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MONITORING OF PRESCRIBING PATTERN AND ADVERSE DRUG REACTIONS OF ANTI-PSYCHOTIC AND ANTIDEPRESSANT MEDICATIONS IN PSYCHIATRIC DEPARTMENT OF A TERTIARYCAREHOSPITAL

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Key Words: Naranjos scale, Adverse drug reaction, Prescribing pattern, Psychiatry, Anti-Psychotics, Anti-Depressants

ABSTRACT:

Objectives: To estimate various Prescribing patterns and to access Adverse drug reaction of Anti-depressants and Anti-Psychotic medications in psychiatric unit of tertiary care hospital.**Materials and Methods:**This Prospective observational study carried out for a duration of six months. Data collected using case proforma for analyzing prescribing patterns. The assessment of causality of adverse drug reactions was done using Naranjo's scale. All the statistical analysis was done by using Graph pad prism.**Results:**A total of 303, mean age of psychiatric patients like Schizophrenia, Depression, Psychosis of males,females were 30±19.16, 31±21.4 respectively. Atypical antipsychotic, among them clonazepam was commonly used i.e., 25.8% followed by

haloperidol 15.8% and risperidone 3.9%. Among antidepressants SSRIs,Amitriptyline was commonly used 24.4% followed by Escitalopram 8.5% and Sertraline 7.9% of patients. The incidence rate of Adverse drug reaction was 76.8%. Around23.34 adverse drug reactions, Weight gain 54(17.8%) and Headache 35(11.8%) was commonly reported in antipsychotic and antidepressants respectively. Atypical antipsychotics like olanzapine 199(85.4%) and risperidone 63(27.0%) implicated in adverse drug reactions. Sertraline 37(15.8%) followed by escitalopram 29(12.4%) were associated with adverse drug reactions.There were statistically significant relationship between the adverse drug reactions and prescriptions.**Conclusion:** It is concluded that incidence of schizophrenia and depression is more in females than in males. Atypical antipsychotics and SSRIs were commonly prescribed. The prescription trend was towards monotherapy. This study enables to reduce the Adverse drug reactions occurrence and enhance the safe use of drugs.

INTRODUCTION:

Mental illness refers to the group of disorders that affect mood, thinking, and behavior. [(1)] According to DSM-V criteria Schizophrenia is a severe and chronic mental disorder characterised by disturbances in thought, perception , behavior. Depression is also known as major depressive disorder or clinical depression characterised by either depressed mood or loss of interest or pleasure. [(2)] Psychosis is characterised by an impaired relationship with reality. It is a symptom of serious mental disorders. [(3)]

Antipsychotics are class of agents which reduce the psychotic symptoms of schizophrenia [(4)]. In appropriate use of drugs represent a potential hazard to patients. To overcome this first generation antipsychotics called typical antipsychotics were discovered in 1950's. First generation antipsychotics used to treat the positive symptoms like hallucinations and delusions. [(5)] Previously most frequently prescribed typical antipsychotics are Chlorpromazine, Fluphenazine, Haloperidol. However, so far no antipsychotic has been shown to be significantly effective than chlorpromazine in treating schizophrenia.[(6)]Fluphenazine is equivalent effect to chlorpromazine. [(7)] Both haloperidol and chlorpromazine are similarly effective in the treatment of schizophrenia. The comparative effects of these drugs seems that haloperidol causes more movement disorders than chlorpromazine, while chlorpromazine is significantly more likely to lead to hypotonia. [(8)] These typical antipsychotics treat the positive symptoms of schizophrenia while the atypical antipsychotics treat the both positive and negative symptoms of shizophenia and minimize the Extrapyramidal syndrome effects.

Atypical antipsychotics also called as second generation antipsychotics. Clozapine is the first medication was found to be more effective than typical antipsychotics medications.Due to serious side effects like blood disordersknown as agranulocytosis, Several other antipsychotics have been developed first was Risperidonefollowed by Olanzepine, (causes more weight gain) Quetiapine, Ziprasidone and Aripiprazole. The use of quetapine, olanzepine and risperidoneis increasing.

The atypical antipsychotics now considered to be first line treatment for schizophrenia and gradually replacing the typical antipsychotics. They generally have lower risk of motor side effects, but are associated with significant weight gain, elevated lipids and prolactin levels and have been associated with the development of type 2 diabetes.[9] Though these are widely prescribed in the treatment of schizophrenia, however not a single atypical antipsychotic drug having any exceptional efficacy and safety profile. The combinations of atypical antipsychotics are Olanzepine +Quetiapine, Risperidone + Olanzepine, Risperidone +Quetiapine in the treatment of schizophrenia. These combinations are beneficial in the reduction of positive symptoms and occasionally negative symptoms.

The first two specifically antidepressants are iproniazid, a monoamine oxidase inhibitor and imipramine, the first drug in the antidepressant family. Decreased pharmacotherapeutic activity and side effects of the monoamine oxidase inhibitors, Tricyclic antidepressants were developed. Tricyclic antidepressants like imipramine, amitryptiline, clomipramine, desipramine. These drugs affect the heart rate and blood pressure include postural hypotension, tachycardia, urinary retention, blurred vision. To minimize these adverse events selective serotonin reuptake inhibitors were introduced includes Fluoxetine,Escitalopram, (most commonly used) Proxetine, sertaline, citalopramare equally effective as tricyclic antidepressants but having decreased side effects. Selective serotonin reuptake inhibitors are preferred over other antidepressants because of their relative lesser side effects.

Bupropion is the first atypical antidepressants frequently associated with sexual side effects.Highest efficacious antidepressants are trazadone and mirtazipine.

MATERIALS AND METHODS:

STUDY DESIGN:

It is a prospective observational study.

STUDY PERIOD:

The present study was carried out for a period of six months from August to January 2023.

STUDY SITE:

Psychiatric Department, Outpatient unit of Government GeneralHospital, Kurnool.

SAMPLE SIZE:

During the study period of six months, the total of 303 cases was collected and studied for the prescription pattern, among them 233 patients were studied for ADRs.

SOURCE OF DATA:

All the patients satisfying the inclusion criteria were selected from a psychiatric department in Government General Hospital, Kurnool.

All the required data was collected from patients through personal interview and case sheets.

Inclusion criteria:

1. Patients diagnosed with diseases like Psychosis, Depression, and Schizophrenia.

2. Patients of age > 18 years are included in our study.

3. Only outpatients are involved in the study, who are coming for regular follow-up.

4. Patients receiving at least one antidepressant or antipsychotics medications.

5. Either gender is considered.

Exclusion criteria:

1. Patients who are receiving medications other than allopathic drugs.

2. The data collection is not possible for aggressive and violent patients.

3. Inpatients are excluded from the study because they are newly diagnosed patients.

4. The patients who underwent/ongoing ECT are excluded.

METHOD OF COLLECTION OF DATA:

All the patients satisfying the inclusion criteria were selected from the psychiatric department in Government GeneralHospital, Kurnool.

All the data of the subjects are collected by using the proforma.

The data collection includes demographic details, chief complaints, History of present illness, treatment history, Past Psychiatric/medical and medication history, Family history, Personal history and allergies, Laboratory investigations, Diagnosis, Drug chart, Adverse drug reactions.

The causality for adverse drug reaction was assessed by using Naranjo's Scale.

STATISTICAL ANALYSIS:

The data collected from the participants were entered into a Microsoft Excel spreadsheet and descriptive statistics were used. All the statistical analysis was done by using Graph pad prism.

Parametric data were summarized as the mean (+) standard deviation for continuous variables. Categorical variables were summarized as percentages.

A prescription pattern was analyzed to determine significance. Chi-square test was used to test for independence of two categorical variables. One way ANOVA was used for continuous variables. Confidence intervals 95% as set as a level of significance.

RESULTS

A total of 303 patients were enrolled in the study are presented to the outpatient department, in which the 118 patients are identified with schizophrenia, 130 are identified with psychosis whereas 27 were identified with depression.

AGEAND GENDER DISTRIBUTION:

A total of 303 patients are presented to the outpatient department, the percentage distribution of the study population showed that 154(50.9%) females and 149(49.2%) males which are represented in the table:

Table 1. AGEAND GENDER DISTRIBUTION

Gender	18-27	28-37	38-47	48-57	>59	Total
Female	38(12.5%)	64(21.1%)	27(9.0%)	12(4.0%)	13(4.2%)	154(50.8%)
Male	43(14.1%)	54(17.9%)	30(10.0%)	12(4.0%)	10(3.3%)	149(49.2%)
Total	81(26.8%)	118(38.9%)	57(18.9%)	24(7.9%)	23(7.6%)	303

DISTRIBUTION OF PATIENTS BASED ON DIAGNOSIS:

A number of patients suffering from a particular disease so the data can be expressed as percentages, not in mean $\pm$ Standard Deviation. A total of 303 patients were enrolled in this study, the percentage distribution of patients based on diagnosis shows that the majority of patients were identified with Psychosis 130(42.9%), followed by Schizophrenia 118(38.9%), Depression 27(8.9%), BPAD with Psychosis 7(2.3%), BPAD with Depression 2(0.6%), whereas in combination diseases shows Schizophrenia + Psychosis 8(2.6%),

Schizophrenia + Depression 3(0.9%), Psychosis + Depression 8(2.6%), majority of the patients in single disease was found to be 275(90.7%) followed by combination diseases 28(9.2%)respectively which is shown in table:

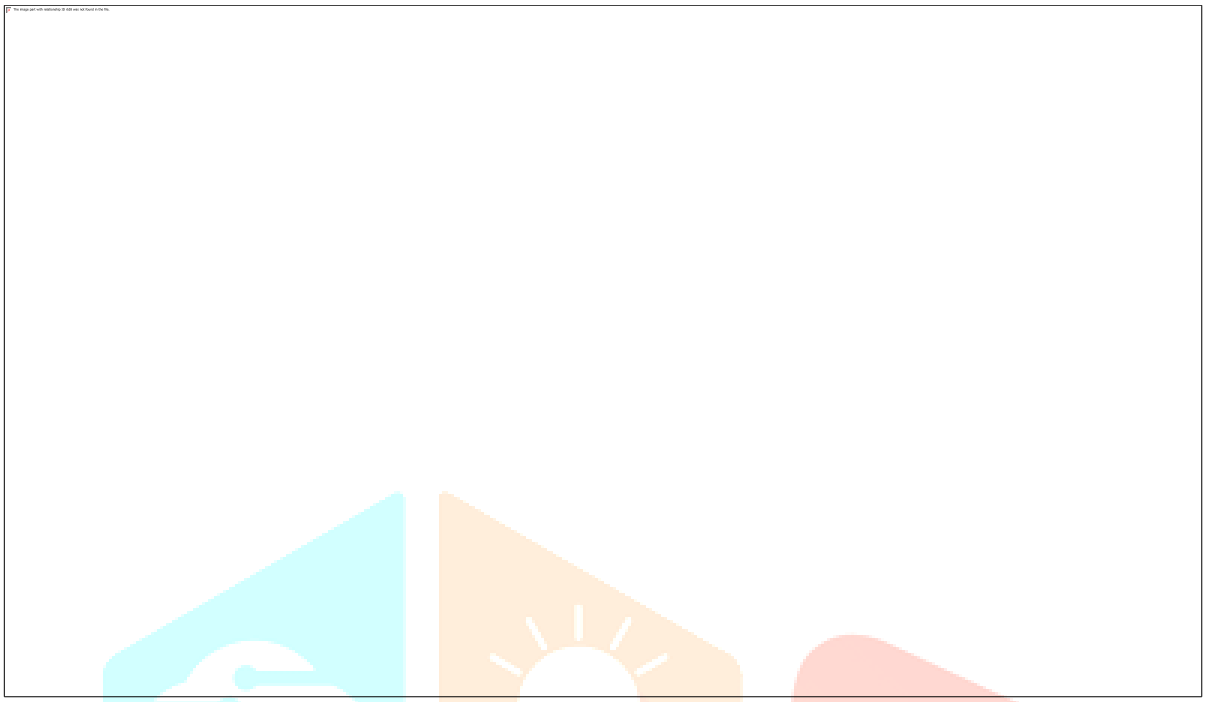

Figure 1. Distribution of Patient Diagnosis

SZ – Schizophrenia	PS – Psychosis
DP- Depression	BPAD – Bipolar Anxiety Disorder

DISTRIBUTION OF PATIENTS DIAGNOSIS BASED ON GENDER:

Among 303 patients, the percentage distribution of patients diagnosis based on gender shows that the majority of patients in Schizophrenia were females 63(20.7%), Psychosis were males 68(22.4%), Depression was females 16(5.2%), BPAD with Psychosis were males 4(1.3%), BPAD with Depression were males 2(0.6%), Schizophrenia+Psychosis were females 5(1.6%), Schizophrenia+Depression were males 2(0.6%), Psychosis+Depression were males 4(1.3%) which were represented in table. No significant difference of diagnosis on gender was found (P> 0.05).

DISTRIBUTION OF PATIENTS DIAGNOSIS BASED ON AGE FREQUENCY:

Among 118 patients in Schizophrenia, the distribution of patients diagnosis based on age shows that the majority of patients were found in between age group 28-37 years 58(49.2%), whereas in Psychosis among 130 patients, were found in between age group 18-27 years 43(33.0%) and whereas in depression among 27 patients

age group 38-47 years 10(37.0%) respectively shown in table. The significant difference of diagnosis on age was found. ($P < 0.05$).

Table 2. DISTRIBUTION OF PATIENTS DIAGNOSIS BASED ON AGE FREQUENCY

Diseases	**18-27**	**28-37**	**38-47**	**48-57**	**>58**	**Total**
Schizophrenia	28(9.2%)	58(19.4%)	16(5.2%)	9(3.0%)	7(2.3%)	118
Psychosis	43(14.1%)	38(12.5%)	24(7.9%)	11(3.6%)	14(4.6%)	130
Depression	4(1.3%)	9(3.0%)	10(3.3%)	4(1.3%)	-	27
BPAD with Psychosis	3(0.9%)	3(0.9%)	1(0.3%)	-	-	7
BPAD with Depression	-	-	-	1(0.3%)	1(0.3%)	2
Schizophrenia+Psychosis	3(0.9%)	4(1.3%)	1(0.3%)	-	-	8
Schizophrenia+Depression	-	2(0.6%)	1(0.3%)	-	-	3
Psychosis+Depression	1(0.3%)	4(1.3%)	3(0.9%)	-	-	8
Total	82	118	56	25	22	303

DISTRIBUTION OF PATIENTS DIAGNOSIS BASED ON DURATION OF ILLNESS:

In Schizophrenia among 118 patients, the distribution of patients diagnosis based on duration of illness includes

Table 3. DISTRIBUTION OF PATIENTS DIAGNOSIS BASED ON DURATION OF ILLNESS

Duration of illness	**SZP**	**PS**	**DP**	**BPAD with PS**	**BPAD with DP**	**SZP + PS**	**SZP + DP**	**PS + DP**	**Total**
6m-5y	59 (19.4%)	67 (22.1%)	15 (4.9%)	-	1 (0.3%)	3 (0.9%)	-	3 (0.9%)	148
6-10y	40 (13.2%)	38 (12.5%)	10 (3.3%)	7 (2.3%)	1 (0.3%)	3 (0.9%)	1 (0.3%)	5 (1.6%)	105
11-15y	14 (4.6%)	13 (4.2%)	2 (0.6%)	-	-	-	-	-	29
16-20y	-	7 (2.3%)	-	-	-	-	1 (0.3%)	-	8
>20y	5 (1.6%)	5 (1.6%)	-	-	-	2 (0.6%)	1 (0.3%)	-	13
Total	118	130	27	7	2	8	3	8	303

SZP – Schizophrenia	DP – Depression
PS – Psychosis	BPAD – Bipolar anxiety disorder

PRESCRIBING PATTERN:

Among 938drugs, a majority of the patients received 560(59.7%) Atypical antipsychotics and 183(19.5%) received SSRIs, followed by 117(12.4%) received Typical antipsychotics, 76(8.1%) were received TCAs and 2(0.2%) received SNRIs which is represented in the table:

Figure 2. Prescribing Pattern

NUMBER OF PRESCRIPTION PER PATIENT:

Among 303 prescriptions, a maximum number of 280 prescriptions was found in one patient. Whereas, the minimum number of 8 prescriptions were found in one patient.

SINGLE DRUG THERAPY AND COMBINATION DRUG THERAPY:

Among 303 patients, majority of the drug prescribed in single drug therapy

Table 4. SINGLE DRUG THERAPY AND COMBINATION DRUG THERAPY

Drugs prescribed	**No of drugs prescribed in patients n=303**	**Percentage (%)**
Single-drug therapy		
Olanzapine	31	10.2%
Risperidone	6	1.9%
Haloperidol	5	1.6%
Escitalopram	2	0.6%
Two drug combination		
Olanzapine+Risperidone	53	17.4%
Haloperidol+Olanzapine	12	3.9%
Olanzapine+Escitalopram	9	2.9%
Olanzapine+Amisulpride	7	2.3%
Three drug combination		
Olanzapine+Quetiapine+Risperidone	23	7.5%
Haloperidol+Olanzapine+Risperidone	16	5.2%
Olanzapine+Escitalopram+Sertraline	10	3.3%
Olanzapine+Quetiapine+Amitriptyline	14	4.6%
Four drug combination		
Amitriptyline+Fluoxetine+Escitalopram+Sertraline	12	3.9%
Olanzapine+Risperidone+Fluoxetine+Sertraline	26	8.5%
Risperidone+Fluoxetine+Amitriptyline+Olanzapine	10	3.3%
Haloperidol+Olanzapine+Amisulpride+Chlorpromazine	13	4.2%
Five drug combination		
Haloperidol+Olanzapine+Risperidone+Aripiprazole+Escitalopram	5	1.6%
Chlorpromazine+Olanzapine+Quetiapine+Risperidone+Sertraline	8	2.6%
Olanzapine+Risperidone+Quetiapine+amitriptyline +Sertraline	12	3.9%
Olanzapine+Risperidone+Fluoxetine+Sertraline+Amitriptyline	7	2.3%

PRESCRIPTION OF DIFFERENT ANTIPSYCHOTIC DRUGS:

A total of 303 patients and 938 drugs were enrolled in this study, of these majority of the patients who received antipsychotics were olanzapine 256(27.2%) followed by risperidone 164(17.4%), haloperidol 72(7.6%), Quetiapine 56(5.9%), Amisulpride 46(4.9%), Chlorpromazine 29(3.0%), Aripiprazole 20(2.1%), Promethazine 16(1.7%), Clozapine 13(1.3%), Trifluoperazine 2(0.2%), Fluphenazine 1(0.1%) respectively shown in table:

Figure 3. Utilization of Different Anti-Psychotic Drugs

PRESCRIPTION OF DIFFERENT ANTI-DEPRESSANTS DRUGS:

Overall 303 patients and 938 drugs in anti-depressants, majority of the patients who received monotherapy were Amitriptyline 74(7.8%) followed by escitalopram 74(7.8%), 73(7.7%) received sertraline, 34(3.6%) received fluoxetine, 2(0.2%) received imipramine and 2(0.2%) received duloxetine, 2(0.2%) received Paroxetine and vilazodone 2(0.2%) respectively represented in table:

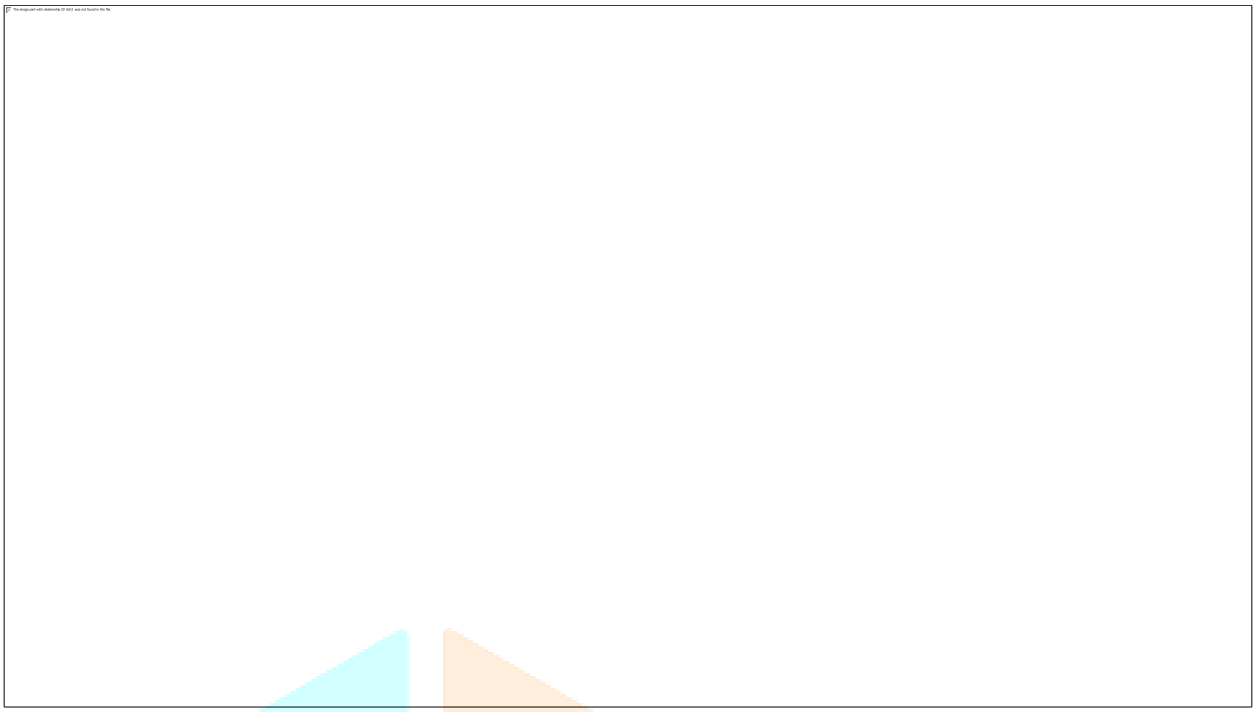

Figure 4. Utilization of Different Anti-Depressants Drugs

AGEAND GENDER WISE DISTRIBUTION OF PATIENTS WITHADVERSE DRUG REACTIONS:

In this study, 303 patients were reported to experience prescribing pattern and adverse drug reaction during the study period.

Of these 233 patients were reported to experience ADR during the study period. Among 233 patients, a majority of the patients in ADRs were females 122(52.3%) compare to males 111(47.6%). Majority of the patient's experienced adverse drug reactions belonged to the age group of 28-37 years 90(38.6%) which is represented in the table. No significant difference of age and gender on ADRs was found. ($P > 0.05$).

Table 5. AGEAND GENDER WISE DISTRIBUTION OF PATIENTS WITH ADRs

Age range	Male	female	Total patients	%
18-27	33 (14.1%)	32 (13.7%)	65	27.8%
28-37	39 (16.7%)	51 (21.8%)	90	38.6%
38-47	25 (10.7%)	24 (10.3%)	49	21.0%
48-57	11 (4.7%)	6 (2.5%)	17	7.2%
>58	3 (1.2%)	9 (3.8%)	12	5.1%
Total	111	122	233	

NUMBER OF ADVERSE DRUG REACTIONS PER PRESCRIPTION:

Among 303 patients, most of the patients 105(45.0%) contained two adverse drug reactions rest followed by 74(31.7%) contained one adverse drug reactions, 35(15.0%) contained three adverse drug reactions, 10(4.2%) contained four adverse drug reactions, 6(2.5%) contained five adverse drug reactions and 3(1.2%) contained six adverse drug reactions respectively shown in table. The overall mean frequency of ADRs is 38.3±42. Adverse Drug Reactions are significant in Most of the prescriptions P (0.06). 233 subjects reported 477 ADRs. Thus 76.8 % (95% confidence interval: 72.06 -81.53) prevalence of ADRs.

Table 6. ADVERSE DRUG REACTIONS PER PRESCRIPTION

No of ADRs	Frequency	Percentage (%)
1	74	31.7%
2	105	45.0%
3	35	15.0%
4	10	4.2%
5	6	2.5%
6	3	1.2%

SPECTRUM OF SUSPECTED ADVERSE DRUG REACTIONS:

Among 303 patients, ADRs were identified in 233(76.8%) patients. 34 different kinds of adverse drug reactions were encountered in the patients.

Of these 28 different kinds of adverse drug reactions were experienced in patients who were receiving Anti-psychotics.

Table 7. SPECTRUM OF SUSPECTED ADVERSE DRUG REACTIONS (n=477)

Type of ADR	No of ADRs in patients using Antipsychotics	%	No of ADRs in patients using Antidepressants	%
Dyspepsia	7	2.3%	2	0.6%
Fatigue	10	3.3%	1	0.3%
Dizziness	45	14.8%	9	2.9%
Amenorrhea	36	11.8%	-	-
Weight gain	54	17.8%	7	2.3%
Increased appetite	15	4.9%	2	0.6%
Sedation	6	1.9%	3	0.9%
Dry mouth	8	2.6%	1	0.3%
Akathisia	10	3.3%	1	0.3%
Somnolence	35	11.5%	-	-
Parkinsonism	26	8.5%	1	0.3%
Hyperprolactinemia	8	2.6%	1	0.3%
Weakness	-	-	2	0.6%
Constipation	10	3.3%	4	1.3%
Tremors	24	7.9%	4	1.3%
Tachycardia	2	0.6%	-	-
Acute dystonia	2	0.6%	-	-
Insomnia	16	5.2%	5	1.6%
Erectiledysfunction	2	0.6%	2	0.6%
Hyperglycemia	9	2.9%	-	-
Numbness	8	2.6%	4	1.3%
Palpitation	2	0.6%	-	-
Seizures	2	0.6%	-	-

A headache	3	0.9%	35	11.5%
Weight loss	2	0.6%	3	0.9%
Nausea	-	-	8	2.6%
Sexual dysfunction	4	1.3%	-	-
Paraesthesia	4	1.3%	11	3.6%
Anxiety	-	-	3	0.9%
Cognitive changes	-	-	2	0.6%
Hypersalivation	7	2.3%	-	-
Vomiting	1	0.3%	-	-
Rashes	-	-	8	2.6%

DRUGS RESPONSIBLE FOR ADVERSE DRUG REACTIONS:

Among the drugs incriminated, Anti-psychotics 358(75.0%) were the commonest group of agents causing adverse drug reactions followed by Anti-depressants 119(85.4%).

Table 8. ANTI-PSYCHOTICS RESPONSIBLE FOR ADRs

Drugs	**No of ADRs (n=358)**	**Percentage (%)**
Olanzapine	199	41.7%
Risperidone	63	13.2%
Quetiapine	12	2.5%
Clozapine	8	1.6%
Amisulpride	3	0.6%
Aripiprazole	6	1.2%
Haloperidol	52	10.9%
Promethazine	5	1.0%
Chlorpromazine	7	1.4%
Trifluoperazine	3	0.6%

Table 9. ANTI-DEPRESSANTS RESPONSIBLE FOR ADRs

Drugs	No of ADRs (n=119)	Percentage (%)
Sertraline	37	7.7%
Escitalopram	29	6.0%
Fluoxetine	24	5.0%
Amitriptyline	27	5.6%
Paroxetine	1	0.2%
Duloxetine	1	0.2%

ASSESSMENT OF ADRs BY USING NARANJO'S SCALE:

According to Naranjo's algorithm scale, 286(59.9%) suspected ADRs were Probable, 144(30.1%) ADRs were Possible and 2(0.4%) ADRs were Definite, whereas 45(9.4%) ADRs were Probable+Possible represented were shown in the table:

Figure 5. Assessment of ADRs by Using Naranjo's Scale

MANAGEMENT OF ADVERSE DRUG REACTIONS:

Among 233 patients, no changes were seen in patients 194(83.2%), dose altered in 30(12.8%) and the drug was withdrawn in 9(3.8%) which is shown in the table:

Table 10. MANAGEMENT OF ADRs

Management	No of ADRs (n=233)	Percentage (%)
Drug withdrawn	9	3.8%
Dose altered	30	12.8%
No changes	194	83.2%

DISCUSSION:

Our prospective observational study which was conducted in 303 patients, shows that the schizophrenia and depression occurs more in females 63(20.7%) and 16(5.2%), similar to the results of chatter et al.,[10] and E. Avanti et al.,[23] The reason for this is because of the biological life cycle, hormonal and psychological factors that women experience may cause women's higher depression and schizophrenia rate.

Psychosis is more in males 68(22.4%) observed similarly reported by Rode SB et al.,[24] has been hypothesized that this difference due to an effect of childbirth, substance-induced and due to the withdrawal of alcohol. No significant difference of disease on gender was found ($P > 0.05$).

In the present study, Age distribution shows that the majority of patients attending the psychiatric outpatient department were 28-37 years 118(38.9%) followed by 18-27 years 81(26.8%) suffering from schizophrenia, psychosis, and depression. The significant difference of diagnosis on age was found. ($P<0.05$).The reason may be due to vulnerable stress, polypharmacy compare to younger patients, more sensitive to the effect of psychiatric medications and are susceptible to adverse drug reactions. Mugada et al.,[25] and poul et al.,[26] study showed similar results.

In our study, Anti-psychotics 677(72.1%) and Anti-depressant 261(27.8%) medication used not only for the psychosis, schizophrenia, depression but also the combination diseased like BPAD with psychosis, BPAD with depression, schizophrenia with psychosis and schizophrenia with depression.

In our study schizophrenia, psychosis, depression patients have a duration of illness 6m-5 yrs. The most of the patients experience illness at the starting of the disease so that treatment at the onset of disease results the rate of occurrence of symptoms falls down and doesn't lead to chronic. Prasanth Ampalam et al[27] and Buoli et al.[28] Study showed similar data.

This study Atypical antipsychotics are preferred a lot when compared to Typical anti-psychotics demonstrates that the clinicians place more importance on the schizophrenic patient quality of life. Atypical antipsychotics are preferred over typical antipsychotics because of lower risk of Extrapyramidal syndrome and control over negative symptoms. Grover et al.,[29] conducted the study having similar findings.

Most frequently prescribed class of Anti-depressants was SSRIs 183(19.5%) followed by TCAs 76(8.1%) because of lesser side effects and better tolerability, similar to the study of chattar K. B et al.,[10] and Abdul Rahman fata Nahas et al.,[30]

In our study, the maximum no of prescriptions was found to be 280 in one patient and minimum no of prescription was found to be 8 in one patient. The reasons for this because psychiatric disorders are chronic mental disorders and require long term therapy and regular visits to the hospital.

In the present study, olanzapine 31(10.2%)) was the most commonly used Anti-psychotic drug followed by risperidone6(1.9%) and haloperidol5(1.6%). The reason for this because of olanzapine reduces hospitalization, minimizes side effects and reduces overall medical costs. [31] Atypical antipsychotics are commonly prescribed owing to their better tolerability; low relapse rate, better control over negative symptoms. RiyazAhmedSiddiqui et al.,[32] conducted study results are comparatively similar. A systemic review showed that the olanzapine is more efficacious than the other second-generation antipsychotics. [33]

Escitalopram 2(0.6%)was the most frequently used Anti-depressant drug having better efficacy, earlier onset of action, more responders to the therapy, definite superiority in the treatment of depression. MichaelBauer et al., [34] study showed similar results.

Atypical antipsychotic with the typical antipsychotic combination is preferred because of control over both positive and negative symptoms and to control the progression of the disease to chronic. Our prescribing pattern showed that the combination of olanzapine+risperidone, olanzapine+haloperidol, olanzapine+amisulpride compared to the study of R. A Siddiqui et al., [35] Most prescribed neuroleptic is olanzapine+risperidone.

The most common use of drugs like Olanzapine 256(27.2%), risperidone 164(17.4%), Quetiapine 56(5.9%), amisulpride 46(4.9%), chlorpromazine 29(3.0%), haloperidol 72(7.6%) is seen. Khalid A.J et al., [35] study has comparative similar findings.

Roopadevi et al., [36] results are comparatively similar to the present study, shows that SSRIs are commonly prescribed antidepressants like Escitalopram 74(7.8%), Amitriptyline 74(7.8%) and sertraline 73(7.7%) because of the first line agents in the treatment of depression.

In our study among 303 patients, 233 patients had developed 477 adverse drug reactions to Anti-psychotics 358(75%) and Anti-depressants 119(24.9%) medications i.e., the overall incidence of Adverse drug reaction in

our study was 76.8%. The incidence of Anti-psychotics in our study was 208(68.6%) and Anti-depressants was 82(27%).

In the present study, on adverse drug reactions among females was estimated to be high 122(52.3%) compare to males 111(47.6%). The difference in prevalence of adverse drug reactions in psychotropics may be due to increasing age, hormonal and psychological factors, females generally have a reduced hepatic clearance, pharmacokinetic and pharmacodynamic differences. No significant difference of age and gender on ADRs was found. ($P > 0.05$).

In the present study, we found that the majority of patients associated with adverse drug reactions to Anti-psychotics and Anti-depressants belonged to the age group of 28-37 years 90(38.6%). The reason may be due to vulnerable stress, more sensitive to the effect of psychiatric medications and are susceptible to adverse drug reactions. Singh et al., [37] and Mukherjee et al., [38] showed that a majority of adverse drug reactions in the age group 25-35 and 20-40 years are similar results to our study.

A total of 477 adverse drug reactions were identified in our study. Hence the average number of ADRs per patient in our study was assessed to be 2 slightly higher compared to the study Lucca et al.,[39] showed that majority of ADRs per patient is 1.6. The prevalence of ADRs may be due to psychotropic agents acts on CNS carry a high probability of causing ADRs whereas psychiatric disorders are chronic mental disorders and may be due to long term therapy and ADRs may occur due to patients non-compliance. Adverse Drug Reactions are significant in Most of the prescriptions P (0.06). 233 subjects reported 477 ADRs. Thus 76.8 % (95% confidence interval: 72.06 -81.53) prevalence of ADRs.

Anti-psychotics 675(71.9%) and Anti-depressants 263(28%) were the most commonly prescribed psychotropic drugs in our study. Anti-psychotics were responsible for most of the adverse drug reactions followed by Anti-depressants. Jayanthi et al., [40] and Lohan K et al., [41] study have similar results.

From the present study, it is clear that most of the Adverse drug reactions in Antipsychotics due to olanzapine 199(41.7%) followed by risperidone whereas, in Typical anti-psychotics most of the ADRs due to haloperidol 51(21.8%) and chlorpromazine. Among ADRs in Anti-depressants of SSRIs are due to Sertraline 37(77%) followed by escitalopram 74(7.8%). In TCAs, Amitriptyline 27(11.5%) was the most common drug causes ADR. P. Lakshmi et al., [42] and Hari Chandran et al., [43] results are comparatively similar.

34 different kinds of adverse drug reactions were encountered in the study. Among the ADRs monitored in Atypical antipsychotics, weight gain 54(17.8%) was found to be most common ADR followed by Amenorrhoea 26(11.8%). The prevalence may be due to a flexible dose of olanzapine, patients with low body mass index and may be due to a lack of serotonin receptors. Amenorrhoea occurs may be estrogen imbalance. Chakravarthy et al., [44] and Sridhar et al., [45] study results have similar findings.

Among the adverse drug reactions monitored in typical antipsychotics, Parkinsonism 26(8.5%) was the most common adverse drug reaction. The reason due to dopamine receptors is widely distributed in brain and typicals acts on dopamine receptors in the striatum. These findings are similar to the study results of Chakravarthy et al., [44] and Sridhar et al., [45]

Among Adverse drug reactions monitored in Anti-depressants, in SSRIs Headache 35(11.8%) was the most common ADR followed by rashes 8(3.6%) whereas in TCAs paraesthesia 11(3.6%). Mukherjee et al., [38] showed similar results.

For the management of these adverse drug reactions like weight gain, dizziness, headache, tremors, paraesthesia drugs like Trihexyphenidyl, Diazepam, and Propranolol drugs were added to the patients.

In our study, the causality assessment of suspected ADRs done by Naranjo's scale revealed that majority of ADRs was probable 286(59.9%). In the management of ADRs, no changes were seen in most of the patients 194(83.2%). Our study comparative with Sengupta et al., [46] and R. J. Lihite et al., [47] in their study reported causality of ADRs to be probable.

CONCLUSION:

Prescribing pattern helps in understanding, changing trends over time. Among all the antipsychotics like typical and atypical, atypical antipsychotics include Olanzapine, Risperidone are preferred than the other atypical antipsychotics. Typical antipsychotics usage is declined in recent years because of associated Extra pyramidal side effects. Among the prescribed antidepressants SSRIs like Escitalopram is preferred because of safer side effect profile, better tolerability, favorable risk-benefit ratio than the other drugs, decreased risk of drug-drug interactions, favorable pharmacokinetic profile. The establishment of an active pharmacovigilance program is essential to prevent possible ADRs and it helps to improve the quality of patient care by ensuring safer use of drugs. Though the Olanzapine is the preferred antipsychotic, better tolerability, low relapse rate, more efficacious in the treatment of negative symptoms and control the suicidal, impulsivity behavior, it is having ADR like weight gain. Sertraline is associated with ADR like a headache. The causality assessment of suspected ADRs done by using Naranjo scale revealed that the majority of ADRs are probable.

Clinical pharmacist takes an active part in the identifying, monitoring, and reporting of ADRs. This helps in early detection, prevention, and management of ADRs which reduces the treatment cost and enhance medication adherence pattern. Under-reporting due to lack of awareness both at the level of health care professionals and patients leads to serious complications so that should be addressed immediately.

ABBREVIATIONS:

ADRs - Adverse Drug Reactions

BPAD – Bipolar Anxiety disorder

CNS - Central Nervous System

DP – Depression

DSM - Diagnostic and Statistical Manual

EPS - Extra Pyramidal Symptoms

FGAs - First Generation Anti-Psychotics

MAOIs - Monoamine Oxidase Inhibitors

NDRI - Norepinephrine and Dopamine Reuptake Inhibitor

NE - Norepinephrine

PS – Psychosis

SGAs - Second Generation Anti-Psychotics

SNRIs - Serotonin and Nor-epinephrine Reuptake Inhibitors

SSRIs - Selective Serotonin Receptors

SZ – Schizophrenia

TCAs - Tricyclic Anti-Depressants

WHO - World Health Organization

Graphical abstract