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# Exploring Neuroglycopenia: A Case Series from A Tertiary Care Hospital

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## ABSTRACT

Neuroglycopenia, is defined as neurological manifestations due to hypoglycemia, leading to neuronal injury, manifesting as, seizures, neurologic deficit, altered sensorium, coma or even death. It is easily and fully reversible on administration of Intravenous or oral glucose. It stems from diverse etiologies such as medication use, critical illness, hormonal deficiencies, tumors, and hyperinsulinemia.[1] Management involves identifying underlying causes, adjusting medications, and implementing dietary modifications to prevent hypoglycemic episodes. Prompt recognition and tailored interventions are crucial in mitigating neurological sequelae and optimizing patient outcomes in this complex condition. This abstract presents insights gleaned from case series, highlighting the diverse presentation and management approaches in clinical practice.

**Keywords**

Neuroglycopenia, Hypoglycemic encephalopathy, Hypoglycemic seizures

## INTRODUCTION

Brain is one of the few organs that depend solely on oxygen for energy and glucose as its primary metabolic substrate. Hence, hypoxia or hypoglycemia can lead to overproduction of intracellular adenosine triphosphate and in turn cell death / irreversible neuronal injury.[2] Manifestations of hypoglycemia can be categorized into Autonomic symptoms, such as tremulousness, anxiety, paresthesias, hunger, diaphoresis, light headedness and palpitations; and Neuroglycopenic symptoms, include fatigue, dizziness, fall risk in elderly, migraine headaches, focal neurologic deficits, seizures, cognitive

impairment, difficulty with speech and concentration, personality change, irritability, altered sensorium, coma and even death. Symptomatic episodes of hypoglycemia affecting nervous system is referred to as Neuroglycopenia. In this case series we study a set of patients with Neuroglycopenia.

The primary etiologies of Neuroglycopenia/ Hypoglycemia encompass [3]

1. Pharmacological Agents: Most commonly associated with type 1 diabetes mellitus, pharmacologically induced hypoglycemia often arises from medications like insulin secretagogues (e.g., Glyburide, Glipizide, Glimepiride, Repaglinide) or insulin itself. Other drugs implicated in hypoglycemia include alcohol, quinolones, quinine, beta blockers, Angiotensin converting enzyme-inhibitors.
2. Critical Illness: Conditions such as sepsis, chronic kidney disease, severe liver failure, and cardiac failure can precipitate hypoglycemia.
3. Hormonal Deficiencies: Deficits in cortisol, glucagon, and growth hormone can contribute to hypoglycemic episodes.
4. Non-Islet Cell Tumors
5. Endogenous Hyperinsulinism: Disorders affecting beta cells, insulinoma, autoimmune hypoglycemia, and other conditions can lead to hyperinsulinemia and subsequent hypoglycemia.
6. Accidental, Surreptitious, or Malicious Hypoglycemia.
7. Glycogen Storage Diseases- 0 to XI

**CASE PRESENTATION**

**CASE 1**: Mr. JT, an 82-year-old male, presented to the medical OPD with complaints of severe headache, poor appetite, fatigue, and blurred vision persisting for approximately two weeks. He had a past medical history of Type II Diabetes Mellitus of 26 years- HbA1c- 6, Systemic Hypertension and Dyslipidemia. At home, his recorded RBS values fluctuated between 80, 120, 180, and 70 mg/dL. He was on H.Mixtard 30-0-25 IU insulin regimen; and recently initiated on Glycomet2 by his GP for a better control. The patient self-discontinued GlycoMet 2 (Glymipride 2/Metformin 500) combination pill on own, due to his episodes of symptomatic hypoglycemia. A diagnosis of Hypoglycemic headache was made. He was advised lifestyle changes and the dosage of H.Mixtard was also reduced to 20-0-15 IU. On subsequent follow ups, he was asymptomatic and blood sugars and HbA1c was within normal range.

**CASE 2:** Mr. SMC, a 58-year-old male, presented to the ED with generalized seizures, followed by diminished responsiveness. There was repeated vomiting, chills, and generalized fatigue for two days prior to admission as reported by wife. He had a past history of Type II Diabetes Mellitus of 16 years- HbA1c- 5.6, Systemic Hypertension, Dyslipidemia, and a history of cerebrovascular accident in the past. He was self -medicating H Mixtard and OAD. Initial blood investigations revealed normal cell counts and inflammatory markers. Random Blood Sugar was recorded as 70 mg/dL in ED, Vitals were normal. A diagnosis of Hypoglycemic seizures was established. He was immediately administered intravenous glucose and observed in ICU. He also received symptomatic management with blood sugar monitoring. He recovered fully, his blood glucose levels stabilized, but renal parameters were deranged, his calculated GFR was 30 mL / min / 1.73m2. So, the dosage of Inj.H Actrapid was adjusted to 8-8-8 IU. He was

discharged after a thorough diabetic education. This case highlights the need for regular follow up of the diabetic subjects; that short acting insulins are safe, while long acting insulins should be used with caution, once a patient has long standing diabetes, has proteinuria, and his eGFR becomes < 60 mL/min /1.73m2.[4] In such cases there is higher chance for hypoglycemia.

**CASE 3**: Mr. AMS, a 71-year-old male, presented to the ED with complaints of unresponsiveness, hypothermia, and a fasting blood sugar of 24 mg/dL. He was not a diabetic on OAD as the previous cases. He had a known medical history of Systemic Hypertension, Dyslipidemia, and bipolar disorder, on treatment. Investigations revealed a very low serum cortisol and TSH levels. Subsequently a diagnosis of hypoglycemic encephalopathy secondary to decreased cortisol level due to hypo-pituitarism and Pituitary adenoma was made. The patient received replacement steroid therapy (Prednisolone) and thyroxin. His blood sugars normalized. Antipsychotic medications (T.Risperidone and T.Quitiapin) were withheld due to the risk of further hypoglycemic episodes. With symptomatic improvement, the patient was discharged with advice to plan for neurosurgery. This case highlights that, even when it is obvious that psychiatric drugs can produce hyper or hypoglycemic adverse events, the clinician must look for secondary causes of hypoglycemia; as Pituitary adenoma was the cause in this case.

**CASE 4**: Mrs. AD, a 78-year-old female, a widow, who stayed alone, was brought to the ED, exhibiting restlessness, profuse sweating, hand stiffness, decreased responsiveness, and frothing from the mouth. She had a history of Type II Diabetes Mellitus- since 22 years- HbA1c- 5.2, Systemic Hypertension, Parkinson's disease, and Chronic Kidney Disease, and was on self - medication of Inj.H Mixtard 40-0-40IU. Her random blood sugar on admission was measured as 46 mg/dL. A diagnosis of Hypoglycemic seizures induced by insulin was made. Symptomatic management was initiated, and insulin was withheld for 2 days. Prior to discharge the dosage of Inj.H Mixtard was reduced to 10-0-6 IU. With improvement in symptoms, the patient was discharged, with proper diet advice and education by a diabetic educator. This case emphasizes the need for connecting diabetic educators to the elderly for role of DSMES- “Diabetes Self- Management Education and Support,” frequent reminders and visits by / to health care personnel.

**CASE 5**: Mrs. LR, a 64-year-old female, presented to the ED with symptoms of irrelevant speech and recurrent vomiting. Her Random Blood Sugar was measured as 50 mg/dL. She had a medical history of Systemic Hypertension, Dyslipidemia, and Type II Diabetes Mellitus of 16 years HbA1c- 8.5. She had dysuria and fever with chills, and so GP had administered Ciprofloxacin 500 mg bd for Urinary Tract Infection. Within 2 days fever responded, however she started sweating profusely and became confused and disoriented. A diagnosis of Neuroglycopenia was established, intravenous 25% Dextrose solution was immediately administered and there was spontaneous remission of complaints. Admission for further evaluation was recommended, but the patient declined and opted for discharge against medical advice. Urine and blood samples were collected for cultures and ciprofloxacin was stopped. Inj. H.Mixtard dose was adjusted to 16-0-10IU from

25-0-20IU. Instructions were provided for timely meals and snacks at 10 am, 4 pm, and bedtime. This case highlights that caution should be used while prescribing quinolones in diabetic patients, due to the possibility of fatal hypoglycemia. Quinolones act by increased insulin release via blockade of ATP sensitive potassium channels in the beta cells of pancreas, and thus leads to hypoglycemia. [5]

**CASE 6**: Mr. VTG, a 76-year-old male, presented to the ED with symptoms resembling seizure activity, characterized by jerky movements of the upper limbs and up-rolling of the eyes lasting 2-3 minutes, followed by decreased responsiveness. The care takers complained of difficulty in feeding him, however his antidiabetic and other medications were given accurately. His blood sugar level was measured at 46 mg/dL. He had a medical history of Parkinson's disease with dementia, Type II Diabetes Mellitus of 28 years- HbA1c- 5.6, BPH, and Systemic Hypertension. Emergency Neurology consultation was obtained. The patient was diagnosed with Hypoglycemic Encephalopathy and received treatment with intravenous glucose, Inj. Levetiracetam along with other supportive measures. The neurologist diagnosed him to have a poor swallowing reflex and progression of Parkinsons disease and dementia, as compared to the previous visit. With symptomatic improvement, the patient was discharged on NG Tube feeding, oral anti diabetics were stopped, and dose of Inj.Glargine was reduced to 6 IU at night, along with other medications. This case highlights the importance of food intake prior to administration of antidiabetic medications, especially insulin. Advanced Parkinsons disease patients experience dysphagia, which can be mitigated by muscle strengthening exercises or by initiation of Nasogastric tube feeding and an adjustment of antidiabetic medication.

**CASE 7**: Mrs. VRCP, a 72-year-old female, arrived at the ED displaying decreased responsiveness, hypotension and symptoms resembling seizures. Her RBS was 55 mg/dL. She had Type II Diabetes Mellitus- of 18 years- HbA1c- 6.2, Systemic Hypertension, and Coronary Artery Disease with Triple Vessel Disease, on insulin, betablockers, statins, and dual anti-platelet agents. Prior to admission, she had fever, poor intake and vomiting of 5 days, due to urinary tract infection. A diagnosis of Neuroglycopenia was made, and she received intravenous glucose, IV antibiotics, IV fluids and symptomatic management. The dosage of Inj.Lantus and Inj.Actrapid was adjusted according to blood sugars during hospital stay. Upon achieving hemodynamic and glycemic stability, the patient was afebrile and subsequently discharged from the hospital. Infections lead to poor glycemic control and dehydration in diabetics. Vomiting may be a sign of Diabetic ketosis. Beta-Blockers lead to hypoglycemia unawareness, and should be used with caution in patients with long standing diabetes. Hence the need for DSMES in all diabetics.

**CASE 8:** Mrs.MR, a 61-year-old female, presented to the outpatient department (OPD) with complaints of headache, slurred speech, and increased fatigue. As home RBS was 42mg%, she received oral glucose management at home. In OPD, RBS was 52mg%. A diagnosis of Neuroglycopenia was made. Patient had a past medical history of Systemic Hypertension, Hypothyroidism, Dyslipidemia, and a previous stroke. She was a “newly detected Type 2 Diabetic”- HbA1c 8- and advised to take Glimepiride to 0.5 mg twice

daily, in addition to Metformin 500 mg twice daily, 2 weeks prior to presentation. Mrs. MR was instructed to regularly monitor her blood glucose levels using SMBG device. Despite this she presented as neuroglycopenia. She was admitted and given IV glucose and discharged with only life-style modification changes for her diabetes. This case highlights the need for the "stepwise approach" towards glycemic control. [6]

**CASE 9:** Mr. KGV, an 80-year-old male patient under palliative care, was brought to ED reporting poor oral intake, insomnia, muttering and abnormal behavior. He had Type II Diabetes Mellitus- of 32 years- HbA1c- 5.2, Parkinson's disease, Systemic Hypertension and Metastatic Prostatic malignancy. The GRBS on admission 50mg/dl. At home, the patient received oral glucose management. The patient was diagnosed to have an episode of Neuroglycopenia and given IV glucose in ED, and there was spontaneous remission of all complaints. Neurology and Psychiatry consults were taken and drugs were titrated. The dosage of Inj. FIASP was drastically reduced, and the relatives were counselled regarding nasogastric tube feeding. Additionally, Tab. Glucovita was prescribed for managing hypoglycemic episodes at home. In this case correction of hypoglycemia itself reverted the patient to normalcy.

**CASE 10**: Mr. MJ, a 74-year-old male, arrived at the ED reporting symptoms of intense headache, sweating, deviation of the angle of the mouth, right sided weakness, of few hours duration. GRBS- 58mg%. The patient had a medical history of Systemic Hypertension, Type II Diabetes Mellitus of 14 years- HbA1c- 5.4, BPH, and CKD. A diagnosis of Neuroglycopenia was established, intravenous 25% Dextrose solution was immediately administered, followed by continuous IV dextrose infusion; and there was spontaneous remission of all complaints. He was taking the oral hypoglycemic agent Linagliptin, which was advised to be discontinued, and advised only life style modification for glycemic control. Mr. MJ was discharged fit from the hospital with his other medications. This case highlights the fact that hypoglycemia and neuroglycopenia are great masqueraders, which mimic serious neurologic disease, however are completely reversed by quick bedside diagnosis and administration of glucose.

**DISCUSSION**

Neuroglycopenia, resulting from low brain glucose levels and manifesting as neurological symptoms, can have diverse origins; if undetected may last several years. Patients with Diabetes, including both type 1 and type 2, can present with symptoms of neuroglycopenia. Insulinoma, a pancreatic tumor overproducing insulin, can also cause neuroglycopenia, however is extremely rare.[7] Excessive insulin use, liver or kidney diseases disrupting glucose regulation, and endocrine disorders affecting insulin levels are additional contributors. Lifestyle factors such as alcohol misuse, malnutrition, and prolonged fasting can deplete glucose stores or impair liver function, resulting in neuroglycopenia. Genetic disorders impacting glucose metabolism, such as glycogen storage diseases, contribute to neuroglycopenia, however, these are rare inherited disorders. [8]

Diagnosing neuroglycopenia involves quick clinical assessment, medical history review, and bedside blood sugar testing. A detailed analysis after hospitalization, would include blood tests measuring glucose, insulin,

and C-peptide levels, HbA1c, eGFR and LFT. Glucose tolerance tests evaluate glucose response over time, while imaging studies like CT scans or MRI identify pancreatic tumors, renal or liver abnormalities. Accurate identification of underlying cause, guided tailored treatment and management strategies prevent neuroglycopenic episodes and minimize neurological complications.[9]

In this case series, we have noted that hypoglycemic seizures and altered sensorium were the predominant presentations of neuroglycopenia. Neuroglycopenia was commonly seen in patients with a history of long-standing Type II diabetes mellitus. Hypoglycemia Unawareness was seen in most diabetic patients presenting with neuroglycopenia, and all were elderly. One patient had a pituitary tumor as cause for neuroglycopenia. Neuroglycopenia can be secondary to decreased cortisol levels, this underscores the importance of identifying various etiologies contributing to neuroglycopenia. Random blood sugar measurement has been the primary diagnostic approach utilized in elderly patients arriving in ED with any neurologic complaint. A bedside RBS distinguishes neuroglycopenia from other neurological abnormalities, and the deficit dramatically responds within minutes, after administering intravenous glucose and / or oral glucose supplements. This vetoes the need for unnecessary neurologic imaging.

## CONCLUSION

In conclusion, it is evident that neuroglycopenia, an easily treatable condition, characterized by a spectrum of neurological symptoms, poses significant challenges in clinical practice. A high index of suspicion is particularly critical in the elderly population, [10] presenting in ED with vague somatic complaints or changes in behavior, which can easily be disregarded by families and the clinician alike. In our series, each case had unique clinical features, comorbidities, and management strategies, highlighting the complexity of diagnosing and treating hypoglycemic events. Despite variations in presentation, timely recognition and appropriate interventions, including adjustments in medication dosages, intravenous glucose administration, DSMES and symptomatic management, were crucial in achieving favorable outcomes. These cases underscore the importance of comprehensive patient assessment, interdisciplinary collaboration, and patient education in optimizing care for individuals at risk of neuroglycopenia. Moving forward, continued efforts in research and clinical practice are essential to enhance our understanding and management of this clinically significant condition.

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## ABBREVIATIONS

**OPD -** OUT PATIENT DEPARTMENT
**RBS -** RANDOM BLOOD SUGAR
**ED –** EMERGENCY DEPARTMENT
**BPH -** BENIGN PROSTATIC HYPERPLASIA
**SMBG-** SELF-MONITORING OF BLOOD GLUCOSE
**DSMES-** DIABETES SELF- MANAGEMENT EDUCATION AND SUPPORT

**GFR-** GLOMERULAR FILTRATION RATE

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