

To Assess the Compliance of Monitoring Metabolic Symptoms Associated with Antipsychotics in an Inpatient Setting in a Tertiary Care Hospital in Karachi, Pakistan

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Abstract: Mental health problems like schizophrenia, bipolar affective disorder and use of second generation antipsychotics (SGA) are linked to the risk of developing metabolic syndrome. The purpose of our study was to determine the level of compliance to monitoring metabolic symptoms associated with second generation antipsychotics according to the standards of NICE guidelines. Secondly, we aim to develop a workable standardized protocol. A total of 385 patients admitted to psychiatric ward from February 2015-January 2016 were included in the study. Case files were reviewed to obtain relevant clinical information. Assessment of height, weight, pulse, blood pressure, movement disorders, level of physical activity and nutritional status were measured in all patients. Fasting blood glucose was measured in 99 (26.5%), glycosylated hemoglobin (HbA1c) in 39 (10.4%), blood lipid profile in 44 (11.8%) and prolactin in 3 (0.8%) patients. Less than half of the patients (118, 31.6%) underwent ECG investigation. Slow titration of medication (331, 88.5%) and a trial at optimum dosage (343, 81.7%) were routinely seen. Overall physical health and patient well-being was recorded in the majority of subjects (310, 82.9%). A significant number of physical and biochemical parameters were not routinely monitored. Our study reports findings consistent with previous literature. With this we hope to highlight important concerns and make recommendations, especially in country like Pakistan where these monitoring systems are non-existing. This will not only reduce the risk of a number of complications secondary to antipsychotic medications, but will also improve patient adherence and compliance to the pharmacological treatment.

Keywords: Metabolic Syndrome, Compliance, Antipsychotics

1. Introduction

1.1. Literature Review

Patients with mental health problems have seen to be associated with a greater risk of developing metabolic syndrome than the general population. Contributing factors include genetic predisposition, developmental problems and environmental stressors including type of life style. [1-3]

Antipsychotics are the usual medications of choice for schizophrenia and bipolar disorder. At some instances they are also employed to improve anxiety or depressive symptoms. Prescription of antipsychotics has increased

considerably as evidenced by several studies. [2, 4-6]

They work via affecting the activity of certain neurotransmitters in the brain. The key one is Dopamine; hyperactivity of which results in psychotic symptoms.

For the past decade or so two main groups of antipsychotics have been used in medical practice: 'Typical' and the 'Atypical'.

Typical antipsychotics also referred to as 'first-generation' antipsychotics, initially appeared in 1950s. Atypical antipsychotics are more recent and are often called "second generation" medications. Though they still block dopamine, but to a lesser degree than the typical antipsychotics. They are also known to influence the level of other

neurotransmitters, including serotonin. [7]

Antipsychotic medications can result in metabolic syndrome, which is a cluster of conditions like high blood sugar, uncontrolled hypertension and obesity. This in turn leads to a greater risk of developing cardiovascular disease, diabetes and cerebrovascular disease. [4, 8, 9]

Apart from some of the other risk factors which include age, stress, weight and coronary heart disease, people with schizophrenia, schizoaffective disorder or bipolar disorder are at risk of developing metabolic syndrome. [4, 6] Additional aggravating factors include limited physical activity, failure of adherence to a healthy diet and limited access to relevant healthcare services. [11, 5]

Metabolic syndrome has become quite prevalent in recent years. Depending on the geographic location, approximately (20-25)% population suffer from metabolic syndrome. For instance, in Australia more than half of the population diagnosed with schizophrenia is also seen to be suffering from metabolic syndrome. Furthermore, women are more commonly affected. And there is no real guidelines for older people. [5, 10, 12]

Different guidelines recommend variable schedule of metabolic risk factor monitoring, but consensus in the literature has been mainly for the assessment of familial risk factors, physical parameters like weight, waist circumference, baseline BMI, vitals including blood pressure, baseline investigations including lipid profile and fasting blood sugar. [9, 13,]

In spite of these guidelines, level of compliance has been low. [14, 13, 15] For instance, in UK only less than a quarter of population had been categorized into obese individuals. In addition, less than one third individuals had their blood sugar monitored. [16, 17] Similar results have been reported in the USA and Australia. [16, 18, 19] There is lack of RCTs in this area. In Pakistan, there is even less of that.

Due to concerns and lack of any sort of screening and proper monitoring of metabolic symptoms in our tertiary care hospital, we aimed to investigate this and make important recommendations.

1.2. Aims and Objectives

To assess the compliance of monitoring metabolic symptoms associated with second generation antipsychotics according to the standards of NICE guidelines.

We aimed to look at the current practice of metabolic monitoring in our inpatient psychiatric ward (C0), comparing them with NICE guidelines and make recommendations to identify patients with increased risk of metabolic syndrome.

2. Methodology

We sought ethical approval from Ethical Review Committee (ERC) in Aga Khan University, before commencing our study. Confidentiality of patient data and identifiers was protected throughout the course of study.

This was a descriptive study carried out in retrospective design in Aga Khan University, hospital (AKUH), Karachi.

The total duration of this study was six months (May, 2017-October, 2017).

A total of 374 patients admitted to psychiatric ward from February 2015-January 2016 were included in the study. The sample comprised of all the inpatients admitted to C0 ward in AKUH for this period.

Inclusion criteria: All the patients commenced or switched on antipsychotics.

Exclusion criteria: Patients not using antipsychotic medications and patients from outside AKUH.

Case files were reviewed by the investigator to obtain the relevant clinical information through a history of medical records, previous admissions, doctor's notes, nurse's notes, assessment forms, relevant investigations and discharge summaries. Medical Record Numbers were used for identification of the patients.

We looked at the sociodemographic variables of our population. There was no previous screening instrument or preexisting protocol that could be employed in our target population. Therefore, the minimum standard we established for the audit purposes was that baseline investigations as outlined below should be carried out whenever a new antipsychotic medication was initiated or switched. These investigations were included in our screening instrument in concordance with NICE guidelines as outlined below: [20]

“Standard 1

Before starting antipsychotic medication, undertake and record the following baseline investigations:

1. *weight (plotted on a chart)*
2. *waist circumference*
3. *pulse and blood pressure*
4. *fasting blood glucose, glycosylated hemoglobin (HbA_{1c}), blood lipid profile and prolactin levels*
5. *assessment of any movement disorders*
6. *assessment of nutritional status, diet and level of physical activity.*

Standard 2

Before starting antipsychotic medication, offer the person with psychosis or schizophrenia an electrocardiogram (ECG) if:

1. *a physical examination has identified specific cardiovascular risk (such as diagnosis of high blood pressure)*
2. *there is a personal history of cardiovascular disease or The service user is being admitted as an inpatient*

Standard 3

Treatment with antipsychotic medication should be considered an explicit individual therapeutic trial. Include the following:

1. *Discuss and record the side effects that the person is most willing to tolerate.*
2. *Record the indications and expected benefits and risks of oral antipsychotic medication, and the expected time for a change in symptoms and appearance of side effects.*
3. *At the start of treatment give a dose at the lower end of the licensed range and slowly titrate upwards.*

4. Justify and record reasons for dosages outside the range.
5. Record the rationale for continuing, changing or stopping medication, and the effects of such changes.
6. Carry out a trial of the medication at optimum dosage for 4–6 weeks

Standard 4

Monitor and record the following regularly and systematically throughout treatment, but especially during titration:

1. response to treatment, including changes in symptoms and behaviour
2. side effects of treatment, taking into account overlap between certain side effects and clinical features of

schizophrenia (for example, the overlap between akathisia and agitation or anxiety) and impact on functioning

3. the emergence of movement disorders
4. weight, weekly for the first 6 weeks, then at 12 weeks, at 1 year and then annually (plotted on a chart)
5. waist circumference annually (plotted on a chart)
6. pulse and blood pressure at 12 weeks, at 1 year and then annually
7. fasting blood glucose, HbA_{1c} and blood lipid levels at 12 weeks, at 1 year and then annually
8. adherence
9. overall physical health"

Table 1. Monitoring as per Standard 4 (NICE).

	Baseline	1 week	2 week	3 week	4 week	5 week	6 week	12 week	1 year	Annually
Personal/Family History	✓									
Weight (BMI)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Waist circumference	✓									✓
Blood Pressure	✓							✓	✓	✓
Fasting Plasma glucose/HbA _{1c}	✓							✓	✓	✓
Fasting lipid profile	✓							✓	✓	✓

Data was analyzed and interpreted using SPSS latest version 21.0. As this was a descriptive study, frequencies and additional descriptive statistics were run to measure the level of metabolic monitoring in different categorical domains. In addition, the sociodemographic characteristics of our population were also studied.

3. Results

3.1. Study Population

The study population included a total of 374 individuals. There were 54.8% males and 45.2% females. As far as age range was concerned, 55.1% were between 21–40 years, followed by 41–60 years, which was 24.6%. There was 0.5% representation of patient with age range 81 years and above.

The most common diagnosis was Schizophrenia/Psychosis (27.3%), followed by bipolar disorder (25.9%). Approximately a quarter of the subjects had completed graduation (26.5%). A significant proportion of our population was either unemployed (24.1%) or house makers (20.1%). (21.9%) patients were students enrolled in an academic program. Other patient characteristics are listed in table 2.

Table 2. Sociodemographic Characteristics.

Subject Characteristic	Subjects / n (%) N=374
Occupation	
Unemployed	90 (24.1)
House maker	75 (20.1)
Student	82 (21.9)
Retired	6 (1.6)
Teacher	7 (1.9)
Businessmen	42 (11.2)
Skilled labour	25 (6.7)
Professional	37 (9.9)

Subject Characteristic	Subjects / n (%) N=374
Unskilled labour	2 (0.5)
Landlord	8 (2.1)
Level of Education	
Illiterate	52 (13.9)
Primary	15 (4.1)
Secondary	35 (9.4)
Matric	43 (11.5)
Intermediate	66 (17.6)
Graduate	99 (26.5)
Postgraduate	64 (17.1)
Diagnosis	
Bipolar disorder	97 (25.9)
Depression	66 (17.6)
Schizophrenia/Psychosis	102 (27.3)
Substance Abuse	53 (14.2)
Panic disorder	6 (1.6)
Personality disorder	6 (1.6)
Conversion disorder	9 (2.4)
Generalized Anxiety disorder	6 (1.6)
Dementia	9 (2.4)
Others	20 (5.3)

3.2. Level of Monitoring

3.2.1. Baseline Investigations (Standard 1)

Height, Weight, Blood Pressure and Pulse were measured in all 374 patients who presented to the psychiatry service. However, waist circumference was not measured in any patient. Evaluation of any movement disorders, level of physical activity and nutritional status was performed and documented in all 374 cases.

Fasting blood glucose was measured in 99 (26.5%), glycosylated hemoglobin (HbA_{1c}) in 39 (10.4%), blood lipid profile in 44 (11.8%) and prolactin in 3 (0.8%) patients.

3.2.2. Cardiovascular Assessment (Standard 2)

Less than half of the patients (118, 31.6%) had their ECG performed in order to detect and address cardiovascular

disease. In some patient's physical examination (40.7%) identified a cardiovascular risk (high BP, for example) whereas in others either the clinical history was remarkable

(94.9%) or the patient was admitted under the specific service as shown in table 3.

Table 3. Rationale for offering an ECG before initiating an antipsychotic medication.

Rationale	Subjects / n (%) N=118
Physical examination revealed a cardiovascular risk (such as diagnosis of high blood pressure).	48 (40.7%)
Personal history of cardiovascular disease or the service user is being admitted as an inpatient.	112 (94.9%)

3.2.3. Pharmacological Treatment and Therapeutic Trial (Standard 3)

Different practices adopted by clinicians when initiating and/or monitoring pharmacological treatment were measured. The number of occasions when these practices were implemented was calculated as shown in table 4. Two

guidelines were seen to be routinely implemented in more than 80% of the patients. These included slow upward titration of the medication (88.5%) and a trial of medication for 4-6 weeks at optimum dosage (91.7%). In (30.2%) of cases, rationale for continuing, changing or stopping medication, and the effects of such changes were recorded.

Table 4. Monitoring of treatment as an explicit therapeutic trial.

Clinical Practice	Number of patients in whom the practice was undertaken / n (%) N=374
Discuss and record the side effects that the person is most willing to tolerate.	30 (8.0%)
Record the indications and expected benefits and risks of oral antipsychotic medication, and the expected time for a change in symptoms and appearance of side effects.	16 (4.3%)
At the start of the treatment give a dose at the lower end of the licensed range and slowly titrate upwards.	331 (88.5%)
Justify and record reasons for dosages outside the range.	8 (2.1%)
Record the rationale for continuing, changing or stopping medication, and the effects of such changes.	113 (30.2%)
Carry out a trial of the medication at optimum dosage for 4-6 weeks.	343 (91.7%)

3.2.4. Monitoring the Treatment and Patient Well-being (Standard 4)

In more than three quarters of the study subjects (347, 92.8%) both clinical and behavioral improvement was recorded. For 296 (79.1%) subjects a note of the *side effects of treatment including overlap between certain side effects and clinical features of schizophrenia and impact on functioning* was made. A subset of our study population comprising 127 subjects suffered from a movement disorder. In a total of 104 (81.9%) subjects a documentation of the emergence of such disorder was made.

Overall physical health and patient well-being was recorded in a significant number of our study subjects (310, 82.9%).

A number of physical and biochemical parameters were not routinely monitored and measured in accordance with the NICE guidelines. These include physical parameters (weight, waist circumference), vitals (heart rate, blood pressure), biochemical investigations (HbA1c, fasting blood sugar, lipid profile).

4. Discussion

According to Cohn et al, there are two over all goals of monitoring: 'Identification of treatable pathology in a high risk population and tracking and linking of metabolic disturbance in relation to antipsychotic medications'. [21]

Although for general population there are recommendations for monitoring and screening of diabetes, dyslipidemia and hypertension. Such monitoring is unfortunately lacking in people with mental illness. In a Catie

trial, metabolic syndrome was highly prevalent with approximately half of the population suffering from dyslipidemia, one third had hypertension and less than a quarter had diabetes. Unfortunately, more than half of the population diagnosed with the medical conditions mentioned above did not receive and further treatment. [22]

A meta-analysis of 48 studies (mainly in US and UK) was conducted in 2012 to look at the level compliance of metabolic screening and monitoring in patients treated with antipsychotic medications. Overall, the baseline screening tests were less than adequate and a significant number of investigations were not done. Blood pressure (BP) was monitored in 69.8%, Cholesterol in 41.5%, Glucose in 44.3%, weight in 47.9% and lipids in less than 25% of the patients before guideline implementation. [23]

For our study, we extracted common guidelines from NICE to measure our local practice with the standard. These guidelines are similar to ADA/APA consensus statement. [24]

Our study however revealed 100% compliance to BP and weight measurement. This observation can be explained in terms of the existence of a standard assessment form commonly used in psychiatry clinics and wards of AKUH, Karachi. Both of these parameters are included in the protocol, which explains the high level of adherence. It is noteworthy that another study found monitoring of BP and BMI higher than that of glucose and lipids and they also concluded that this could be because of part of routine clinical practice, monitoring BP, along with height and weight. [25]

As far as glucose and lipid were concerned, our study showed glucose monitoring of 26.5% and that of lipid was

11.8%. There was another study, which had similar results. [26, 27]

Another review article looked at seven studies that investigated the level of compliance of metabolic monitoring. Again the results were not promising with compliance level almost negligible. The only baseline investigations offered included lipids and glucose testing. [28, 29]

One thing that became highlighted in our study was the complete absence of waist circumference measurement. Other studies show that although this was monitored but rates were lower at 5.2% and 1.7%. This low rate indicates that doctors may not be aware of the importance of waist circumference as a strong independent predictor of cardiovascular disorder. [30] This appears to be the similar reason in our local circumstances too. This is an important component as people with mental illness are at risk of cardiac abnormalities due to genetic predisposition, environmental and life style factors and this risk is enhanced with atypical antipsychotics. (Hasnain *et al.*, 2008). [31, 32]

As far as recording ECG was concerned, although 40.7% had identifiable risk factor and 94.9% were admitted (both of which is a criteria to do an ECG), but only 31.6% had their ECG done. One of the other study also revealed poor recording of ECGs at baseline and following questioning clinical staff, the most common explanation was the lack of trained nurses and follow up of orders by the doctors. [33, 34]

Prolactin level measurement was also poorly performed (0.8%) in our study. Though this was the case in another study by (Prashar *et al.*). [34] They mentioned that it could be due to either due to less awareness regarding its risks and methods of screening for hyperprolactinaemia. This is important as because high levels of prolactin places the patients at higher risk of osteoporosis, menstrual irregularities and sexual dysfunction.

A similar observation across various articles above suggested that the compliance of metabolic monitoring is not sufficient. Our study reports similar results. In our subjects the highest level of monitoring and screening was reported in standard 1 of our screening instrument. In contrast, the lowest level was reported in standard 4. A possible reason is that in order to carry out the guidelines in standard 4 it is important to call the patient on a regular basis. This inevitably leads to more frequent visits to the psychiatry clinic and higher healthcare expenses.

It is important to interpret the findings from a patient's and a clinician's perspective. Our study represents patients of a developing country where socioeconomic instability has a negative impact on the overall lifestyle. A majority of individuals are unable to afford quality health services. Moreover, a significant proportion of Pakistan's population resides in rural areas with limited access to healthcare centers. So, even when tests are advised and offered, a number of patients are actually unable to utilize these services due to the issues highlighted above.

Also there is a belief that there is shortage of staff and lack of time, so little knowledge on emphasis of medical needs in

mental health settings can be a barrier. [35, 36]

However, we can't ignore the idea that clinician plays a significant role in ensuring optimal metabolic monitoring and treating possible complications in an efficient manner. This process requires the establishment of standard guidelines and protocols. Assessment forms need to be formulated.

The issue of responsibility remains the ongoing and long debate; psychiatrists or physicians. It may not be possible for Psychiatrists to carry out the tests themselves, but with prescription comes the responsibility so they should at least be able to delegate the tasks to physicians. In country, like Pakistan with huge stigma attached to mental health, visiting Psychiatry clinics is not considered a priority and rather a financial burden. In this situation there is a dire need of communication with the family/ general physicians to care out this very important monitoring and this role needs to be made specific as in one of the study, there was an uncertainty amongst clinician that whether this monitoring was the role of psychiatrists or general physicians. [37]

It is extremely important for the psychiatrists to be up to date with their medical knowledge. Although treatment of medical conditions does not always come under the realm of psychiatric practice. But still there is a need to adopt a proper method of monitoring these symptoms as metabolic side effects are common in people with mental health issues and antipsychotic medications can further contribute. It's important that patients should be assessed prior to initiation of antipsychotics. This can also serve as guide with regards to choice of antipsychotics.

In one of the studies, it was concluded that physicians trained in both family medicine and psychiatry had the highest rate of screening, followed by other medical specialties. Psychiatrists had the lowest rate of screening. [38, 39]

If we look overall, even with guidelines in place, clinicians fail to implement these. This carries a potential risk of overlooking serious health concerns and not addressing them on time. Moreover, there is a possibility of poor patient compliance to the medications. In other words, the treatment regimen is compromised. It is important to monitor and evaluate the implementation of guidelines once incorporated into the service.

In short, this study has both short and long term implications in patient care. These interim findings represent the first step, which defines the magnitude of the problem. At the same time, it provides a rationale and reasoning to the clinicians to work on creating standardized protocols. Lastly, it will be useful to carry out a periodic evaluation post implementation to identify and address the major obstacles.

5. Conclusion and Limitations

This study aimed to look at the level of compliance of metabolic monitoring in one of the tertiary care hospitals of Pakistan in accordance with NICE guidelines. There were some limitations of the study methodology. Firstly, the population sample is limited to one tertiary care hospital so it

limits the generalizability of the findings. Secondly, a larger sample size would have aided further in reporting important conclusive findings. Thirdly, it would be even more beneficial if a post implementation survey were carried out to compare the level of compliance before and after the establishment of standardized workable protocol.

To the best of our knowledge a study of this nature has not been conducted before in this region. We believe this study is an important first step and with these findings we have highlighted important concerns and made recommendations for inpatient clinical practice. We want to emphasize the dearth of metabolic monitoring in countries like Pakistan and the need to work pro-actively to improve and follow international guidelines. We do comprehend the risk of metabolic syndrome in psychiatric patients and it's the combination of factors that contribute including, iatrogenic effects of psychotropic medication, unhealthy life style, lack of medical care and genetic vulnerability. Further efforts should focus on improving physician implementation of the guidelines. As with increased use of atypical antipsychotics and the observed increase in the risk of metabolic disorders, it is crucial that metabolic parameters recommended by the guidelines are regularly monitored. Apart from physicians, patients should be educated in detail about the risks associated with their prescribed medications and the reasons for the recommended monitoring to ensure compliance post discharge.

Subsequently, a second part of this will be to carried out as a post implementation survey to measure and evaluate the level of compliance. This will not only reduce the risk of a number of possible complications secondary to antipsychotic medications, but will also improve patient adherence and compliance to the pharmacological treatment and monitoring.

Conflict of Interest

The authors declare that they have no competing interests.

References

- [1] Mehrul Hasnain WVRV. Clinical monitoring and management of the metabolic syndrome in patients receiving atypical antipsychotic medications.. Primary care Diabetes 3. 2009: 5-15.
- [2] Bozyski, K. M., Whitten, J. A., Blair, M. E. et al. Monitoring and Treating Metabolic Abnormalities in Patients with Early Psychosis Initiated on Antipsychotic Medications. Community Ment Health J (2018) 54: 717. <https://doi.org/10.1007/s10597-017-0203-y>
- [3] Priyanthi B. Gjerde et al. Increase in serum HDL level is associated with less negative symptoms after one year of antipsychotic treatment in first-episode psychosis. Schizophrenia Research. 2018; 197: 253-260.
- [4] Mary Coughlin et al. Enhancing metabolic monitoring for children and adolescents using second-generation antipsychotics. International Journal of Mental Health nursing. 2017; 27: 1188-1198.
- [5] Fanny Etchepare et al. Compliance of psychotropic drug prescription with clinical practice guidelines in older inpatients. Fundamental and Clinical Pharmacology. 2015; 30.
- [6] Lee Seng Esmond Seow. Metabolic syndrome and cardiovascular risk among institutionalized patients with schizophrenia receiving long term tertiary care. Comprehensive Psychiatry. 2017; 74: 196-203.
- [7] G. P Reynolds MJH, S. L. The 5-HT2C receptor and antipsychotic induced weight gain- mechanisms and genetics. J Psychopharmacology. 2006; 20: 15-8.
- [8] Roman Balōtšev. et al. Antipsychotic treatment is associated with inflammatory and metabolic biomarkers alterations among first-episode psychosis patients: A 7-month follow-up study. early intervention in Psychiatry. 2017; 13; 101-109.
- [9] Sarah Wakefield et al. Metabolic Monitoring of Child and Adolescent Patients on Atypical Antipsychotics by Psychiatrists and Primary Care Providers. American Journal of Therapeutics. 2019. DOI: 10.1097/MJT.0000000000000853.
- [10] Nasrallah H ME, J Meyer, Goff D, Davis S. Low rates of treatment for metabolic disorders in the CATIE schizophrenia trial at baseline: healthcare disparities in Schizophrenia. Neuropsychopharmacology. 2005; 165: 2631.
- [11] John APK, R.; Dragovic, M.; Lim, S. C.. Prevalence of metabolic syndrome among Australians with severe mental illness. The Medical journal of Australia. 2009; 190 (4): 176-9.
- [12] Narasimhan M RJ. Evidence-based perspective on metabolic syndrome and use of antipsychotics. Drug Benefit Trends. 2010; 22: 77-88.
- [13] Julie Kreyenbuhl et al. A Randomized Controlled Trial of a Patient-Centered Approach to Improve Screening for the Metabolic Side Effects of Antipsychotic Medications. Community Mental Health Journal. 2017; 53: 163-175.
- [14] J. Lee Pharm D Candidate et al. Persistence of metabolic monitoring for psychiatry inpatients treated with second-generation antipsychotics utilizing a computer-based intervention. Journal of clinical Pharmacy and therapeutics. 2016; 41: 209-213.
- [15] Jennifer L. Mc Laren et al. Monitoring of Patients on Second-Generation Antipsychotics: A National Survey of Child Psychiatrists. Psychiatric services. 2017. <https://doi.org/10.1176/appi.ps.201500553>
- [16] Barnes TRE PC, Cavanagh M-R, Hancock E, Taylor DM. A UK audit of screening for metabolic side effects of antipsychotics in community.. Schizophrenia Bull 2007; 33: 1397-403.
- [17] Andrew Thompson S, Mario Álvarez-Jiménez, et al. Targeted Intervention to Improve Monitoring of Antipsychotic-Induced Weight Gain and Metabolic Disturbance in First Episode Psychosis, Australian and New Zealand Journal of Psychiatry, 45 (9). 740 - 748. ISSN 0004-8674.
- [18] Morrato EH DB, Hartung DM et al. Metabolic testing rates in three states Medicaid programs after FDA warnings and ADA/ APA recommendations for second generation antipsychotic drugs. Arch Gen Psychiatry 2010; 67: 17-24.

- [19] Walter G DA, Soh N et al. Side effects of second generation antipsychotics: The experiences, views and monitoring practices of Australian child psychiatrists. *Australas Psychiatry* 2008; 16: 253-62.
- [20] Nice.org.uk/guidance/cg178/chapter/Recommendations.
- [21] Tony a Cohn MJS. Metabolic Monitoring for patients treated with antipsychotic medications. *Can J Psychiatry*. 2006; 51 (8).
- [22] Nasrullah HA. Atypical antipsychotics induced metabolic side effects: Insights from receptor- binding profiles. *Mol Psychiatry*. 2008; 13: 27-35.
- [23] Mitchell AJ DV, Vancampfort D, Correll CU, De Hert M. Guideline concordant monitoring of metabolic risk in people treated with antipsychotic medication: systematic review and meta-analysis of screening practices. *Psychol Med*. 2012; 42 (1): 125-47.
- [24] EH Morrato., Metabolic testing rates in 3 state Medicaid programs after FDA warnings and ADA/APA recommendations for second-generation antipsychotic drugs. *Archives of general*. 2010, DOI: 10.1001/archgenpsychiatry.2009.179.
- [25] Dhamane, Amol D., et al, Metabolic monitoring of patients prescribed second- generation antipsychotics,. *Journal of Psychiatric Practice®*: September 2013- Vol 19- Issue 5-p 360- 37. doi: 10.1097/01.pra.0000435035.45308.03.
- [26] Haupt DW, Rosenblatt LC, Kim E, et al. Prevalence and predictors of lipid and glucose monitoring in commercially insured patients treated with second-generation antipsychotic. *Psychiatry online*, 2009 <https://doi.org/10.1176/appi.ajp.2008.08030383>
- [27] L Pereira. Monitoring of Metabolic Adverse Effects Associated With Atypical Antipsychotics Use in an Outpatient Psychiatric Clinic. 2018, *Journal of Pharmacy*.
- [28] Young SL TM, Lawrie SM.. “First do no harm.” A systematic review of the prevalence and management of antipsychotic adverse effects.. *Psychopharmacology* 2014; 29 (4): 353-62.
- [29] Morrato EH et al., Prevalence of baseline serum glucose and lipid testing in users of second-generation antipsychotic drugs: a retrospective, population-based study of Medicaid claims data. *J Clin Psychiatry*. 2008 Feb; 69 (2): 316-22.
- [30] Alberto et all, The metabolic syndrome- a new worldwide definition. *The lancet*, volume 336, Issue 9491, September 24, 2005.
- [31] Brixner D, Said Q, Kirkness C, et al.. Assessment of cardiometabolic risk factors in a national primary care electronic health record database. *Value in Health*. 2007; 10: S29–36.
- [32] Daniel. E Casey. *Metabolic issues and cardiovascular disease in patients with psychiatric disorders*. The American Journal of Medicine Supplements. Volume 118, Supplement 2, April 2005, Pages 15-22.
- [33] Parashar Pravin Ramanuj et al., Improving blood and ECG monitoring among patients prescribed regular antipsychotic medications. *Ment Health Fam Med*. 2013 Jan; 10 (1): 29–36.
- [34] M Y H Moosa et al. ECG changes in patients on chronic psychotropic medication. Department of Neurosciences, University of the Witwatersrand, Johannesburg. Volume 12 No. 3 September 2006 – SAJP.
- [35] TA Cohn et al, Metabolic monitoring for patients treated with antipsychotic medications. *The Canadian Journal of Psychiatry*, 2006.
- [36] Jesjeet Singh Gill et al. Adherence to metabolic monitoring guidelines in atypical antipsychotic treated subjects: Do physician comply? *African Journal of Pharmacy and Pharmacology* Vol. 6 (1), pp. 13-16, 8 January 2012.
- [37] Thomas R. E Barnes et al., A UK Audit of Screening for the Metabolic Side Effects of Antipsychotics in Community Patients. *Schizophrenia Bulletin*, Volume 33, Issue 6, November 2007, Pages 139-1403, <https://doi.org/10.1093/schbul/sbm038>.
- [38] Charles Mosinger et al., Physician Patterns of Metabolic Screening for Patients Taking Atypical Antipsychotics: A Retrospective Database Study. *Prim Care Companion J Clin Psychiatry*. 2006; 8 (4): 220–223.
- [39] Paul Mackin et al., A prospective study of monitoring practices for metabolic disease in antipsychotic-treated community psychiatric patients. *BMC Psychiatry* 7, Article number: 28 (2007).
- [40] Ahsan Yaqoob Khan et al., To examine the extent of compliance to the proposed monitoring protocol among practicing psychiatrists for second generation antipsychotics. Department of Psychiatry & Behavioral Health, University of Kansas School of Medicine, Wichita, JPMA, Vol. 60, No. 6, June 2010.