

Prescribing Pattern of Tablet form Antihistamines: An Overview of Cost and Expenditure in A Dermatology Clinic in Malaysia

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Abstract

In the management of dermatological disorders, antihistaminic drugs are one of the most frequently used systemic medications other than corticosteroids and antibiotics. Therefore, it is important to evaluate the prescribing patterns of antihistamine along with the subsequent cost and expenditure which can advise the prescribers on the rational and optimize drug use and improve therapeutic efficacy. Thus, this study main objectives are to determine;

- the prescribing pattern of solid dosage form *i.e.*, tablet for antihistamines among patients attending a dermatology clinic in Malaysia and;
- the cost for each type of antihistamines prescribed.

Method: A retrospective cross-sectional study was conducted with data of 648 prescriptions collected anonymously from the electronic Information System (eIS) from 1st of January to 31st of March 2021. **Findings:** The data suggests that loratadine (42.75%) is the most prescribed antihistamine while levocetirizine (1.39%) the least. Second generation antihistamine is the most prescribed antihistamine (60.96%) compared to the first-generation antihistamine (39.04%). The dermatology clinic also recorded the highest expenditure for loratadine (RM 3142.54) compared to other antihistamines which is 50% of the total expenditure. Other costs include hydroxyzine (RM 1729.92), desloratadine (RM 582.76), chlorpheniramine (RM 433.69), cetirizine (RM 385.79) with levocetirizine (RM 81.93) costing the lowest, which corresponds to 1% of the total expenditure. Moreover, eczema (46.14%) was the most common skin disorder reported. **Conclusion and further research:** Statistical analysis reveals that the type of antihistamine prescribed is associated with indications or type of skin disorder. Other factors *i.e.*, patients' gender and age do not influence the type of prescribed antihistamine specifically in the locality of the parameter set. Since the clinic in the study is subsidized by the government, the cost of expenditure does not play a major role in

the prescribing pattern. The follow up research can focus on all dosage forms of antihistamine and can be widen to all department of the hospital.

Keywords: Antihistamines, Pattern, Dermatology Clinic, Malaysia.

Introduction

Antihistaminic drugs are one of the most commonly and widely used systemic medications in the management of dermatological disorders (Kolasani *et al.*, 2016). They are good in treating itching caused by histamine release (Ahmed & Menshaw, 2021) and mostly used for the symptomatic relief of allergic reactions like urticaria, angioedema, rhinitis, conjunctivitis, and pruritus that are associated with skin problems (Kolasani *et al.*, 2016). There are two general types of antihistamines; first-generation antihistamines (sedating antihistamines e.g. chlorphenamine, hydroxyzine and promethazine) and second-generation antihistamines (non-sedating antihistamines e.g. loratadine, desloratadine, cetirizine and levocetirizine). In the initial choice of therapy, the prescribers prefer the second-generation antihistamines more, over the older first-generation antihistamines because they cause less sedation and cholinergic side effects (Ahmed & Menshaw, 2021).

All dermatological disorders are persistent and need lifelong treatment. As a result, antihistamine drugs are commonly prescribed in dermatology clinics. Due to the prolonged nature of the use, prescribers should undertake appropriate diagnosis and provide rational prescription of drugs by understanding both benefit and risk of drugs for patients as these are predominant in drug therapy (Suhaina, 2018). It is important to understand whether the prescriber's decision in prescribing antihistamine is influenced by factors, such as gender, age, or indication. The wide range of antihistamine availables, choices of other treatment modalities, and the complexity of interpreting specialist treatment algorithms may also influence prescribing patterns of appropriate antihistamine for each patient (Baharudin *et al.*, 2019). Evaluation of the prescribing patterns of antihistamine can advise the prescribers on the rational drug use and improve therapeutic efficacy. Thus, this study aims are to determine;

- the prescribing pattern of solid dosage form *i.e.*, tablet (tab) for antihistamines among patients attending a dermatology clinic in Malaysia and;
- the cost for each type of antihistamines prescribed.

Material and Methods

A retrospective cross-sectional study was carried out using patients' medical records who attended a dermatology clinic in Malaysia. Data was collected from electronic Information System (eIS) during the study period in 3 months from 1 January to 31 March 2021 in the dermatology clinic. The study participants included all patients who visited the dermatology Clinic during the period. Data collected consists of patients' ID (kept anonymous), prescription number, age, gender, dosage form, prescribed antihistamines, strength, dose, frequency, duration, total tablet dispensed, indications and prices of the drugs.

Collected data is entered in Microsoft Excel and analyzed for the demographic, tablet types and count, as well as cost of all the total of antihistamine that is used in dermatology Clinic. Then, the collected data also will be exported into Statistical Package for Social Science, SPSS version 26 for Windows. Pearson's Chi-square test was used to prove and show the

relationship between two categorical variables (if any). The categorical variables that showed a relationship between them and were statistically significant will be the confounding factors in contributing to the prescribing pattern. A p -value of $< .05$ is considered significant. The collected indications were observed of antihistamine and the quantity of each antihistamine use in that particular disorder were recorded. Demographic variables, total utilization of antihistamines and use rate of first and second-generations of antihistamine among patients in Dermatology Clinic will be analyzed and summarized as frequency as well as percentages.

Result and Discussion

A total of 648 prescriptions were analyzed during the study period from 1st January to 31st March 2021. There were 301 male patients (46.45%) and 347 female patients (53.55%) who received antihistamine in the dermatology Clinic.

The ratio of male to female patients who have been prescribed antihistamines is close to 1:1, which reflects the overall general population in Malaysia (Mahidin, 2021). The number of male patients is slightly lesser than female patients, however the difference is not significant. Either gender has been reported to have a slightly larger sum (Kolasani *et al.*, 2016, Kumar & Beenta, 2009). Age demographic data (Figure 1) revealed that the highest demographic age group prescribed with antihistamines were in the age group of adults (25-59 years) followed by the elderly (60 years and above). Studies from Sarkar *et al.* (2003) and Kolasani *et al.*, (2016) show similarities with our finding where their subjects were mostly in the age group of adults, however the 60 years and above patients were recorded as the least in receiving antihistamines.

The age group of patients are divided into five categories: children (0-9 years), teenagers (10-19 years), young adults (20-24 years), adults (25-59 years) and elderly (60 years and above) majority of patients are in the age group of adults (25-59 years) with 46.76%, followed by elderly, 60 years and above (37.19%) while the lowest number of patients who have been prescribed with antihistamines were children (0-9 years) is 2.31% (Figure 1).

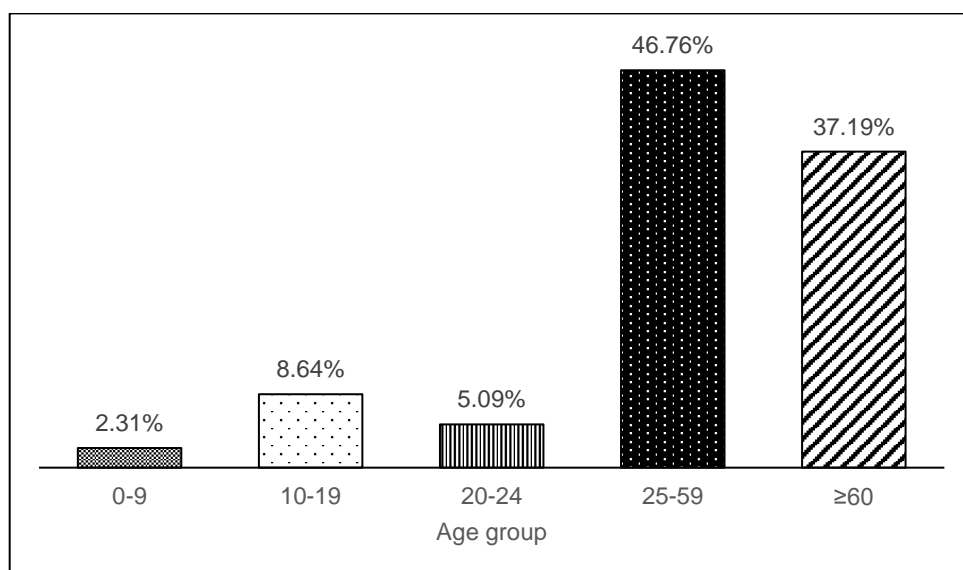


Figure 1: Patients distribution based on age groups

The total number of prescriptions that included antihistamines were 648 which accounts for a total of 51917 tablets (Table 1). Each prescription contains either cetirizine, chlorpheniramine maleate, desloratadine, hydroxyzine, loratadine or levocetirizine. Loratadine is the most prescribed antihistamine in the dermatology clinic over the three months' period with 277 prescriptions (42.8%) overall. Chlorpheniramine is the second highest with 185 prescriptions (28.55 %), followed by cetirizine (12.12%), hydroxyzine (10.50%), desloratadine (3.70%) and levocetirizine with 1.39%.

Table 1: The total number of prescriptions that include antihistamines and tablet count for each

Type of Antihistamine	Prescription number	(%) over total prescription	Tablet count	(%) over total tablet
Loratadine	277	42.8	22772	43.9
Chlorpheniramine	185	28.6	13990	26.9
Cetirizine	85	13.1	7419	14.3
Hydroxyzine	68	10.5	5406	10.4
Desloratadine	24	3.7	1714	3.3
Levocetirizine	9	1.4	616	1.2
Total	648	100	51917	100

In terms of the actual tablets count, 22772 tablets or 43.9% of the prescribed antihistamines were loratadine tablets. This is followed by chlorpheniramine (13990 tablets, 26.9%), cetirizine (7419 tablets, 14.3%), hydroxyzine (5406 tablets, 10.4%), desloratadine (1714 tablets, 3.3%) and levocetirizine with 616 totals of tablets (1.2%). Both prescription and tablet count tally suggest that the most prescribed antihistamine in this study is loratadine.

Tallies of the total number of prescriptions that include antihistamines and tablet count for each (Table 1) revealed that loratadine is the highest antihistamine prescribed in the dermatology clinic in Malaysia. However, previous reports suggest that the most prescribed antihistamines vary between studies. Kumar & Beenta (2009) found that chlorpheniramine was the most prescribed among antihistamine prescriptions. Manjusha et al. (2014) reported levocetirizine as the highest antihistamines type, in contrast to our data by which levocetirizine represented the least prescribed antihistamine.

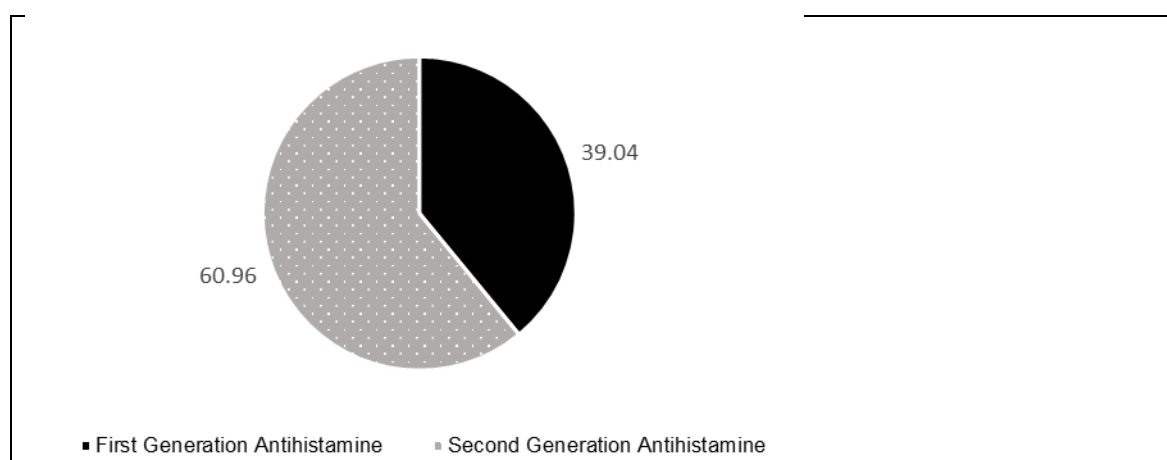


Figure2: Distribution of antihistamine prescriptions based on generation

The second-generation antihistamines are prescribed more compared to the first-generation antihistamines with a percentage of 60.96% and 39.04% respectively (Figure 2). Four main second generation antihistamines prescribed in the dermatological clinic are loratadine, desloratadine, levocetirizine and cetirizine (Table 2). The most second-generation antihistamine that is prescribed by doctors is loratadine with 70.1%. (Table 2). Meanwhile, hydroxyzine and chlorpheniramine are the major prescribed first generation of antihistamine. Chlorpheniramine with 74.14% is the most prescribed antihistamine between the two.

Table 2: Proportion of first and second generations antihistamine

Classification of Antihistamine	Antihistamine	Total Prescribed Antihistamine	Percentage (%)
First Generation	Chlorpheniramine	185	73.12
	Hydroxyzine	68	26.88
Total of prescribed 1 st generation antihistamine		253	100
Second Generation	Loratadine	277	70.13
	Cetirizine	85	21.52
	Desloratadine	24	6.07
	Levocetirizine	9	2.28
Total of prescribed 2 nd generation antihistamine		395	100

Second-generation antihistamines are preferred over first-generation antihistamines (Figure 2) mainly due to their favourable efficacy/safety ratio, pharmacokinetics, and lack of anticholinergic and sedative side effects, second-generation antihistamines are preferred over first-generation antihistamines (Kolasani *et al.*, 2016). Prescriber often choose the second-generation due to having the property of being more lipophobic or hydrophilic. Furthermore, second-generation antihistamines have fewer central nervous system and anticholinergic side effects, such as sedation and dry mouth, than first-generation antihistamines (Kolasani *et al.*, 2016). Their longer half-life allows for a more patient-friendly dosing regimen, which improves patient compliance (Kolasani *et al.*, 2016). Therefore, the second-generation of antihistamines is more effective as they also act through different mechanisms as well.

Table 3 showed the price per tablet for each type of antihistamine prescribed in the dermatological clinic. Desloratadine (RM 0.34) is the most expensive while chlorpheniramine (RM 0.03) is the cheapest antihistamine priced per tablet. The total cost for each type is calculated based on the total tablet dispensed. The total cost of prescribed antihistamine and in use in dermatology clinic from 1st January until 31st March 2021 showed that loratadine has spent the highest cost (RM 3142.54) among other antihistamines with 22772 tablets prescribed, which is 50% of the total expenditure. However, the total cost of each antihistamine does not depend on its total utilisation or number of tablets prescribed. Data also suggest that the price of antihistamine per tablet dictates the total cost (Table 3), as chlorpheniramine showed that even though the total tablet prescribed is the second highest with 13990 tablets, its total cost is only the fourth highest (RM 433.69) due to price per tablet is the cheapest (RM 0.031/tab). In addition, the total cost of hydroxyzine becomes the second highest (RM 1729.92) although its total tablets prescribed (5406 tablets) is not as high as the

total utilization of chlorpheniramine and cetirizine, again due to its costlier price per tablet (RM 0.32/tab).

Table 3: Tablet price total cost of prescribed antihistamine

Type of Antihistamine	Total Tablet Dispensed	Price per Tablet (RM)	Total Cost (RM)
Cetirizine	7419	0.052	385.79
Chlorpheniramine	13990	0.031	433.69
Desloratadine	1714	0.340	582.76
Hydroxyzine	5406	0.320	1729.92
Levocetirizine	616	0.133	81.93
Loratadine	22772	0.138	3142.54
TOTAL (RM)			6356.63

The highest indication for dermatological disorder prescribed with antihistamine (Figure 3) is eczema with 46%. Psoriasis (20%), dermatitis (13%), tinea (7%) and urticarial (5%) completes the top five dermatological disorders prescribed with antihistamine in the dermatological clinic.

The account on dermatology disorder and antihistamine prescription (Figure 3) is in agreement with previous studies. Manjusha et al (2014) suggests that the most common dermatological diseases were acne problems (31.25%) followed by eczema and psoriasis. Meanwhile, Kolasani *et al.* (2016) reported that psoriasis, eczema, and allergic contact dermatitis were the most common skin disorders for which antihistamines were prescribed in their study. These reports are again, in line with our finding, bar acne as most Malaysians do not seek clinic advice for the management of acne, but rather self-treat using over the counter cosmetics.

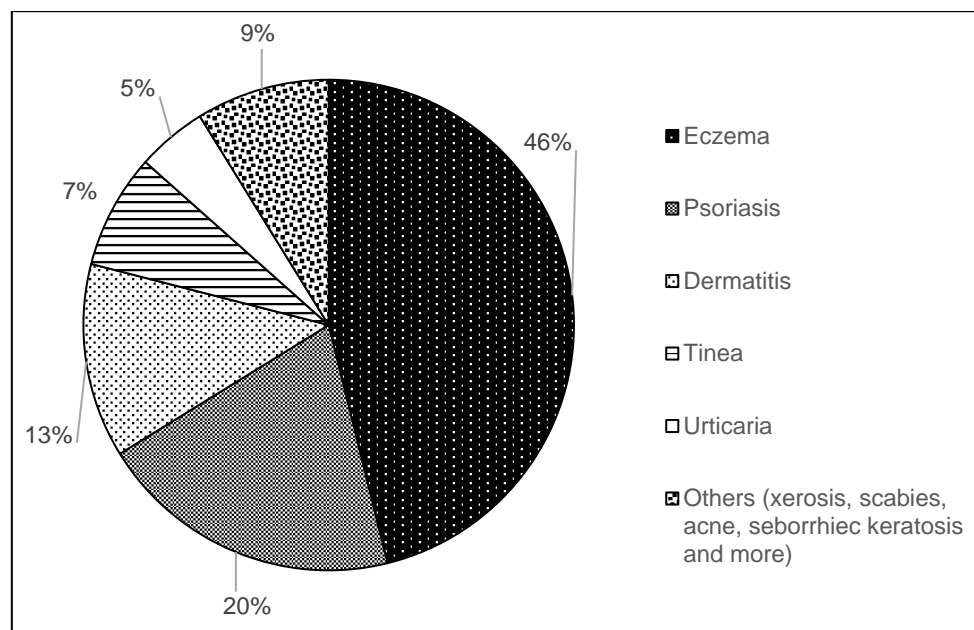


Figure 3: Percentage of indications (dermatological disorders) prescribed with antihistamine

The specific nature of this study limits direct comparison to other studies as there are not many recent studies that perform cost analysis (Table 3) which just focus on antihistamine in a dermatology clinic. The prescribed antihistamine that spends the highest cost in this study was loratadine, which is in contrast with the report by Kumar & Beenta (2009), which stated that diphenhydramine hydrochloride is the highest average cost in their study, followed by promethazine, chlorpheniramine maleate and cetirizine. This might be because their study was implemented to find out the cost of antihistamine use in different problems at the University Health Centre and not focused on skin diseases only. The cost cannot be the confounding factor that contributes to the prescribing pattern because there is no obvious relationship between the price and prescribing pattern. For example, loratadine is the most prescribed antihistamine although its price is not the cheapest among others. In short, the proper treatment guidelines for antihistamines prescribing may be needed to provide the cost-effective treatment by antihistamines (Kumar & Beenta, 2009).

When the types of prescribed antihistamines are analysed or broken down based on the indications (Table 4), loratadine recorded 124 prescriptions (41.47%) to treat eczema. In fact, loratadine is the most prescribed antihistamine for all indications bar for urticaria which cetirizine recorded the highest antihistamine with 9 prescriptions compared to loratadine (with 6 prescriptions).

Table 4: Prescribed antihistamine based on the different indications

Type of Antihistamine	Indications					
	Eczema *(%) ¹ **(%) ²	Psoriasis	Dermatiti s	Tinea	Urticari a	Total antihistamin e (%)
Loratadine 10mg	124 (41.47) (47.69)	66 (50.77) (25.38)	37 (44.58) (14.23)	27 (55.10) (10.39)	6 (20) (2.31)	260 (100)
Chlorpheniramine 4mg	87 (29.10) (54.04)	33 (25.38) (20.49)	23 (27.71) (14.29)	11 (22.45) (6.83)	7 (23.33) (4.35)	161 (100)
Cetirizine 10mg	39 (13.04) (51.32)	9 (6.92) (11.84)	13 (15.66) (17.11)	6 (12.25) (7.89)	9 (30) (11.84)	76 (100)
Hydroxyzine 25mg	32 (10.70) (53.34)	17 (13.08) (28.33)	7 (8.43) (11.67)	2 (4.08) (3.33)	2 (6.67) (3.33)	60 (100)
Desloratadine 5mg	14 (4.68) (53.85)	4 (3.08) (15.38)	3 (3.62) (11.54)	2 (4.08) (7.69)	3 (10) (11.54)	26 (100)
Levocetirizine 5mg	3 (1.01) (37.5)	1 (0.77) (12.5)	0 (0) (0)	1 (2.04) (12.5)	3 (10) (37.5)	8 (100)
Total indications	299(100)	130(100)	83(100)	49(100)	30(100)	

*(%)¹ = % calculated over total indication

**(%)² = % calculated over total antihistamine tab

There is no policy for antihistamine prescriptions in dermatology clinics in Malaysia. However, Table 4 revealed that the trend for each antihistamine prescribed follow the dermatological disorder, recording the highest number eczema, followed by psoriasis (bar cetirizine-higher for dermatitis, and levocetirizine-higher in urticaria) and the other indications. This possible trend is confirmed by running a Chi-Square test between the indications and type of antihistamines.

The Pearson Chi-Square test showed that the p -value is less than $< .05$ ($p = .00$). The analysis affirms that indications are associated with the type of antihistamine; thus, an indication (dermatological disorder) is the confounding factor that contributes to the prescribing pattern of antihistamine in the dermatology clinic.

As a comparison, other confounding factors are analysed. Pearson's Chi-Squared test was carried out to assess whether gender and age indication also bare influence on the type of antihistamine prescribed. The Pearson Chi-Square test shows that both factors have p -value $> .05$ ($p = .053$, for gender, $p = .051$ for age). Hence, we accept the null hypothesis as it was proved that gender and age is not related to the type of antihistamine being prescribed.

Conclusion

In conclusion, the association between indications (dermatology disorder) and type of antihistamines which was confirmed statistically saw similar outcomes reported by which the physicians prescribed the suitable antihistamine not only based on its indication but also based on patient's diagnosis as well as condition. According to Korfitis et al (2017), urticaria treatment is recommended to give preference for the second-generation H1 antihistamines as first-line therapy compared to first-generation antihistamines. This is in line with our report (Table 4) that shows second-generation antihistamines (21 prescriptions) are more prescribed in urticaria than first-generation antihistamines (hydroxyzine and chlorpheniramine with 9 prescriptions). Our study findings have shown that an indication/ type of skin disorder is the factor that contributed to the prescribing pattern while gender and age are not the factors which are similar to the study carried out by Wang et al. (2013) stating that there was no relationship between gender, age, patients' financial situation and job satisfaction with the prescription quality. In addition, the significance of the result is to appraise the rationality of antihistamine prescribing patterns. This is important to ensure rational drug use and avoid inappropriate medication to the patients.

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