A Systematic Review, Audit of "Prescriptions and Adherence to Prescribing Guidelines" for Selective Serotonin Reuptake Inhibitors in A Tertiary Care Hospital

K. Nithiyapriya[*], P. Renuga[1], P. Pragatheesvarar[2], M. Robert Selvin[3], S. Nirmal Kumar[4], C.B. Salin[5], S. Kannan[6,] A. Anandhasayanam[7], B. Sangameswaran[8]

*Associate Professor, Department of Pharmacy Practice, SSM College of Pharmacy,

[1]Associate Professor, Department of Pharmacy Practice, SSM College of Pharmacy,

[2,3,4,5] Pharm D Fifth Year Students, SSM College of Pharmacy,

[6]Professor & HOD Department of Pharmacy Practice, SSM College of Pharmacy,

[7]Professor, Department of Pharmacy Practice, SSM College of Pharmacy,

[8]Professor, Department of Pharmacognosy, SSM College of Pharmacy,

Dr. M.G.R. Medical University, Tamil Nadu, India.

ABSTRACT

This study conducts a systematic review of adverse drug reactions (ADRs) associated with selective serotonin reuptake inhibitors (SSRIs) in patients with major depressive disorder (MDD). Additionally, it evaluates adherence to Clinical Practice Guidelines (CPG) through a prescription audit in a tertiary care hospital. A total of 230 prescriptions were analyzed over six months, with 513 drugs prescribed, including **Escitalopram** (22.22%), **Clonazepam** (18.13%), and **Dosulepin** (11.11%) being the most frequent. Results indicate high adherence (93.48%) to clinical guidelines, while a smaller percentage (6.52%) did not comply. Common ADRs associated with SSRIs included weight gain (50%), somnolence (60%), and sexual dysfunction (70%). Severe adverse reactions like serotonin syndrome and QT prolongation were also reported. The study highlights the importance of monitoring for ADRs and improving practices such as recording allergy status and weight for pediatric patients. Although adherence to guidelines was generally high, there is scope for improving documentation, especially in follow-up care and drug interaction warnings. Regular audits and proper prescription practices are essential for optimizing patient outcomes and minimizing risks associated with antidepressant treatment.

KEYWORDS: SSRIs, Depression, Antidepressants, Prescribing guidelines adherence, Prescription audit

INTRODUCTION:

Major depressive disorder (MDD) was ranked as the third leading cause of disease burden worldwide by the WHO in 2008, and it is projected to become the leading cause by 2030.[1] It is diagnosed when an individual has a persistently low or depressed mood, anhedonia or decreased interest in pleasurable activities, feelings of guilt or worthlessness, lack of energy, poor concentration, appetite changes, psychomotor retardation or agitation, sleep disturbances, or suicidal thoughts.[2] Nearly 15% of Indian adults require active intervention for one or more mental health issues, and one in 20 Indians suffers from depression.[6] In 2012, India was estimated to have had over 258,000 suicides, with the 15-49 age group being the most affected.[6] This study conducts systematic review based on the ADR of SSRI's, 'guideline adherence based on the CPG and audit' of patient's prescriptions diagnosed with depression.

A systematic review on the adverse drug reactions (ADRs) of SSRIs involves a comprehensive and methodical approach to collecting, analyzing, and summarizing data from multiple studies on the side effects and negative outcomes associated with this class of medications.

Clinical Practice Guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.

A prescription audit is a part of the holistic clinical audit and is a quality improvement process that seeks to improve patient care and outcomes through a systematic review of care against explicit criteria and the implementation of change.

MATERIALS AND METHODS:

A retrospective study was conducted in the psychiatric out -patient department in a tertiary care hospital (Sudha Institute of Medical Science, Erode) after obtaining ethical clearance from the institutional ethics committee (Approval number: ECR/948/Inst/TN/2018/RR-22). The study was done for a period of 6 months in 2024. A total of 230 patient's prescription data were included with respective to study criteria. Complete confidentiality of the patient's data was maintained throughout the research study. Around 60 prescriptions per month which were collected which covers both male and female in the OPD. The information of the patients diagnosed with depression is collected using an optimized data collection form.

STUDY CRITERIA:

Systematic Review:

Inclusion Criteria:

❖ Patients of any age or sex using SSRIs for any indication.

❖ Use of any SSRIs (fluoxetine, sertraline, citalopram, escitalopram, paroxetine, fluvoxamine).

❖ Observational study (case-controlled study, cohort study) randomized controlled trials (RCTs), review articles, book.

❖ studies published from a certain period – (2019-2024).

Exclusion Criteria:

❖ Non-human studies (exclude animal studies or in vitro studies).

❖ Non-English language articles.

❖ Exclude studies that have high risk of bias or inadequate reporting standards (missing data, poor methodology).

CLIINICAL PRACTICE GUIDELINE ADHERENCE AND PRESCRIPTION AUDIT

Inclusion Criteria:

❖ Patients with a clinical diagnosis of depression.

❖ Prescriptions issued in outpatient, inpatient

❖ Patients of any age or sex.

Exclusion Criteria:

❖ Patients with significant comorbid psychiatric disorders (e.g., schizophrenia, bipolar disorder) that might influence the prescription practices beyond standard depression treatment.

❖ Patients with incomplete or missing prescription records.

❖ Patients prescribed antidepressants for conditions other than depression (e.g., anxiety disorders, chronic pain).

Process of Systematic Review:
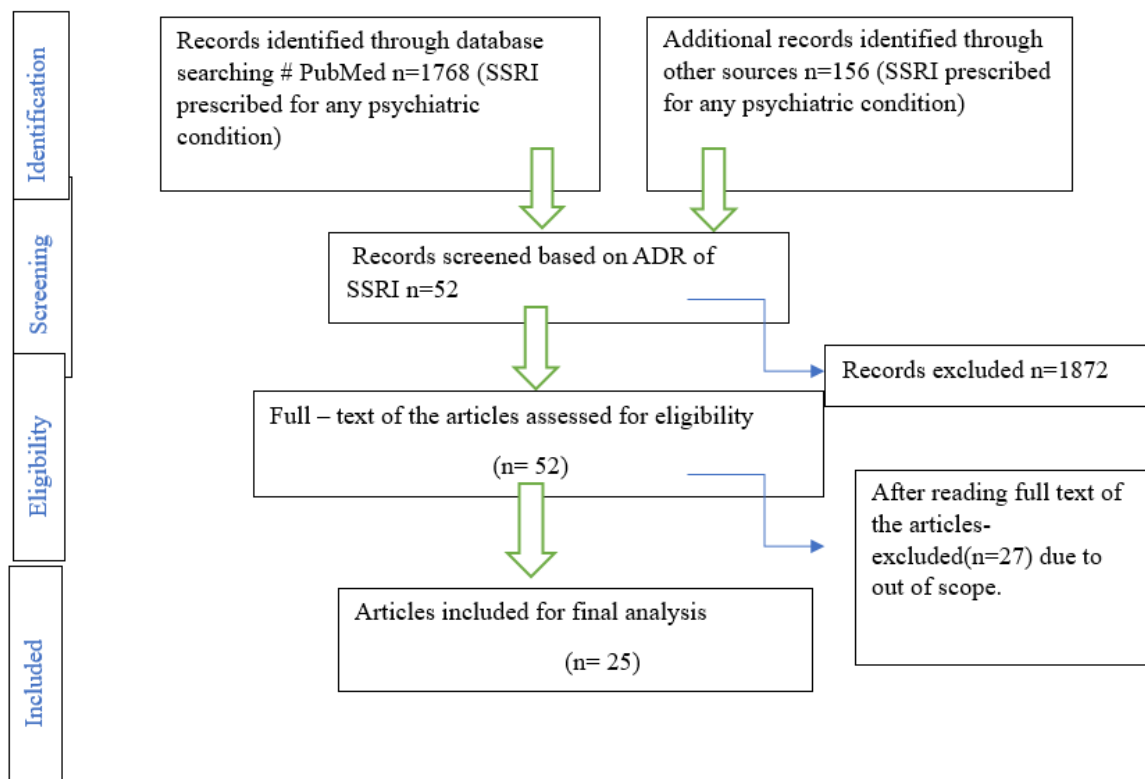
Statistical Analysis:

Descriptive statistics were used to analyse this study. Graphical representation was included.

Descriptive statistics were performed in MS EXCEL version 2021.

RESULTS AND DISCUSSION:

Systematic Review:

This data provided outlines the adverse drug reactions (ADRs) associated with SSRIs (selective serotonin reuptake inhibitors) and other drugs. Common ADRs are Anxiety: 14%, Headache: 10%, Alteration in appetite: 10%, Weight gain: 50%, Somnolence: 60%, Tremor: 45%, Diarrhoea: 20%, Nausea/Vomiting: 15%, Constipation: 2%, Sleep disturbance: 3%, Sedation: 8.5%, Sexual dysfunction: 70%. Reported with various SSRIs, Gastritis: 10.6%, Restlessness: 6.3%, Oral ulcer: 6.3%, Erectile dysfunction: 4.2%, Dizziness: 2.1%, Abdominal discomfort/distension: 2.1%, Postural hypotension: 2.1%, Sweating: 2.1%. Severe or Rare ADRs: Serotonin Syndrome, Extrapyramidal Symptoms, QT Prolongation, Hyponatremia, Suicidal Ideation, Acute hepatic failure (Escitalopram), Seizures (Fluoxetine and Escitalopram).

Table no.1: Systematic review of SSRI and ADR.

Author	Year of Publication	Topic	Drugs	Indication	ADR	
Neelam Sharma Et.al.	2019	Analysis Of Prescribing Pattern And Adverse Drug Reactions of Selective Serotonin	sertraline, escitalopram and fluoxetine	Psychiatric disorder	Anxiety (14%), Dysphoric mood (12%), Headache (10%), Alteration in appetite (10%), Sleep disturbance (3%), Constipation (2%), Vomiting (2%), Giddiness (2%), Weakness	

		Reuptake Inhibitors (SSRIS) In A Psychiatry Out-Patient Department of A Tertiary Care Teaching Hospital			(1%), Body pain (1%), Vertigo (1%), Erectile dysfunction (1%)
Andy R. Eugene Et.AL	2019	Optimizing drug selection in psychopharmacology based on 40 significant CYP2C19- and CYP2D6- biased ADRs of S SRIs	SSRIs	-	Anxiety, Nightmare, panic attack, QT prolongation, Small for dates baby
Ali Shaku et al.	2020	Prescription pattern and ADR of drugs prescribed in the department of Psychiatric in a tertiary care hospital	escitalopram, paroxetine, sertraline	Psychiatric disorder	Weight gain, somnolence, paliptation, headache, nausea, skin rash, tremor, constipation.
Sabina Sankhi et al.	2020	Adverse Drug Reaction due to Antidepressants among Patients with Depression in a Private Psychiatric Hospital of Nepal	SSRIs	Depression	Gastritis (10.6%), sedation (8.5%), oral ulcer (6.3%), restlessness (6.3%), weight gain (6.3%), erectile dysfunction (4.2%), tremor (4.2%), anxiety (4.2%), insomnia (2.1%), dizziness (2.1%), headache (2.1%), vomiting (2.1%), abdominal discomfort (2.1%), abdominal distension (2.1%), diarrhea (2.1%), postural hypotension (2.1%), sweating (2.1%), problem with urination (2.1%)
Moza Salem Rashed Al Zaabi, Sathvik B Sridhar,	2020	Assessment of incidence, causality, severity, and preventability of suspected adverse drug reactions to antidepressant medications in a psychiatry outpatient setting of a secondary care hospital	escitalopram, paroxetine, FLUOXETINE , FLUVOXAMINE	Depression	weight gain ,headcahe, flushing, sexual dysfunction, abdominal pain, excessive dreams, tremors, palipatation, somnolence, weight loss.
Tariku Sisay a,* , Roza Wami b	2021	Adverse drug reactions among major depressive disorders: patterns by age and gender	SSRI	MDD	Diarrhea-20% , Drowsiness-60%,Headache-25%, Nausea or vomiting-15%, Problem with urination-10 %,Sexual dysfunction-70%, Tremor -45%, Weight gain-50%
Bernhard J. Connemann et.al;	2021	Risk of Bleeding Associated With	SSRI	Depression	Upper GI bleeding.

		Antidepressants: Impact of Causality Assessment and Competition Bias on Signal Detection			
Amber N. Edinoff et.al;	2021	Selective Serotonin Reuptake Inhibitors and Adverse Effects: A Narrative Review	SSRI	Psychiatric disorder	Extrapyramidal Symptoms, Serotonin Syndrome, QT Prolongation, Rash, Congenital Malformations, Hyponatremia, Cataracts, Suicidal Ideation
VIRENDRA KUSHWAHA et.al.;	2022	Assessment of adverse drug reaction of antidepressants used in psychiatric department of tertiary care hospital.	SSRI	Psychiatric disorder	Anxiety,insomnia ,constipation, gastritis, sedation, weight gain, oral ulcer, restlessness, erectile dysfunction, and tremor
Chris F Johnson et.al;	2022	Dose-response effects of selective serotonin reuptake inhibitor monotherapy for the treatment of depression: systematic review of reviews and meta-narrative synthesis	SSRI	Depression	nausea, sexual dysfunction, fatigue, anxiety, and insomnia
Karin M. Egbert et.al;	2022	Serious Adverse Drug Reactions in Children and Adolescents Treated On- and Off-Label with Antidepressants and Antipsychotics in Clinical Practice	sertraline and fluoxetine		nausea, sexual dysfunction, insomnia
William J Scotton Et. Al	2019	Serotonin Syndrome: Pathophysiology, Clinical Features, Management, and Potential Future Directions	SSRI	Induce serotonin syndrome (SS)	central nervous system (CNS), including modulation of attention, cognition, behaviour, memory, and thermoregulation, as well as in the peripheral nervous system (PNS), where it regulates, gastrointestinal (GI) motility, uterine contraction, vasoconstriction, and bronchoconstriction.
MIrabwlaRoman escu Et.al,	2022	Sex-Related Differences in Pharmacological Response to CNS Drugs: A Narrative Review	SSRI	CNS Diseases	Sexual dysfunction

Jaspreet kaur sidhu Et. Al	2022	Adverse Drug Reactions in Psychiatry Outpatient Department of a Tertiary Care Hospital in Western Uttar Pradesh	SSRI	Depression	Spascticity, Delurium,Hemoptysis, Seizure, Urinary frequency, Gritty Sensation, Oculogic, Hair loss, CURLING, Awakeing, Constipation, Weight loss, weight gain, Amenorrhoea, Glactorrhoea, facial edema Tremors, Hypertension, Sedation, Headche	
Yan Wang Et. Al	2023	Exploring the association between selective serotonin reuptake inhibitors and rhabdomyolysis risk based on the FDA pharmacovigilance database	SSRI	Depression	Rhabdomyolysis	
Diana Durbrall Et. Al	2023	Selective serotonin reuptake inhibitors and suicidality in children and young adults: analyses of pharmacovigilance databases	SSRI	_	Suicidality	
Michael V. et al.	2022	Association of Selective Serotonin Reuptake Inhibitor Use With Abnormal Physical Movement Patterns as Detected Using a Piezoelectric Accelerometer and Deep Learning in a Nationally Representative Sample of Noninstitutionalized Persons in the US	SSRI	_	Abnormal Physical,Movement Patterns	
Chao Ran et al.	2020	Detection and Evaluation of Adverse Drug Reaction Signals of Antidepressants Based on FDA Adverse Event Reporting System Database	fluoxetine, fluvoxamine, paroxetine, sertraline and citalopram	_	anxiety, depression, suicidal ideation, 5-HT syndrome, withdrawal syndrome	
Tyra Lagerberg et al.	2021	Selective serotonin reuptake inhibitors and suicidal behaviour: a	SSRIs.	_	The results do not suggest that SSRI-treatment increases the risk for suicidal behaviour in either youths	

		population-based cohort study			or adults; rather, it may reduce the risk.
Mia Aakjaer Et.AL.,	2021	Surveillance of Antidepressant Safety (SADS): Active Signal Detection of Serious Medical Events Following SSRI and SNRI Initiation Using Big Healthcare Data	SSRI	Psychiatric	Escitalopram - Acute hepatic failure ,Acute kidney injury, Cardiomyopathy, Delusions, Seizures, Fluoxetine - delusions , seizures, MI, Paroxetine - Cardiomyopathy, Delusions, Ischemic stroke , Sertraline - Cardiomyopathy, seizures, hepatotoxicity
Sanju Trizah Saji ET.AL.,	2024	Assessment of Medication Adherence and Adverse Drug Reactions in Depressive Patients Taking Selective Serotonin Reuptake Inhibitors in Tertiary Care Hospitals in Kerala	SSRI	Psychiatric	Nausea,insomnia,lethargy,headache, fatigue
Alice Fabbri Et,Al.,	2020	Media coverage of drug regulatory agencies' safety advisories: A case study of citalopram and denosumab	Citalopram and Denosumab	Psychiatric	(cardiac arrhythmia
Stefania Chiappini ET, AL.,		A Focus on Abuse/Misuse and Withdrawal Issues with Selective Serotonin Reuptake Inhibitors (SSRIs): Analysis of Both the European EMA and the US FAERS Pharmacovigilance Databases	SSRI	Depression	ataxia,fall,mixed hallucinations,dissociation,substance -induced psychotic disorder
Xiaomei I. Liu ET,AL.,	2019	A Comparison of Pediatric and Adult Safety Studies for Antipsychotic and Antidepressant Drugs Submitted to the United States Food and Drug Administration	Antidepressants	_	Sedation, respiratory tract infection, abdominal pain, and increased appetite

Chiara Gastaldon Et,Al.,	2022	Withdrawal Syndrome Following Discontinuation of 28 Antidepressants: Pharmacovigilance Analysis of 31,688 Reports from the WHO Spontaneous Reporting Database	Antidepressants	Depression	Withdrawal syndrome

Prescribing Guidelines Adherence & Prescription Audit:

Table.2: List of Drugs Prescribed to Patients with Depression:

S.NO	DRUGS	NO. OF DRUGS PRESCRIBED	% OF DRUGS PRECRIBED
1	ESCITALOPRAM	114	22.22
2	FLUOXETINE	14	2.73
3	FLUOXAMINE	7	1.36
4	SERTARLINE	8	1.56
5	MIRTAZEPINE	20	3.90
6	CLONAZEPAM	93	18.13
7	LORAZEPAM	36	7.02
8	CLOBAZAM	3	0.58
9	DOSULEPIN	57	11.11
10	DESVENALAFAXINE	9	1.75
11	QUETIAPINE	23	4.48
12	ARPIPRAZOLE	1	0.19
13	TRAZODONE	19	3.70
14	PANTOPRAZOLE	27	5.26
15	AGOMELATINE	8	1.56
16	MELATONIN	4	0.78
17	PROPRANOLOL	9	1.75
18	SODIUM VALPORATE	2	0.39
19	OLANZAPINE	21	4.09
20	METHYL COBALAMIN	1	0.19
21	AMITRIPTYLLINE	9	1.75
22	BACLOFEN	2	0.39
23	RESPERIDONE	2	0.39
24	ACAMPROSATE	2	0.39
25	DISULFIRAN	1	0.19
26	LITHIUM CARBONATE	2	0.39
27	HALOPERIDOL	2	0.39
28	PROMETHAZINE	1	0.19
29	ZOLPIDEM	7	1.36
30	NUROKINE PLUS	1	0.19
31	LEMBOREXANT	1	0.19
32	DULOXETINE	1	0.19
33	CLONIDINE	1	0.19
34	THYROXIME SODIUM	1	0.19
35	CLOMIPRAMINE	1	0.19
36	CHLORDIAZEPOXIDE	1	0.19

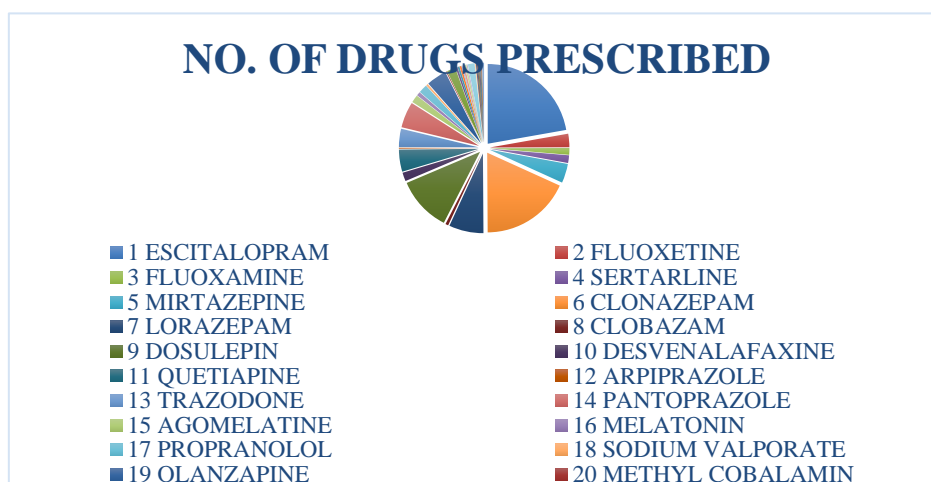| 37	VENALAFAXINE	2	0.39
	TOTAL	513	100

FIGURE NO.1: LIST OF DRUGS PRESCRIBED

DISCUSSION:

FIGURE 1.

A total of 513 drugs were prescribed, encompassing a diverse range of medications from various classes. The most frequently prescribed drugs were escitalopram (22.22%), clonazepam (18.13%), and dosulepin (11.11%). Escitalopram (22.22%) is a SSRI, the most commonly prescribed antidepressant. Clonazepam (18.13%) is a benzodiazepine, often used for its anxiolytic and sedative effects. Dosulepin (11.11%) is a TCA, used less frequently than SSRIs but still a significant component of treatment regimens.

Other notable medications included:

Lorazepam (7.02%), another benzodiazepine used for short-term anxiety relief.

Mirtazepine (3.90%), a NaSSA prescribed for its sedative and antidepressant effects.

Quetiapine (4.48%), an atypical antipsychotic used for mood stabilization and antipsychotic effects.

Desvenlafaxine (1.75%) and Duloxetine (0.19%), both NSRIs, potentially prescribed for patients who have not responded to SSRIs.

A systematic review and network meta-analysis conducted by Andrea Cipriani et al., 2018 reported that in head-to-head studies, agomelatine, amitriptyline, escitalopram, mirtazapine, paroxetine, venlafaxine, and vortioxetine were more effective than other antidepressants whereas fluoxetine, fluvoxamine, reboxetine, and trazodone were the least efficacious drugs. For acceptability, agomelatine, citalopram, escitalopram, fluoxetine, sertraline, and vortioxetine were more tolerable than other antidepressants whereas amitriptyline, clomipramine, duloxetine, fluvoxamine, reboxetine, trazodone, and venlafaxine had the highest dropout rates.

Table.3: Classification of Prescriptions Based on CPG:

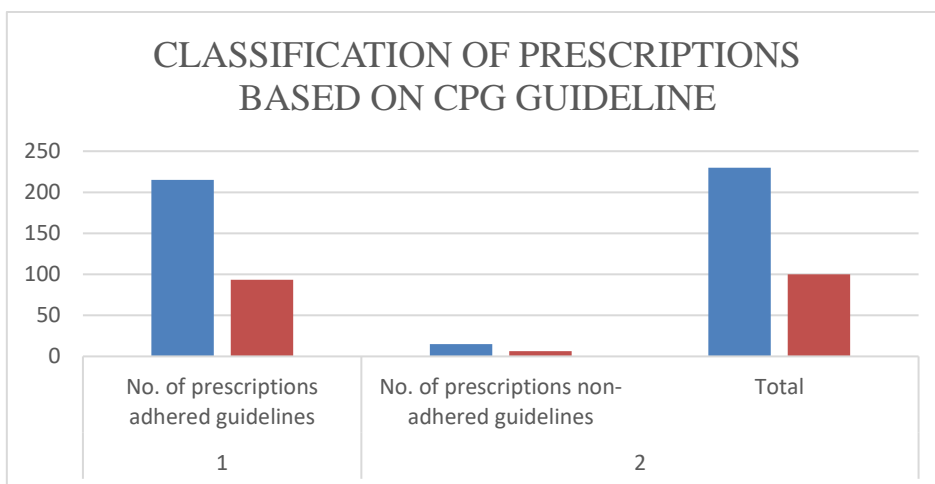| S.NO	ADHERED / NON-ADHERED		% OF PRESCRIPTION
1	No. of prescriptions adhered as per the guideline	215	93.48
2	No. of prescriptions non-adhered	15	6.52
	Total	**230**	**100.00**

FIGURE NO :2 CLASSIFICATION OF PATIENT BASED ON CPG ADHERENCE

DISCUSSION:

FIGURE NO :2

The data indicates that a high percentage of patients (93.48%) adhered to their prescribed treatment regimen, while a smaller proportion (6.52%) did not adhere. This high adherence rate suggests that most patients are following their prescribed treatment plans. Adhered Patients (93.48%): Discuss the implications of this high adherence rate. This is generally a positive outcome, indicating that patients are following their treatment plans. Non-Adhered Patients (6.52%) despite the overall high adherence rate, a small percentage of patients did not adhere to their treatment.

Table.4: Prescribing Indicators:

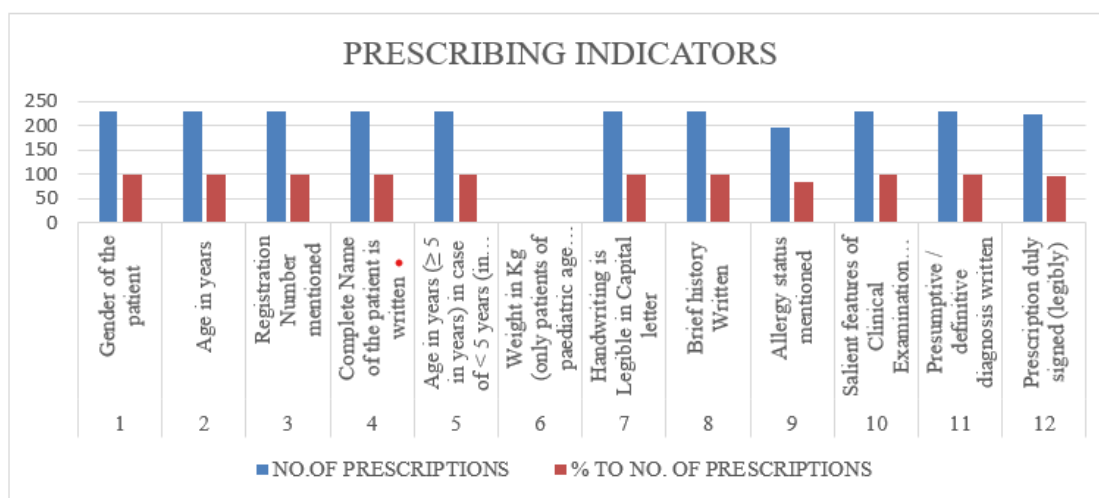| S.NO	PRESCRIBING INDICATORS	NO. OF PRESCRIPTIONS	% TO NO. OF PRESCRIPTIONS
1	Gender of the patient	230	100.00
2	Age in years	230	100.00
3	Registration Number mentioned	230	100.00
4	Complete Name of the patient is written	230	100.00
5	Age in years ($\geq$ 5 in years) in case of < 5 years (in months)	230	100.00
6	Weight in Kg	0	0.00
7	Handwriting is Legible in Capital letter	230	100.00
8	Brief history Written	230	100.00
9	Allergy status mentioned	197	85.65
10	Salient features of Clinical Examination recorded	230	100.00
11	Presumptive / definitive diagnosis written	229	99.57
12	Prescription duly signed (legibly)	223	96.96

FIGURE NO: 3 PRESCRIBING INDICATORS

DISCUSSION:

FIGURE NO:3

The table indicates strong adherence to recording critical patient details such as gender, age, registration number, and name (100% compliance).

Despite high compliance in other areas, allergy status was only mentioned in 85.65% of prescriptions, and weight was not recorded for any patients.

The majority of prescriptions (96.96%) were signed legibly, suggesting good adherence to this essential practice.

Table.5: Patient-care Indicators:

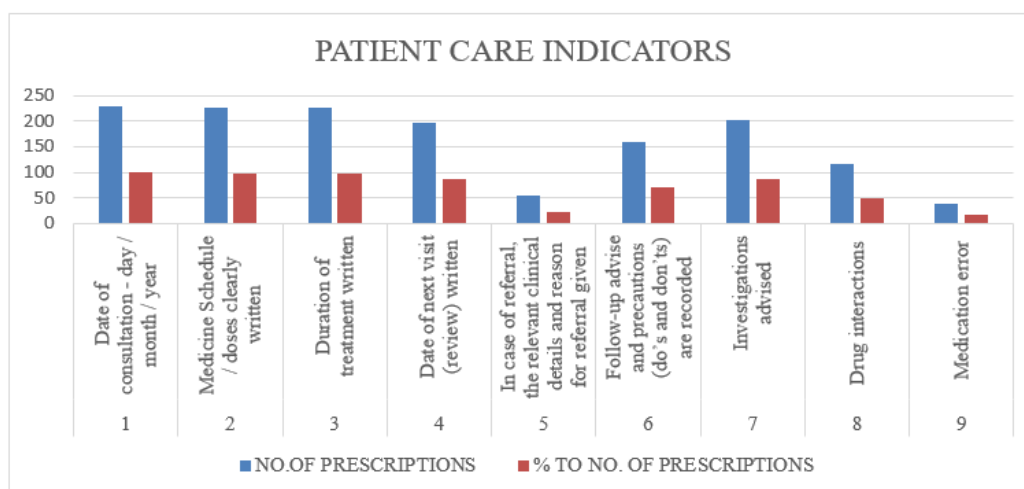| S.NO	PATIENT CARE INDICATORS	NO. OF PRESCRIPTIONS	% TO NO. OF PRESCRIPTIONS
1	Date of consultation - day / month / year	229	99.57
2	Medicine Schedule / doses clearly written	225	97.83
3	Duration of treatment written	227	98.70
4	Date of next visit (review) written	198	86.09
5	In case of referral, the relevant clinical details and reason for referral given	55	23.91
6	Follow-up advise and precautions (do's and don'ts) are recorded	160	69.57
7	Investigations advised	201	87.39
8	Drug interactions	116	50.43
9	Medication error	38	16.52

FIGURE NO: 4 PATIENT CARE INDICATORS

FIGURE NO :4

Nearly all prescriptions included the date of consultation, medicine schedule, duration of treatment, and advised investigations, demonstrating high compliance with essential prescription elements.

A significant number of prescriptions lacked specific clinical details and reasons for referrals, and only half included information on potential drug interactions.

Despite high compliance in other areas, medication errors were noted in 16.52% of prescriptions.

Table.6: Facility Indicators:

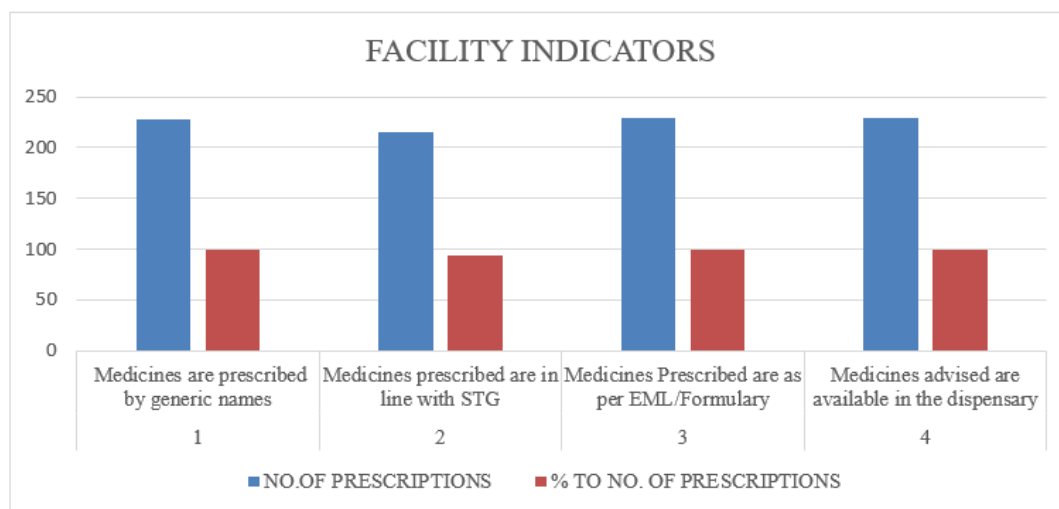| S.NO	FACILITY INDICATORS	NO. OF PRESCRIPTIONS	% TO NO. OF PRESCRIPTIONS
1	Medicines are prescribed by generic names	228	99.13
2	Medicines prescribed are in line with STG	215	93.48
3	Medicines Prescribed are as per EML/Formulary	229	99.57
4	Medicines advised are available in the dispensary	229	99.57

FIGURE NO :5 FACILITY INDICATORS

FIGURE NO :5

A high percentage (99.13%) of prescriptions used generic names, demonstrating a commitment to cost-effectiveness and simplifying medication management.

A significant majority (93.48%) of prescriptions aligned with Standard Treatment Guidelines (STG), indicating strong adherence to established treatment protocols.

99.57% of prescribed medicines were included in the Essential Medicines List (EML) or formulary, ensuring effective and cost-efficient treatments.

99.57% of prescribed medicines were available in the dispensary, minimizing delays in patient care.

STATISTICAL ANALYSIS				
	MEAN	MEDIAN	MODE	STANDARD DEVIATION
AGE	28.75	29	-	17.34
RISK FACTOR	38.33	30	-	20.93
MOOD	12.11	3	2	20.66
THOUGHT	8.85	2.5	1	16.35
CLASS OF DRUGS	57	49	-	50.61
NO. OF DRUGS	13.86	3	1	24.87

CONCLUSION:

The findings highlight that middle-aged women represent a significant portion of the population affected by depression. SSRIs, particularly Escitalopram, are commonly prescribed in such cases. Moreover, the majority of prescriptions about 93.48% align with established guidelines, emphasizing proper clinical practice, though some instances of non-adherence about 6.52% were noted without clarification of the causes. Regular monitoring is essential for adverse effects like suicidal ideation, serotonin syndrome, and severe gastrointestinal symptoms.

ACKNOWLEDGEMENT

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How to cite this article:
K. Nithiyapriya et al. Ijppr.Human, 2024; Vol. 30 (12): 560-573.
Conflict of Interest Statement: All authors have nothing else to disclose.
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