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Original Research Paper

Psychiatry

AN OBSERVATIONAL STUDY ON VARIOUS PHYSICAL COMORBIDITIES AND MEDICATION USAGE IN PATIENTS ATTENDING TO PSYCHIATRY OUTPATIENT DEPARTMENT IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: This study aims to assess physical co-morbidities and medication usage in patients attending to psychiatric services.

Methodology: A hospital-based prospective observational study was conducted by assessing the physical co-morbidities and medication usage in patients, who attended Psychiatry Out-patient department at Sri Padmavathi Medical College for Women,Tirupati over 6 months(June 2019 - December2019). Microsoft excel 2010 was used for analyzing physical comorbidiites and psychiatric illnesses. Descriptive statistics like mean and percentage were used to calculate gender, age, co-morbidities, and severity of drug interactions. SPSS version 25 was used to calculate the Chi-square test and p-value. Results with a p-value <0.05 were considered significant.

Results: The sample size of our study was 355. Among them 176 males (49.57%) and females 179 (50.42%) were with mental illness. physical co-morbidities and medications were evaluated in all participants. The mean age of psychiatric patients with physical co-morbidities and without physical co-morbidities were (45.11 ± 16.82) and (43.97 ± 27.35) respectively. Depression 104(29.29%) was seen in the maximum number of patients followed by Anxiety 65(18.30%), Schizophrenia 64(18.03%). Drug drug interactions were identified in 48 participants.Among them 4 major, 42 moderate and 2 minor drug drug interactions were observed.

Conclusion: Drug drug interactions must be considered while selecting treatment options in patients with multiple co-morbidities. This can be helpful for achieving optimal patient compliance and outcomes. Psychiatrists in collaboration with clinical pharmacists must make sincere efforts to overcome their sense of inadequacy in these conditions.This can save both time and money for patients and the healthcare system.

KEYWORDS : Psychiatric medications, Physical Co-morbidities, Drug Interactions, Anxiety, Depression, Schizophrenia, Psychosis,Mental illness,Anti psychotics,Anti depressants,Mood stabilizers.

INTRODUCTION

Mental illness affects a person's cognition, emotion, and behavior that leads to dysfunction in the psychological and developmental process underlying mental functioning.[1]The diagnostic and statistical manual of mental disorders (DSM-5) is the most widely used handbook by psychiatrists and physicians for the diagnosis and management of mental disorders. Over 9.8 million teenagers in the age group of 13-17 years are affected with depression and other mental health disorders.[2] Almost 4.4% and 3.6% of the world population suffers from depression and anxiety disorders by affecting health and quality of life[3].

Physical Comorbidity is defined as a disease or condition that coexists with another disease. Most of the participants have at least one physical comorbidity(diabetes mellitus, hypertension, rheumatoid arthritis, hyperthyroidism, hypothyroidism, cardiac arrhythmias, and epilepsy).[4] If a person is diagnosed with Major depressive disorder, Social anxiety disorder, and Diabetes Mellitus-II, there will be chances of developing other comorbidities like anxiety disorder, Bipolar disorder.[5] Even concomitant use of multiple medications may result in adverse drug events and drug-drug interactions. The majority of antipsychotic medications interact with other comorbid drugs like antihypertensives, hypoglycemics, anti-epileptics, and antiarrhythmics causing serious Drug drug interactions.[6].A retrospective study of mental health in Qatar stated that patients with serious mental disorders have a high prevalence of Diabetes. This is one of the highest among psychotic illness.[7] Also, elderly patients with depression have high-frequency rates of physical comorbidities like Diabetes mellitus and Hypertension.[8]

If the effect of one drug is altered by other drugs, then it is called drug-drug interaction. The outcome can be harmful if the interaction leads to increase in the toxicity of the drug.[9] Drug drug interactions are classified as pharmacokinetic and pharmacodynamic interactions. Pharmacodynamic interactions cause either an additive pharmacological effect or antagonistic pharmacological effect. Pharmacokinetic interactions occur primarily through metabolic processes in the liver. Drugs are mainly metabolized by the Cytochrome (CYP450) enzymes. If two drugs are metabolized by the same isoenzyme, then co-administration may lead to increased concentration of one or both drugs.[10][11]The potential DDIs have leads to the central nervous system(CNS) depression and anticholinergic effect in Mexican patients due to concominant use of antipsychotics, benzodiazepines, and antidepressants.[12]

The main objective of the study is to examine various physical co-morbidities and medication usage in outpatient department and to identify Drug drug interactions.

MATERIALS AND METHODS

Ethical Consideration ans study site

A prospective observational study was conducted in the Department of Psychiatry at Sri Padmavathi Medical College for Women, a tertiary care teaching hospital, Tirupati, Andhra Pradesh, India.This study was approved by the institutional ethics committee with IEC NO.919 from Sri Venkateswara institute of medical sciences. The study duration was 6 months(June 2019-December 2019).

Sample size

Three hundred and fifty-five participants with physical co-morbidities and mental illnesses were included in the study.

Selection criteria

Patients of all age groups with mental illness, co-morbidities, and patients who were willing to give their informed consent were included. Patients who were not willing to participate and who were admitted to IP were excluded from the study.

Method of collection of data

Written informed consent was obtained from all the participants. Data and demographic details such as age, gender, diagnosis, co-morbid conditions, and medications were collected from case files in the department. Medications were analyzed for drug-drug interactions by using drug information softwares like Stockley drug interaction checker, Medscape drug interaction checker, and drug.com checker.

Statistical analysis

Microsoft excel 2010 was used for analyzing physical comorbidiites and psychiatric illnesses. Descriptive statistics like mean and percentage were used to calculate the gender, age, co-morbidities, and severity of drug interactions. SPSS version 25 was used to calculate the Chi-square test and p-value. Results with a p-value$<$0.05 were considered significant.

RESULTS

Distribution of patients on gender

Among 355 cases, 176 males (49.57%) and 179 females (50.42%) have come with mental illness to the psychiatry OP(Figure 1). They were evaluated for physical co-morbidities and medication usage.

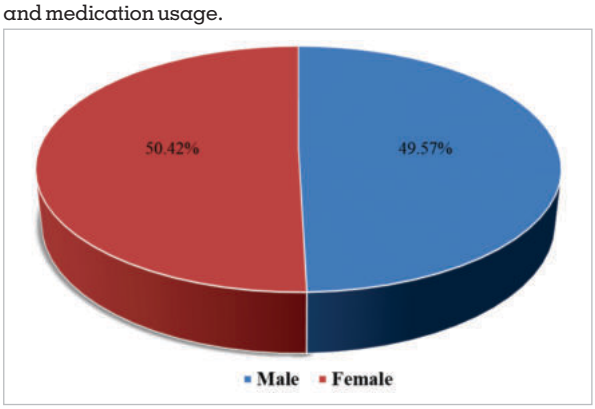

Figure .1 Distribution of patients based on gender

Age-wise distribution of mental illness patients with and without physical co-morbidities

The age range of the study population was 7-91 years. The mean value of age in psychiatric patients with physical co-morbidities and without physical co-morbidities are (45.11± 16.82) and (43.97±27.35) respectively. Psychiatric illness patients with physical co-morbidities were high in age groups of 41-60 years followed by 21-40yrs, 61-80yrs, <20yrs and 81-100yrs. Psychiatric illness patients without physical co-morbidities were high in the age group of 41-60years followed by 21-40yrs, <20yrs, 61-80yrs, and 81-100yrs (Figure 2).

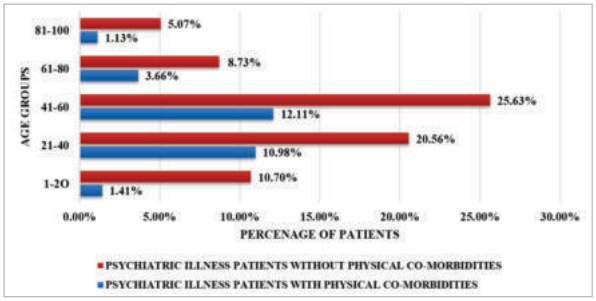

Figure 2: Age-wise distribution of mental illness patients with and without physical co-morbidities

Distribution of patients on basis of psychiatric illness

The first most diagnosed disorder was depression(29.29%). It was followed by Anxiety(18.30%), Schizophrenia (18.03%), Mixed anxiety and depression(3.94%), Psychosis (3.10%) and other psychiatric illnesses(27.32%) (Table 1).

Table 1 Distribution of patients on basis of psychiatric illness

Psychiatric diagnosis	No. Of patients (n=355)	Percentage (%)
Depression	104	29.29
Anxiety	65	18.30
Schizophrenia	64	18.03
Psychosis	11	3.10
Mixed anxiety and depression	14	3.94
Other psychiatric illneses	97	27.32

Distribution of patients based on physical comorbidities.

Among 104 depression patients, 47 participants were with physical co-morbidities. Patients with hypertension (13.46%) were highest and then followed by thyroid abnormality (11.53%), other co-morbidities (11.53%), diabetes mellitus (5.77%), and epilepsy (2.88%).In a total of 65 anxiety patients, 25 participants have physical co-morbidities. Among them, other co-morbidities(12.30%) was highest followed by hypertension (10.77%), thyroid abnormality (9.23%), diabetes mellitus (4.61%), and epilepsy (1.54%). In 64 schizophrenia patients, 15 participants were with physical co-morbidities. Of them, other co-morbidities (9.37%) was highest followed by thyroid abnormality (6.26%), hypertension (3.12%), diabetes mellitus (3.12%), and epilepsy(1.56%).5 patients with physical co-morbidities were observed in 11 psychotic individuals. Of them epilepsy (18.19%) was highest followed by hypertension (9.09%), diabetes mellitus (9.09%), thyroid abnormality 1(9.09%), and other co-morbidities (9.09%) (Table 2).

Table 2 ; Distribution of patients based on physical comorbidities.

Physical co-morbidities	Depression n (%)	Anxiety n (%)	Schizophrenia n (%)	Psychosis n (%)	P-value
Hypertension	14(13.46)	7(10.77)	2(3.12)	1(9.09)	0.0005
Thyroid abnormality	12(11.53)	6(9.23)	4(6.26)	1(9.09)	0.01
Diabetes mellitus	6(5.77)	3(4.61)	2(3.12)	1(9.09)	0.198
Epilepsy	3(2.88)	1(1.54)	1(1.56)	2(18.19)	0.66
Other physical co-morbidities	12(11.53)	8(12.30)	6(9.37)	1(9.09)	0.03

Psychiatric medications used in the sample of patients with physical comorbidities

As per the study antidepressants (48.12%) were the most frequently prescribed class of medications .Among them,

(12.86%) were with thyroid abnormality,(12.86%) were hypertensive, (5.35%) were co-morbid, (4.09%) were epileptic and 7 (4.09%) were diabetic. Mood stabilizers were prescribed for (45.07%)participants . Of them(11.87%) were hypertensive patients, 16 patients (10%) were co-morbid, 14 patients (8.75%) were with thyroid abnormality, (3.12%) patients were diabetic and (3.12%) were epileptic. Antipsychotics were prescribed for (42.25%) participants. Among them (4.66%) were with thyroid abnormality, (4%) were diabetic, (3.33%) were hypertensive, (3.33%) were co-morbid and 3 patients (2%) were epileptic (Table 3) (Figure 3).

Table 3. Psychiatric medications used in the sample of patients with physical comorbidities

Diseases/ Medications	Antipsychotics n (%)	Antidepressants n (%)	Mood stabilizers n (%)
Hypertension	5 (3.33)	22 (12.86)	19 (11.87)
Diabetes mellitus	6 (4)	7 (4.09)	5 (3.12)
Thyroid abnormality	7 (4.66)	22 (12.86)	14 (8.75)
Epilepsy	3 (2)	7 (4.09)	5 (3.12)
Other co-morbidities	5 (3.33)	19 (5.35)	16 (10)

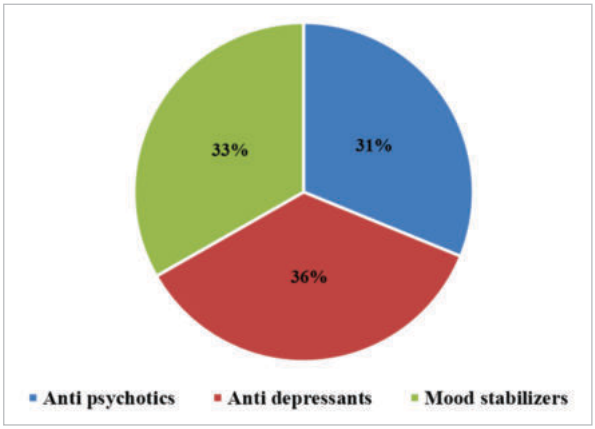

Figure 3. Classification of patients based on the type of medications prescribed

Types of drug-drug interactions observed in mental illness patients with physical co-morbidities.

Drug drug interactions were identified in 48 patients.Among them, 4 major,42 moderate and 2 minor drug drug interactions were observed (Table 4)(Table 5).

Table 4. Types of drug-drug interactions observed in mental illness patients with physical co-morbidities.

Drug combination	No of cases	Consequences of DDI	Severity
Sertraline + Propranolol	1	Sertraline increase the level of propranolol by affecting hepatic enzyme CYP2D6 metabolism	***Major***
Hydroxychloroquine + Escitalopram	1	Risk of an irregular heart rhythm	***Major***
Amitriptyline + Escitalopram	2	Increase the risk of serious condition called Serotonin syndrome .	***Major***
Risperidone + Metformin	6	Risperidone may interfere with blood glucose control and reduce the effectiveness of metformin	***Moderate***
Risperidone + Formoterol	1	Both increase QT_c interval.	***Moderate***
Telmisartan/Amlodipine+ Clonazepam/ Quetiapine/ Risperidone	9	Both may have additive effects in lowering blood pressure	***Moderate***
Propranolol/ Atenolol + Chlordiazepoxide/ Amitriptyline/ Clonazepam	3	Decreases blood pressure by additive effect.	***Moderate***
Fluvoxamine + Glimepiride	1	Decreases blod sugar levels	***Moderate***
Naproxen + Escitalopram	3	Increases risk of bleeding	***Moderate***
Quetiapine + Levodopa	1	Quetiapine decreases the effects of levodopa by pharmacodynamics antagonism.	***Moderate***
Amlodipine + Phenytoin	1	Amlodipine will increase the level or effect of phenytoin by affecting hepatic/intestinal enzyme CYP3A4 metabolism.	***Moderate***
Clobazam + Aripiprazole	2	Clobazam decreases plasma concentration of aripiprazole.	***Moderate***
Quetiapine + Pregabaline	2	Increases side effects such as dizziness, drowsiness, confusion.	***Moderate***
Levocetrizine + Valproic acid	3	Valproic acid increases the side effects of levocetrizine	***Moderate***
Carbamazepine + Amitriptyline	2	Carbamazepine decreases the effect of amitriptyline by altering metabolism	***Moderate***
Valproic acid + Clonazepam	1	This combination may affect seizure control and cause drowsiness	***Moderate***
Amitriptyline + Pheniramine	2	Increases side effects such as drowsiness, blurred vision, flushing	***Moderate***
Phenytoin + Risperidone	1	Phenytoin will decrease the level/effect of Risperidone by MRD-1 efflux transporter	***Moderate***
Salmeterol + desvenlafaxine	1	Both increases blood pressure	***Moderate***
Atorvastatin + Risperidone	1	Atorvastatin will increase the level of Risperidone by P-Glycoprotein (MDR-1) efflux transporter	***Moderate***
Omeprazole + Escitalopram	1	Omeprazole will increase the level/effect of Escitalopram by affecting hepatic enzyme CYP2C19 metabolism	***Moderate***

Flavoxate + Risperidone	1	Flavoxate decreases levels of Risperidone by inhibition of GI absorption	***Moderate***
Escitalopram + Propranolol	1	Escitalopram increases the levels of propranolol by decreasing metabolism	***Minor***
Rabeprazole + Levothyroxine	1	Rabeprazole decreases levels of levothyroxine by increasing gastric pH.	***Minor***

Table 5 Classification of drug interactions on the basis of severity

Severity	No of drug interactions(n=24)	Percentage (%)
Major	3	12.5
Moderate	19	79.17
Minor	2	8.33

Chi-square test result was 53.69 and the p-value was found to be 0.08. This shows that it is statistically non-significant.

DISCUSSION

This study presents the frequency rates of concurrent physical co-morbidities in psychiatric illness patients. A total of 355 patients were diagnosed with psychiatric illness.Of them 104 cases were presented with physical co-morbidities. The most frequently occurred psychiatric illnesses were observed in the age group of 41-60 years.

Among 355 study population, females were 179(50.42%) and males were 176(49.57%). This shows that females were more prone to psychiatric illness when compared to males. This might be because of increased stress and hormonal changes in premenopausal women, which is similar to an Indian study done by Savita Malhotra and Ruchitha Shah.[13]

Depression(29.29%) was seen in the majority of patients.But statistical differences were not present among the psychiatric disorders (Depression, Anxiety, and Schizophrenia). These findings were similar to a study reported by Sokal[14] in the USA. Even they did not find any significant differences in their prospective study.

According to few international studies, hypertension was the most common physical co-morbidity (13.46%).The Medicaid database of USA reported that more than half of the patients who were diagnosed with psychiatric illnesses also had diabetic mellitus, cardiovascular disorders, and pulmonary diseases. However medical comorbidities such as thyroid abnormality (11.53%) and diabetes mellitus (5.77%) were lesser when compared with a study by Bener.[15] in Qatar.

Among medications, anti-depressants(48.12%) were the most widely prescribed class of drugs for psychiatric disorders.The second most prescribed class were mood stabilizers(45.07%) and followed by antipsychotics(42.25%).

This was similar to a study conducted by Thomas.J.Moore.[16]In the case of co-morbid associated psychiatric illness, anti-depressants were used widely in both Hypertension and Thyroid abnormality .

A total of 24 drug drug interactions were identified in our study. The identified rates of major, moderate, and minor drug drug interactions were 12.5%, 79.17%, and 8.33%, respectively. They were lower than the ones reported in an Euthopian study by Mezgebe[17].This shows that older adults are more prone to adverse drug events and drug drug interactions because of their higher likelihood to have multiple comorbidities and multiple medications. This was similar to a study by Gurwitz[18] and Fick DM[19].

The combination of Amitriptyline and Escitalopram was the majorly observed serious drug drug interaction . Using Escitalopram together with amitriptyline can cause Serotonin syndrome.A study by Jacaqueline Volpi-Abadie[20] stated that the concomitant use of Escitalopram with Amitriptyline leads to accumulation of more serotonin causing serotonin syndrome.Other major drug drug interaction was observed between hydroxychloroquine and escitalopram .Using Hydroxychloroquine together with Escitalopram may prolong QT interval and increases the risk of irregular heartbeat.This is similar to a study by Karuppiah Arunachalam[21].

In moderate drug drug interactions, the CYP3A4-mediated metabolism of clonazepam is accelerated by Valproic acid, leading to increased clonazepam clearance that may affect seizure control which is similar to a study conducted by Yukawa E[22]. Among minor drug drug interactions, Rabeprazole decreases the levels of Levothyroxine by increasing gastric pH.

CONCLUSION

From the data obtained, it has been concluded that a total of 29.2% of the psychiatric out-patients were found to have physical co-morbidities. In terms of a specific illness, depression was the major psychiatric illness,observed in about 29.29% of the participants and this was followed by anxiety and schizophrenia. Major physical co-morbidity detected in this study was hypertension followed by thyroid abnormality.The results of our study have revealed that the rate of antidepressants prescription was high. The frequency of chronic physical conditions and depression is very common. The potential drug drug interactions must be considered while selecting treatment options in patients with multiple co-morbidities. This can help in achieving optimal patient adherence and outcomes. Psychiatrists in collaboration with clinical pharmacists must make sincere efforts to overcome their sense of inadequacy in these conditions. This can save both time and money for patients and the healthcare system.

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