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# A case report on atypical antipsychotic polypharmacy induced diabetic ketoacidosis (DKA): Need for a pharmacy care programme to improve medication related outcomes

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**Abstract**
The 1st line agents for the management of schizophrenia are the Second-Generation Antipsychotics (SGAs) due to the superior efficacy in comparison to First-Generation typical antipsychotics. Associated with metabolic disturbances. People with schizophrenia have an excess mortality, 2 to 3 times higher than the general population and is primarily associated with metabolic disturbances and poor adherence to the therapy. Diabetic ketoacidosis (DKA) is a rare, but potentially fatal hyperglycemic emergency from dysregulated acute glucose metabolism, which may be associated with the use of SGAs. We report a case of 63-year-old Females chizophrenic patient who presented with DKA along with metabolic abnormalities from antipsychotic poly-pharmacy.

**Keywords:** second generation antipsychotics, diabetic ketoacidosis, schizophrenia, non adherence

## Introduction
According to the American Psychiatric Association, Atypical Antipsychotics (AAPs) are the choice for first-line treatment of schizophrenia, than conventional agents as they cause less extrapyramidal side effects [1, 2]. Most SGAs are associated with significant weight gain and the development of glucose intolerance, thus causing diabetes mellitus, metabolic syndrome, and overall increased risk of cardiovascular diseases and related morbidity and mortality [3]. Individuals who have at least three of these risk factors have been described as having metabolic syndrome (MS) [4]. The mechanisms behind Atypical Anti Psychotics (AAP)-induced metabolic syndrome are complex and variable [5]. MS is relatively common with a prevalence varying from 6% to over 60% in people on long-term antipsychotictherapy [4]. Antipsychotic-induced hyperglycemic emergencies are rare (about 1-2 events per 1000 person per years of exposure) [2]. Increasing numbers of cases on comorbid illnesses like diabetes, ketoacidosis, hyperglycemia and lipid dys-regulation in patients taking second-generation (or atypical) antipsychotics have gradually raised concerns about a possible relation between these metabolic adverse problems and treatment with these medicines [6].

## Case report
### Presentation
A 63-year-old female patient on treatment for schizophrenia (for 2 years) attended the psychiatric OP department with complaints of violent behavior since 2 weeks. Patient's vitals where normal and was drowsy with Glasgow coma scale score of 9.
She was on Haloperidol 0.25 mg and Quetiapine 25 mg for past 2 years. She is onAspirin, Clopidogrel, and Atorvastatin for CAD, Type II DM, Metoprolol and Ramipril for Mild LV dysfunction.
During her Laboratory investigations, an elevated level of fasting blood sugar of 449mg/dl (normal 70-110 mg/dl), positive sugar and ketone bodies (+++) in urine were observed. A pH 7.1 and $HCO_3^-$ level 9mEq/L (normal 23- 30 mEq/L) and $PCO_2$mEq/L (normal 35-45mmHg) from ABG analysis. Fasting lipid profile test results revealed elevated levels of Total cholesterol 260 mg/dl (normal <200 mg/dl) and Triglycerides 190mg/dl (normal <150 mg%). An elevated $HbA_1c$ level of 7.4 mg% indicated poor glucose management. Moreover, total leukocyte count was found to be 13, 640 cells/$mm^3$ (normal 5000-11000 cells/$mm^3$), differential leukocyte count with elevated polymorphs 87% (normal 40-60%) and decreased lymphocyte count 5% (normal 20-60%). Patient presented with decreased level of sodium 124mEq/L (normal 130-150 mEq/L). Patient was managed according to the DKA protocol with insulin therapy (NPH and insulin Isophane), and intravenous fluids (10%NS, dextrose).

## Discussion
In comparison to first-generation antipsychotics, atypical antipsychotics have better tolerability and a lowered risk of extrapyramidal side effects which are attributable to their increased popularity in recent years.[7] Schizophrenia patients have a 15-20 year shorter life expectancy compared to the general population [8]. The mortality gap is even worsening and is increased prevalence primarily related to burden of metabolic syndrome from antipsychotic therapy.[9] This of metabolic syndrome and obesity contributes to the lower life expectancy and increased mortality rates in schizophrenia.[10] Antipsychotic induced metabolic abnormalities include obesity, cardiovascular illnesses causing arterial hypertension from impaired lipid levels, hyperglycemia. Risperidone, Quetiapine, Amisulpride and Zotepine generally show low to moderate levels of mean weight gain and a modest risk of clinically significant increases in weight [11].
The use of SGAs is also associated with new onset of type 2 diabetes mellitus (T2DM), worsening of pre-existing T1DM or T2DM, and rare cases of diabetic ketoacidosis and hyperosmolar-hyperglycemic state [14]. Diabetic Ketoacidosis

(DKA) is a medical emergency with considerable mortality and morbidity characterized by hyperglycemia over 250 mg/dL, a bicarbonate level <18 mEq/L, and a pH <7.30, with ketonemia and ketonuria [12]. The incidence of diabetes presenting as DKA in schizophrenia has been calculated as 10-fold higher than the calculated risk for the general population [13]. Risk factors include male gender, middle age (45-50) years, obesity, positive family history of DM, polypharmacy from treatment resistance schizo-active disorder [14]. Our patient has a known complaint of pre-existing diabetes and poor compliance to glycemic control methods such as Insulin regimen, and diabetic diet. A better compliance to self-management strategies is a crucial factor of concern in pre-existing DM who are on antipsychotic therapy.

## Conclusion

India being a diabetes rich country, researches should be undertaken on the prevalence of diabetes in Indian population among patients exposed to antipsychotics. Adherence to pharmacological therapy is vital for the alleviation of DM complications. Metabolic side effects of antipsychotic therapy can further contribute to lack of adherence. Collaborated interventions such as pharmacist led counseling and self-care training should be initiated to improve glycemic control.

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