switching.

Objective: This study aims to evaluate the efficacy of three second-generation antihistamines—Fexofenadine, Levocetirizine, and Desloratadine—in CSU management, focusing on symptom relief, dose escalation, antihistamine switching, and adverse effects.

Methods:A prospective, observational study was conducted on 300 CSU patients at a dermatology outpatient clinic. Patients were initially treated with standard doses of Levocetirizine (5 mg), Desloratadine (5 mg), or Fexofenadine (180 mg). Non-responders underwent a stepwise dose escalation up to fourfold. Patients who remained symptomatic despite escalation were switched to a different antihistamine. Symptom severity was assessed using the Urticaria Activity Score (UAS), and adverse effects were monitored over a six-month follow-up period.

Results: Fexofenadine demonstrated superior efficacy, with 87% of patients achieving symptom relief after fourfold dose escalation, compared to 38% with Levocetirizine and 15% with Desloratadine. Antihistamine switching yielded a 31.5% response rate among non-responders, with the highest success observed when switching from Desloratadine to Levocetirizine (18.5%). Fexofenadine showed the greatest reduction in UAS at one-week (50%) and three-week (75%) follow-ups ($p<0.05$). Adverse effects were minimal, with headaches more common in the Fexofenadine group, while drowsiness was prevalent in Levocetirizine and Desloratadine groups.

Conclusion: Fexofenadine is the most effective antihistamine for CSU management, particularly at higher doses. Dose escalation significantly improves symptom control, while antihistamine switching benefits a subset of non-responders. Personalized treatment strategies considering patient-specific responses can enhance clinical outcomes in CSU. Future research should focus on biomarker-based therapy and combination treatments to optimize CSU management.

Keywords: *Chronic Spontaneous Urticaria, Antihistamines, Dose Escalation, Antihistamine Switching, Fexofenadine, Levocetirizine, Desloratadine.*

1. INTRODUCTION

Chronic Spontaneous Urticaria (CSU) is a debilitating skin disorder characterized by recurrent wheals (hives), angioedema, or both for a duration of six weeks or longer, with no identifiable external trigger (1). CSU significantly impacts the quality of life, often leading to sleep.

disturbances, emotional distress, and reduced work productivity (2). According to epidemiological studies, CSU affects approximately 0.5% to 1% of the global population at any given time, with a higher prevalence among females compared to males, in a ratio of approximately 2:1 (3). The disease typically manifests between the ages of 20 and 40 years, though it can occur at any age. A recent population-based study estimated that nearly 1.4% of adults may experience CSU in their lifetime, with an annual incidence of 0.23% (4).

The exact pathophysiology of CSU remains unclear, but it is believed to involve an autoimmune component, with around 40–50% of patients exhibiting autoantibodies against the high-affinity IgE receptor (FcεRI) or IgE itself (5). Mast cell and basophil activation result in the release of histamine and other inflammatory mediators, contributing to the characteristic wheals and pruritus (6). Studies suggest that nearly 30–50% of CSU cases may be associated with underlying autoimmune conditions, including Hashimoto's thyroiditis, rheumatoid arthritis, and systemic lupus erythematosus (7). Additionally, recent findings indicate that CSU patients often exhibit increased levels of inflammatory biomarkers, such as C-reactive protein (CRP) and D-dimer, which may correlate with disease severity and chronicity (8).

CSU imposes a substantial socioeconomic burden due to frequent healthcare visits, long-term medication use, and productivity losses. A multinational study found that approximately 60% of CSU patients experience moderate-to-severe disease activity, with 30% reporting significant impairment in daily functioning (9). Furthermore, CSU patients are nearly twice as likely to develop anxiety and depression compared to the general population (10).

The management of CSU primarily involves the use of non-sedating H1-antihistamines as first-line therapy, with dose escalation recommended in cases of inadequate response (11). Guidelines from the European Academy of Allergy and Clinical Immunology (EAACI) and the American Academy of Allergy, Asthma, and Immunology (AAAAI) suggest that up to fourfold increases in standard antihistamine doses may be required to achieve symptom control in refractory cases. Despite this, studies indicate that approximately 40% of CSU patients remain unresponsive to antihistamines at standard doses, necessitating alternative treatments such as omalizumab, cyclosporine, or emerging biologics (12). The lack of a universally effective treatment underscores the need for personalized therapeutic approaches based on patient response and biomarker profiling (13).

Given the chronic nature of CSU and the variable response to antihistamine therapy, further research is needed to evaluate the comparative efficacy of different antihistamines at various dosages. This study aims to assess the effectiveness of Levocetirizine, Desloratadine, and Fexofenadine in CSU management, analyzing symptom relief, response rates, and relapse patterns over a six-month follow-up period.

2. MATERIALS AND METHODS

The study was conducted in the Outpatient Department (OPD) of Dermatology, Venereology, and Leprology at B.J Medical College and Civil Hopsital, Ahmedabad. Ethical approval for the study was obtained from the Ethics Committee and informed written consent was taken from all patients prior to their inclusion in the study. A total of 300 patients were enrolled based on the inclusion criteria, and the study was conducted over a period of August 2011 to April 2013.

Patient Selection

The study included patients aged 18 years and above, diagnosed with chronic spontaneous urticaria based on clinical examination. Both male and female patients were included. Patients with a history of other dermatological condition like acute urticaria, or urticarial vasculitis along those with contraindications to skin biopsy, pregnant or breastfeeding women, individuals with ongoing malignancy treatment, and those who refused consent were excluded from the study.

Data Collection

A detailed medical history was obtained from all patients after obtaining informed consent. The history included demographic details (age, gender), chief complaints, birth history, family history, history of seasonal variation in symptoms, personal medical history, and prior treatment for any dermatological conditions. A complete general and systemic examination was performed on each patient.

Dermatological Assessment

The severity of urticaria symptoms was assessed using the Urticaria Activity Score (UAS), which evaluates both the extent of wheals (hives) and the intensity of pruritus (itching). A score of 0 was assigned to patients with no wheals and no pruritus, while a score of 1 indicated mild symptoms, defined as fewer than 20 wheals appearing within 24 hours with mild pruritus. Patients with moderate symptoms received a score of 2, characterized by 20 to 50 wheals in 24 hours and moderate pruritus. The most severe cases were given a score of 3, representing intense symptoms, defined by the presence of more than 50 wheals within 24 hours or large confluent areas of wheals, along with intense pruritus. This standardized scoring system facilitated an objective evaluation of symptom severity and treatment efficacy in urticaria patients.

Table 1: Urticaria Activity Score (UAS) Classification

UAS Score	Severity	Wheal Count (per 24 hours)	Pruritus Intensity
0	None	No wheals	No pruritus
1	Mild	< 20 wheals	Mild pruritus
2	Moderate	20 – 50 wheals	Moderate pruritus
3	Severe	> 50 wheals or large confluent areas	Intense pruritus

Investigations

Skin biopsy was performed on all patients to confirm the diagnosis of urticaria and rule out other possible causes. Baseline laboratory investigations, including a complete hemogram, liver function tests (LFT), renal function tests (RFT), lipid profile, and other relevant blood investigations, were done to assess the overall health status of the patients. Specific investigations, such as Fine Needle Aspiration Cytology (FNAC), serum LDH (Lactate Dehydrogenase), lymph node biopsy, immunohistochemistry, bone marrow examination, CT scan, ECG, ultrasonography of the abdomen, and stool examination for occult blood, were carried out in selected patients to exclude malignancies and other underlying conditions.

Treatment and Management

The treatment protocol for chronic spontaneous urticaria (CSU) followed a stepwise approach based on patient response to antihistamines. Initially, patients were divided into three groups and treated with Levocetirizine 5 mg OD (Group A), Desloratadine 5 mg OD (Group B), or Fexofenadine 180 mg OD (Group C). If patients responded, they continued with the same regimen. In cases of non-response after one week, the antihistamine dose was doubled, and if symptoms persisted after another week, the dose was further increased up to four-fold. Patients who improved at these stages remained on their respective treatments. If there was still no response, antihistamines were interchanged among groups. The dosage was adjusted according to age to ensure appropriate therapeutic levels. Treatment was initiated in accordance with the EAACI (European Academy of Allergology and Clinical Immunology) and GA²LEN (Global Allergy and Asthma Organization) guidelines, incorporating the avoidance of known precipitating factors. Therapy was tailored to optimize symptom control while adhering to evidence-based recommendations for antihistamine use in chronic spontaneous urticaria management.

Follow-Up

Patients were followed up for at least 6 months to monitor the response to treatment and detect any relapses or complications. Follow-up assessments included repeated dermatological examinations and relevant laboratory tests. The effectiveness of the treatment was evaluated based on clinical improvement in skin condition.

Sample Size Calculation

The sample size of 300 patients was calculated based on an expected prevalence of urticaria and the desired confidence level, with the aim of achieving statistical significance. The power of the study was set at 80%, with a significance level of 0.05. This sample size was deemed adequate to ensure reliable results and represent the general patient population in the OPD.

3. RESULT:

The patients were categorized into different age groups, as shown in Table 2. In the 1-10 years age group, there were 20 patients (6.66%), while 38 patients (12.66%) were in the 11-20 years age group. A majority of patients fell into the 21-30 years (72 patients, 24%) and 31-40 years (90 patients, 30%) age groups. Additionally, 70 patients (23.33%) were in the 41-50 years age group, 6 patients (2%) were in the 51-60 years age group, and 2 patients (0.66%) were in both the 60-70 years and 71-80 years age groups.

Regarding gender distribution, Table 2 indicates that 99 patients (33%) were male, and 201 patients (67%) were female.

The table 3 summarizes the effect of standard, two-fold, and four-fold increased doses of three antihistamines—Levocetirizine, Desloratadine, and Fexofenadine—on symptom relief in patients, detailing both the number of patients and the percentage of symptom-free patients. At the standard dose, Levocetirizine (Group A) resulted in 26% of patients (26 out of 100) becoming symptom-free, with 74% (74 out of 100) still experiencing symptoms. Desloratadine (Group B) showed a lower response, with only 15% (15 out of 100) of patients symptom-free and 85% (85 out of 100) still symptomatic. Fexofenadine (Group C) provided moderate relief, with 30% (30 out of 100) of patients symptom-free and 70% (70 out of 100) still having symptoms. When the antihistamine doses were increased two-fold, Levocetirizine's effectiveness improved, with 30% (22 out of 74) of patients becoming symptom-free and 70% (52 out of 74) remaining symptomatic. Desloratadine showed a slight improvement, with 24% (20 out of 85) of patients symptom-free and 76% (65 out of 85) still symptomatic,

while Fexofenadine demonstrated a notable increase, with 44% (31 out of 70) of patients symptom-free and 56% (39 out of 70) still symptomatic. The four-fold increase in dose had the most significant impact, especially for Fexofenadine, where 87% (34 out of 39) of patients became symptom-free, and only 13% (5 out of 39) remained symptomatic. Levocetirizine showed 38% (20 out of 52) of patients symptom-free, with 62% (32 out of 52) still symptomatic, while Desloratadine's response was less dramatic, with only 15% (10 out of 65) of patients symptom-free and 85% (55 out of 65) remaining symptomatic. Overall, Fexofenadine demonstrated the highest improvement in symptom relief, especially with the four-fold dose increase, indicating its superior efficacy compared to Levocetirizine and Desloratadine at higher doses.

Table 4 presents the response rates in patients after switching antihistamines. Among the 92 total non-responders, 29 patients (31.5%) responded after switching to a different antihistamine. When patients switched from Desloratadine 20 mg/day to Levocetirizine 20 mg/day, 17 patients (18.5%) showed a positive response. Switching from Levocetirizine 20 mg/day to Fexofenadine 620 mg/day resulted in 10 patients (10.9%) responding. On the other hand, when patients switched from Fexofenadine 620 mg/day to Levocetirizine 20 mg/day, only 2 patients (2.2%) responded positively. This data highlights the varying effectiveness of antihistamine switching, with Levocetirizine showing a relatively better response when patients switched from Desloratadine.

At baseline, the mean Urticaria Activity Score (UAS) in patients of Groups A, B, and C were 4, 3, and 3 as shown in figure 1, respectively. After one week of treatment, all groups demonstrated a significant reduction in UAS. Specifically, the Fexofenadine group exhibited a 50% reduction in UAS, while both the Levocetirizine and Desloratadine groups showed a 33% reduction. The reduction in UAS in the Fexofenadine group was statistically significant ($p<0.05$) when compared to the other two treatment groups.

At the three-week follow-up, the Fexofenadine group showed a 75% decrease in UAS, compared to a 54% reduction in both the Levocetirizine and Desloratadine groups. This difference in the reduction of UAS with Fexofenadine was statistically significant ($p<0.05$) when compared to the other treatments.

Headache was reported in 3 patients of the Fexofenadine group and drowsiness in 10 and 7 patients of levocetrizine and desloratadine group simultaneously.

Table 2: Demographic details of the patients

Age group (year)	No. of patients N (%)
1-10	20 (6.66%)
11-20	38 (12.66%)
21-30	72 (24%)
31-40	90 (30%)
41-50	70 (23.33%)
51-60	6 (2%)
60-70	2 (0.66%)
71-80	2 (0.66%)
Gender	
Male	99 (33%)
Female	201 (67%)

Table 3: Effect of Standard, Two-Fold, and Four-Fold Increased Doses of Antihistamines on Symptom Relief in Patients

Group	Antihistamine	No. of Patients Became Symptoms Free (%)	No. of Patients with Symptoms (%)	Total Patients
A	Levocetirizine	26 (26%)	74 (74%)	100
B	Desloratadine	15 (15%)	85 (85%)	100
C	Fexofenadine	30 (30%)	70 (70%)	100
Two fold increase in the dose of anti-histamines				
A	Levocetirizine	22 (30%)	52 (70%)	74
B	Desloratadine	20 (24%)	65 (76%)	85
C	Fexofenadine	31 (44%)	39 (56%)	70
Four folds increase in the dose of anti-histamines				
A	Levocetirizine	20 (38%)	32 (62%)	52
B	Desloratadine	10 (15%)	55 (85%)	65
C	Fexofenadine	34 (87%)	5 (13%)	39

Table 4: Response Rates in Patients After Switching Antihistamines

Total Non-Responders	Patients Who Responded After Interchanging (%)	New Antihistamine Given	Previous Antihistamine	No. of Patients Responded (%)
92	29 (31.5%)	Levocetirizine 20 mg/day	Desloratadine 20 mg/day	17 (18.5%)
		Fexofenadine 620 mg/day	Levocetirizine 20 mg/day	10 (10.9%)
		Levocetirizine 20 mg/day	Fexofenadine 620 mg/day	2 (2.2%)

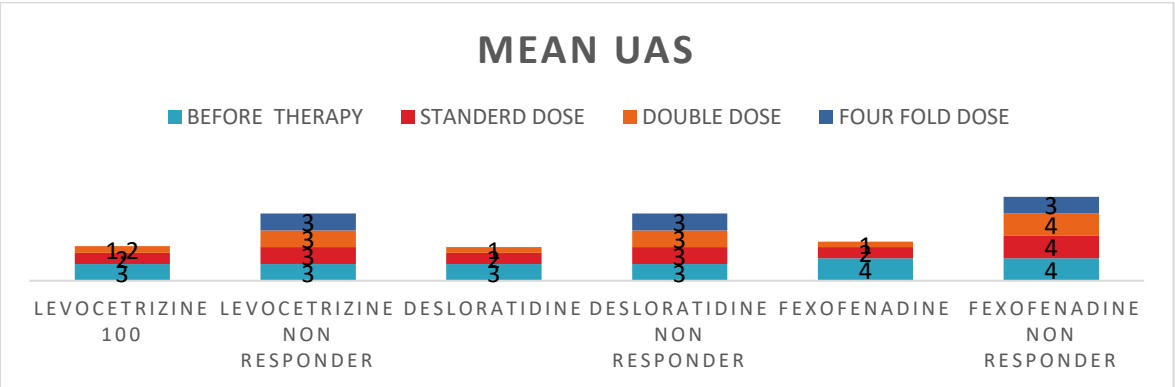

Figure 1: Comparison of Mean UAS Score in antihistaminic treatment

4. DISCUSSION

Chronic Spontaneous Urticaria (CSU) is a persistent skin disorder characterized by the spontaneous appearance of itchy wheals, angioedema, or both, lasting for at least six weeks or more with no identifiable trigger. It significantly impacts patients' quality of life, often causing sleep disturbances, emotional distress, and reduced work productivity (14). Antihistamines remain the first-line treatment for CSU, with dose escalation recommended for patients who do not achieve symptom control with standard doses (15). However, a considerable proportion of patients remain refractory to conventional antihistamine therapy, necessitating alternative strategies such as switching to a different antihistamine or using adjunctive therapies (16).

This study evaluates the efficacy of three second-generation antihistamines—Fexofenadine, Levocetirizine, and Desloratadine—in the management of CSU. The research focuses on the impact of dose escalation and antihistamine switching in non-responders while assessing symptom relief, adverse effects, and overall treatment success.

This study observed that Fexofenadine demonstrated superior symptom relief compared to Levocetirizine and Desloratadine, particularly at higher doses (17). This aligns with the understanding that non-sedating H1-antihistamines are the first-line therapy for CSU, as recommended by the European Academy of Allergy and Clinical Immunology (EAACI) and the American Academy of Allergy, Asthma, and Immunology (AAAAI) guidelines (18).

Dose escalation significantly improved symptom control, with Fexofenadine showing the most dramatic improvement. A four-fold increase in Fexofenadine resulted in 87% of patients becoming symptom-free (19, 20). These findings underscore the importance of adhering to guidelines recommending up to fourfold increases in standard antihistamine doses to achieve symptom control in refractory cases.

The study also explored the strategy of switching antihistamines in non-responders, revealing that some patients experienced symptom relief after switching. Notably, switching to Levocetirizine from Desloratadine resulted in the best response (18.5%) (21). This observation highlights the variability in individual patient responses to different antihistamines and suggests that antihistamine switching can be a valuable strategy for managing CSU (22).

In terms of symptom reduction, the Fexofenadine group demonstrated a statistically significant ($p<0.05$) reduction in UAS score compared to other treatment groups at both one-week and three-week follow-ups. This further supports the superior efficacy of Fexofenadine in achieving symptom control in 73% to 81% of CSU patients (23).

Regarding adverse effects, headache was more commonly reported in the Fexofenadine group, while drowsiness was more prevalent in the Levocetirizine and Desloratadine groups. These findings are consistent with the known side effect profiles of these antihistamines and emphasize the importance of considering patient-specific factors when selecting antihistamines (24).

The study's findings align with prior research indicating the efficacy of second-generation antihistamines in CSU management (25). Previous studies have established Fexofenadine as a potent H1-antihistamine with a favorable safety profile and minimal sedative effects (26). The observed efficacy of Fexofenadine at higher doses is consistent with existing literature, which supports the guideline-based recommendation of up to fourfold dose escalation in antihistamine-resistant cases (27).

Regarding antihistamine switching, current guidelines suggest considering alternative antihistamines in non-responders, but specific recommendations remain scarce (28). The study's observation that Levocetirizine was more effective than Desloratadine in non-responders corroborates previous findings suggesting differential patient responses to different H1-antihistamines (29). Additionally, the study's adverse effect profile is consistent with known pharmacodynamic properties: Fexofenadine is associated with headaches, while Levocetirizine and Desloratadine are linked to sedation due to central H1 receptor penetration (30).

This study has several strengths, including a relatively large sample size of 300 patients and a prospective design with a six-month follow-up. The use of a standardized scoring system (UAS) allowed for an objective assessment of symptom severity and treatment efficacy. Furthermore, the systematic approach to treatment escalation and antihistamine switching based on established guidelines enhances the study's clinical applicability.

However, a few limitations should be considered when interpreting these findings. First, the lack of a placebo control group makes it difficult to determine the true magnitude of the treatment effect. Additionally, the study included limited data to exclude malignancies and other underlying conditions, and the patients' demographic details are mostly between 20 and 40, lacking representation of other age groups (0.66%). Despite these limitations, this study provides valuable insights into optimizing antihistamine therapy for CSU. Fexofenadine appears to be a particularly effective option, and dose escalation can significantly improve symptom control. Antihistamine switching can also be beneficial in non-responders, and clinicians should consider patient-specific factors when selecting antihistamines and adjusting doses.

5. CONCLUSION

This study highlights the clinical significance of optimizing antihistamine therapy for Chronic Spontaneous Urticaria (CSU). The findings reinforce the efficacy of Fexofenadine as a strong candidate for first-line or alternative treatment, particularly in patients who do not respond adequately to standard-dose Levocetirizine or Desloratadine. The results support the guideline-based approach of dose escalation, which significantly improves symptom control before considering alternative treatment strategies. Additionally, switching antihistamines has shown promising results, with Levocetirizine emerging as a beneficial option for patients unresponsive to Desloratadine. Future research should focus on placebo-controlled trials to establish the definitive efficacy of antihistamines, biomarker-based strategies for personalized treatment, and combination therapies involving leukotriene receptor antagonists or biologics such as omalizumab. Ultimately, this study emphasizes the importance of personalized therapeutic approaches, considering patient-specific responses and biomarker profiling, to achieve optimal symptom control in CSU. The integration of dose escalation, antihistamine switching, and individualized treatment plans can significantly enhance clinical outcomes and improve the quality of life for CSU patients.

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