Impact of Clinical Pharmacist Interventions in Resolving Drug-Related Problems in Patients with Systemic Autoimmune Disorders

Systemic autoimmune disorders are one of the leading causes of death and disability. They include a heterogeneous group of inflammatory diseases such as rheumatoid arthritis, systemic lupus erythematosus (SLE), systemic vasculitis, scleroderma, psoriasis, and Sjogren's syndrome that affects multiple organ systems.[1] The pharmacotherapy of systemic autoimmune disorders is rather challenging due to chronic treatment regimens and a higher disease relapse rate.[2] The complex drug regimen is associated with a high risk of drug-related problems (DRPs).[3] As DRPs are becoming one of the major concerns in modern clinical practice, timely identification and their resolution are critical in lowering the therapeutic related harm. Patient satisfaction can be enhanced through drug therapy optimization, reducing economic and iatrogenic burdens.[4]

Through individualized pharmaceutical care plans, clinical pharmacists play an essential role in the early identification and resolution of DRPs and are capable of suggesting safer and cost-effective alternatives to optimize the intense drug therapies.[5] The collaborative approach in modern medical practice has been successful and the acceptance of pharmacist interventions has raised to 52%–100%.[6] Several studies have shown that the occurrence of DRPs was common in multiple chronic diseases and the participation of clinical pharmacists in the management of DRPs had a significant impact in resolving it.[4,7,8] However, a literature search revealed the lack of published data on the identification and resolution of DRPs, through clinical pharmacists' participation among systemic autoimmune disorder patients in developing and underdeveloped countries. This study was conducted to assess the impact of clinical pharmacist-led detection and management of DRPs among systemic autoimmune disorders patients in the Indian setting.

A prospective, interventional study was carried out between July 2019 and June 2021, at the department of rheumatology, of a tertiary care teaching hospital. The study was approved by the Institutional Human Ethics Committee (JSSCPM/IHEC/2019/015). Patients of any gender, aged above 16 years and diagnosed with at least one systemic autoimmune disorder (rheumatoid arthritis, SLE, systemic vasculitis, and psoriasis) and receiving at least one medication for the same were included. All the necessary data such as demography, clinical manifestations, medical history, past and current medications, and laboratory data were collected and documented by a clinical pharmacist on daily basis. The data were carefully reviewed for any discrepancies. The international guidelines for the management of autoimmune disorders, practice guidelines for pharmacists, systematic reviews and meta-analysis, research publications, electronic databases such as Micromedex® and Medscape® were consulted for identifying and resolving the DRPs.[9] All DRPs detected were categorized into primary domains according to the Pharmaceutical Care Network Europe (PCNE V8.02) DRP classification system adopted from Pharmaceutical Care Network Europe foundation.[10]

Further, the identified DRPs and proposed clinical pharmacists' interventions to resolve DRPs were notified to a Multi-Disciplinary Care Team (MDCT) on a real-time basis. The team included the treating rheumatologist, two clinical pharmacists, and two nursing staff. Following that, clinical pharmacist interventions were implemented as per the collective decision taken by the MDCT. The clinical significance of the interventions was evaluated and categorized adopting Alderman's classification system.[11] The descriptive data were analyzed and expressed as frequencies and percentage values.

Of the 860 patients enrolled, the mean age of the study population was 48.8 ± 18.06 years. Majority (n = 348, 40.4%) of the patients belonged to the age group of 40–59 years. The study observed female predominance (n = 718, 83.4%). Rheumatoid arthritis was the most frequent diagnosis (n = 528, 61.3%), followed by SLE (n = 188, 21.8%), systemic vasculitis (n = 100, 11.6%) and psoriasis (n = 44, 5.1%). Of the 7955 drugs prescribed, the average number of drugs per patient was 9.25 (range: 3–17 drugs). The demographic and clinical characteristics of the study population are presented in Table 1. A total of 1297 DRPs and 1330 contributing factors (causes) were identified from 765 (88.9%) patients giving an average of 1.69 DRPs per patient. The categories and causes of identified DRPs are presented in Table 2. All the identified DRPs were intervened and 1245 (93.6%) interventions were accepted and 1173 (90.4%) DRPs were resolved. Majority of the interventions were at drug-level (n = 560, 42.1%) followed by patient-level (n = 468, 35.2%) and prescriber-level (n = 302, 22.7%). Of the total interventions accepted, majority belonged to moderate (n = 504, 40.4%) followed by minor (n = 486, 39.1%) and major (n = 255, 20.5%) in their clinical significance.

In this study, the frequency of DRPs was 1.69 per patient. A similar finding (1.5 per patient) was reported by Ma *et al*.; however, they assessed the DRPs in RA patients alone.

Various factors can affect the frequency of DRPs such as study population, sample size, study design, active clinical pharmacist participation, and patient-related factors such as age, gender, polypharmacy, and comorbidities.[12] We observed a high prevalence (n = 718, 83.4%) of systemic autoimmune disorders among females. The similar observations (96.5%) were reported in a study conducted in North-east India.[13] In general, the increased frequency of systemic autoimmune disorders among females could be due to the differences in the metabolism of sex hormones as compared to males.[14] In our study, the majority (38.3%) of the DRPs were associated with treatment safety indicating a high frequency of adverse drug events. This is due to polypharmacy and the use of complex treatment regimens owing to the presence of multiple comorbid conditions in systemic autoimmune disorder patients. Further, in our study, the most frequent causes of DRPs were patient-related (n = 326, 24.5%). Although there are no studies reported among systemic autoimmune disorder patients, a study conducted by Zhu *et al*. reported similar findings (25.8%) in patients with respiratory illnesses.[7] This indicates that patients' involvement in drug selection and adequate awareness about the appropriate use of drugs

Table 1: Demographic and clinical characteristics of the study populations (n=860)

Categories	Variables	Total (n=860; 100%), n (%)
Gender	Male	142 (16.5)
	Female	718 (83.4)
Age-group distribution (years)	Above 16-39	332 (38.6)
	40-59	348 (40.4)
	≥60	180 (20.9)
Marital status	Single	119 (13.8)
	Married	719 (83.6)
	Widowed or divorced	22 (2.5)
Residence locality	Rural	533 (61.9)
	Urban	327 (38.0)
Social habits	Alcoholic	30 (3.4)
	Smoking	18 (2.0)
	Both alcoholic and smoking	62 (7.2)
BMI level (kg/m^2)	≤18.5-24.9	374 (43.4)
	25.0-29.9	234 (27.2)
	≥30.0	252 (29.3)
Clinical diagnosis	RA	528 (61.3)
	SLE	188 (21.8)
	Systemic vasculitis	100 (11.6)
	Psoriasis	44 (5.1)
Disease duration (years)	<1	207 (24.0)
	1-5	473 (55)
	>5	180 (20.9)
Polypharmacy (drugs)	≤5	95 (11.0)
	>5	765 (88.9)
Comorbidities	No comorbidities	154 (17.9)
	1-3	618 (71.8)
	>3	88 (10.2)
Most common comorbidities	Hyperlipidemia	300 (24.61)
	Hypertension	265 (21.73
	Type 2 diabetes mellitus	255 (20.92)
	Kidney disease	107 (8.78)
	Hypothyroidism	98 (8.04)
Number of drugs prescribed (drugs/patient)	<5	106 (12.3)
	≥5	754 (87.6)
Patients' prescribed with the most common class of drugs	Disease-modifying antirheumatic drugs	718 (86.1)
	Glucocorticoids	673 (69.6)
	Analgesic and antipyretic drugs	520 (63.8)
	Gastroprotective drugs	458 (55.3)
	Vitamins and minerals	413 (47.3)
	Hypoglycemic agents	270 (38.2)

RA=Rheumatoid arthritis, SLE=Systemic lupus erythematosus, BMI=Body mass index

by the patients is important. Therefore, we recommend a multi-disciplinary approach involving patients along with the prescriber and clinical pharmacist during drug selection to minimize the patient-related DRPs.

Most (40.4%) of the interventions in our study were of moderate clinical significance indicating adjustments required to enhance the effectiveness of drug therapy. There is no published literature in this regard among systemic autoimmune disorder patients. However, a study conducted by Lombardi *et al*. in the internal medicine unit reported that a majority (63.2%) of the interventions were of moderate clinical significance.[8]

In our study, 93.6% of clinical pharmacist interventions were accepted and led to the resolution of 90.4% of DRPs. A study conducted in the respiratory unit also reported a similar rate (96.2%) of acceptance of interventions; however, the rate of resolution of DRPs was much less (81.9%) as compared to our study.[7] This difference is because, only 85.6% of the

Table 2: Categories and causes of identified drug-related problems based on pharmaceutical care network Europe V8.02

Categories of identified DRPs			
Primary domain	**Subdomain code**	**Nature of DRPs**	**Frequency, *n* (%)**
Treatment effectiveness	P1.1	No effect of drug treatment	119 (9.1)
	P1.2	Effect of drug treatment not optimal	198 (15.2)
	P1.3	Untreated symptoms or indication	155 (11.9)
Treatment safety	P2.1	Adverse drug event (possibly) occurring	497 (38.3)
Others	P3.1	Problem with the cost-effectiveness of the treatment	108 (8.3)
	P3.2	Unnecessary drug treatment	220 (16.9)
		Total number of DRPs	1297 (100)
Causes of identified DRPs			
Primary domain	**Subdomain code**	**Nature of causes**	**Frequency, *n* (%)**
Drug selection	C1.1	Inappropriate drug according to guidelines/formulary	9 (0.6)
	C1.2	Inappropriate drug (within guidelines but otherwise contra-indicated)	13 (0.9)
	C1.3	No indication for drug	29 (2.1)
	C1.4	Inappropriate combination of drugs or drugs and herbal medication	133 (10)
	C1.5	Inappropriate duplication of the therapeutic group or active ingredient	24 (1.8)
	C1.6	No drug treatment in spite of existing indication	66 (4.9)
	C1.7	Too many drugs prescribed for an indication	28 (2.10)
Drug form	C2.1	Inappropriate drug form (for this patient)	5 (0.3)
Dose selection	C3.1	Drug dose too low	19 (1.43)
	C3.2	Drug dose too high	31 (2.33)
	C3.3	Dosage regimen not frequent enough	45 (3.38)
	C3.4	Dosage regimen too frequent	38 (2.86)
	C3.5	Dose timing instructions wrong, unclear, or missing	61 (4.57)
Treatment duration	C4.1	Duration of treatment too short	22 (1.65)
	C4.2	Duration of treatment too long	43 (3.23)
Dispensing	C5.1	Prescribed drug not available	35 (2.63)
	C5.2	Necessary information not provided	22 (1.65)
	C5.3	Wrong drug, strength, or dosage advised (OTC)	34 (2.56)
	C5.4	Wrong drug or strength dispensed	46 (3.46)
Drug use process	C6.1	Inappropriate timing of administration and/or dosing interval	161 (12.1)
	C6.2	Drug under-administered	38 (2.85)
	C6.3	Drug over-administered	33 (2.48)
	C6.4	Drug not administered at all	29 (2.18)
	C6.5	Wrong drug administered	40 (3.01)
Patient-related	C7.1	Patient uses/takes less drug than prescribed or doesn't take the drug at all	41 (3.08)
	C7.2	Patient uses/takes more drugs than prescribed	39 (2.93)
	C7.4	Patient uses unnecessary drug	79 (5.94)
	C7.6	Patient stores drug inappropriately	44 (3.31)
	C7.7	Inappropriate timing or dosing intervals	72 (5.41)
	C7.8	Patient administers/uses the drug in a wrong way	36 (2.71)
	C7.9	Patient unable to use drug/form as directed	15 (1.13)
		Total number of causes *	1330 (100)

DRPs=Drug-related problems, PCNE=Pharmaceutical care network Europe, OTC=Over-the-counter drugs, *One DRP may have one or more causes

accepted interventions were implemented in their study, in contrast to our study where all of the accepted interventions were implemented. This demonstrates that the clinical pharmacist participation is needed in identifying, resolving and optimizing pharmacotherapy in systemic autoimmune disorder patients among the Indian or other settings.

This study concluded that the prevalence of DRPs in patients with systemic autoimmune disorders is high and clinical pharmacists' intervention can greatly help in the early detection and adequate management of DRPs in systemic autoimmune disorder patients.

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Conflicts of interest

There are no conflict of interest.

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