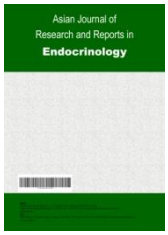

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Diabetes Insipidus: A Report of Three Cases in a Tertiary Health Facility in North Western Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Background: Diabetes Insipidus (DI) is a condition characterized by excessive thirst (polydipsia) and passage of a large volume of dilute urine (polyuria).
Methods: The report was a case study involving three subjects from the Federal Teaching Hospital Kastina, Nigeria. Subjects were aged 20, 21 and 10years. All presented with polydipsia and polyuria. A clinical assessment was done. Investigations include routine laboratory and radiological assessments, thyroid function tests, blood glucose, 24hrs urine quantification, water deprivation test, and brain MRI were done among others.
Results: Two cases had primary complaints of polydipsia and polyuria while one was secondary to head trauma. All preliminary routine investigations were essentially normal. 24-hour urine collection of 18.6 litres (134mOsmol/kg), 9.6 litres (292.6mOsm/kg) and 6.9 litres (250mOsmol/kg) were reported in cases 1,2 & 3 respectively. The urine deprivation test shows a less than 50% increase in urinary osmolality after administration of DDVAP in cases 1& 2, while the urinary osmolality values continued to increase throughout the test period in case 3.
Conclusion: Partial Central Diabetes Insipidus was diagnosed in the first and second cases and were managed with desmopressin nasal spray with significant improvements. However, the third

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case was referred to the paediatric mental health clinic where she also responded well to treatment.

Keywords: Diabetes Insipidus; polyuria; polydipsia; Katsina; Nigeria.

1. INTRODUCTION

Diabetes insipidus (DI) is a rare illness caused either by vasopressin deficiency (central diabetes insipidus) or by a lack of kidney sensitivity to vasopressin (nephrogenic diabetes insipidus) [1]. The prevalence of diabetes insipidus is 3 cases per 100,000 population with no sex predilection. Central diabetes insipidus is the result of damage to the supraoptic nuclei in the hypothalamus where vasopressin is secreted which usually leads to permanent DI [1–3].

It is a rare endocrine disorder in children and results from the destruction or degeneration of arginine vasopressin, (AVP) secreting neurons in the supraoptic and paraventricular nuclei of the hypo-thalamus or from impairment to the release or transport of AVP [4]. In rare cases, for example, when a patient suffers from either post-operative infundibulum hypothalamus damage or rear hypothalamus lobe damage, the disorder may be transient. Central diabetes insipidus is caused in most cases by hypothalamic tumors (craniopharyngiomas, invasive pituitary macroadenomas); hypothalamic-pituitary injury following trauma, post-operative condition or post-radiotherapy (RTH), empty sella syndrome [2,5]. Central diabetes insipidus may also be idiopathic, genetic, or immunologically in origin [6].

On the other hand, Nephrogenic diabetes insipidus is mainly caused by a genetic defect in the vasopressin receptors in the kidneys and occurs usually in males. Acquired forms of nephrogenic diabetes insipidus may be seen in chronic lithium therapy, chronic kidney disease, urinary tract obstruction, hypokalemia, or hypercalcemia [6]. The Symptoms of diabetes insipidus may include the following: excessive thirst (polydipsia), polyuria (passing >3-4 litres of urine a day), the passage of dilute urine, and nocturia. In addition, symptoms of the hypothalamic-pituitary tumour may occur [1,5,6].

Diagnosis is made by a two-stage water deprivation test; dehydration and vasopressin test. The dehydration test excludes the presence of psychogenic polydipsia while the vasopressin test differentiates central from nephrogenic diabetes insipidus as shown below in Table 1.

The treatment of diabetes insipidus depends on its cause. Central diabetes insipidus responds to desmopressin while nephrogenic DI treatment usually does not respond to desmopressin and treatment is based on the cause. Intravenous fluids, decreased dietary solute, and diuretics have been used to treat nephrogenic DI. Experimental approaches such as V2 receptor chaperones and V2 receptor bypass have also been used [1,6]. Though DI is a rare disease, it has been found in children and adult populations worldwide. In Nigeria, it has been reported in adults following burns and surgery [7]. Not much cases has been reported on DI in this area, therefore this study presented three cases DI in Federal Teaching Hospital Katsina, Northwestern Nigeria.

2. PRESENTATION OF CASES

2.1 Case 1

Patient IA is a 20-year-old man who was referred on account of excessive urination and excessive drinking of water for six months duration. The patient was apparently well until six months prior to presentation when he noticed excessive urination from 2-3 times in a day to 15-20 times and overnight urination from none to 7-9times at night. The patient also had excessive thirst which made him ingest large amount of water, initially from about 3-5litres to about 10-15 litres per day. He also complained of easy fatiguability. There was no history of urgency, hesitancy, dysuria, fever, weight loss, chronic cough, headache, vomiting, abdominal pain, no uremic symptoms, and no symptoms suggestive of thyroid dysfunction, blurred vision, photophobia, abnormal body movement or abnormal behavior. There was no history of trauma to the head, no radiation to the head region and was not on any medications before onset of symptoms. His symptoms affected his studies as he could not go to school anymore. Past medical history was not remarkable. He is not a known diabetic or sickle cell disease patient. He does not take alcohol, smoke cigarette or use illicit drugs. He is the second born of his mother and has 3 other siblings who are all males and all in good condition of health. Examination findings were essentially normal.

Table 1. Diagnostic criteria for DI using water deprivation and DDAVP as adapted from crook's [6]

Post-water restriction		Post-DDAVP	
Plasma osmolality (mmol/kg)	**Urine osmolality (mmol/kg)**	**Urine osmolality (mmol/kg)**	**Interpretation**
285-295	>750	>750	Normal
>295	<300	>750	Cranial DI
>295	<300	<300	Nephrogenic DI

DDAVP, 1-desamino-8-D-arginine vasopressin

Preliminary investigations**:** Fasting plasma glucose was 4.8mmol/l, and serum urea, electrolyte and creatinine were within reference limits. Corrected serum calcium was also within the reference limit. The result of urine microscopy culture and sensitivity yielded no growth of organism. Hemoglobin electrophoresis was AA. The thyroid function test was within the reference limit. Abdominal ultrasound scan and plain x-ray (KUB) of the abdomen were essentially normal.

Further evaluation observed 24-hour urine collection of 18.6 litres, random serum osmolality of 293mOsmol/ kg with a corresponding urine osmolality of 134mOsmol/kg.

With the above findings the following provisional diagnoses were made; Primary polydipisia, Central DI and Nephrogenic DI.

A water deprivation test was conducted using Fishberg concentration technique as shown in Table 2. Patient was admitted a day prior to the investigation. Patient was instructed not take anything after 10pm of the preceding night (overnight fasting) and collection of the samples started around 8:37am the following morning after full examination of the patient with the weight, height, BMI, blood pressure, respiratory rate and pulse rate. Urine was also collected and serum osmolality and urine osmolality were calculated every hour and after 3 consecutive samples collection, DDAVP 2mg was given intramuscularly and samples were collected hourly for another 3 hours. The result showed progressive increase in urinary osmolality (although less than 50% increase in serum osmolality).

The above findings were consistent with partial Central DI. Subsequently, a brain imaging (MRI) was done which showed the absence T1W posterior pituitary bright spot in keeping with Central DI.

A diagnosis of Central Diabetes Insipidus was made and he was placed on Intranasal Desmopressin spray. He responded tremendously well and has since resumed his academic activities.

Table 2. Result summary for case 1

Time	Na mmol/L	K mmol/L	Urea mmol/L	Glucose mmol/L	Osmolality mOsmol/kg
Plasma					
8:37am	141	4/1	1.8	4.1	298
9:37am	143	4.4	3.0	4.4	302
10:37am	144	5.0	2.8	4.3	305
11:37am	146	4.1	2.0	3.3	306
1:20pm	141	4.1	3.2	3.0	296
2:20pm	140	3.8	3.2	4.9	296
3:20pm	141	4.0	2.8	5.1	298
Urine					
8:37am	100	17	80	N/A	314
9:37am	196	37	97	N/A	563
10:37am	246	46	94	N/A	678
11:37am	242	48	96	N/A	676
1:20pm	354	89	179	N/A	1,063
2:20pm	367	86	230	N/A	1,136
3.20pm	318	70	265	N/A	1,037

NB: 2mg of DDAVP was given intramuscularly at 12:20pm

2.2 Case 2

Patient MA is a 21year old male undergraduate who was referred on account of excessive drinking of water and excessive urination of two months duration which followed shortly after a head injury. He had no seizures but lost consciousness for an hour with full regain of consciousness after the injury. Following the head injury, he noticed a drastic change in the amount of fluid he takes daily and overnight. He also noticed an increased frequency and volume of urine voided both during the day and at night. He had polyphagia and easy fatiguability. He had no early morning headaches, vomiting or seizures. He was unable to continue his academic activities as a result of this condition. He does not take alcohol, smoke cigarette or use illicit drugs. He is the fourth born of his mother. His other siblings are in good health condition and there is a positive family history of DM (his mother)

Examination findings were essentially normal.

An assessment of ? DI likely cranial was made.

Investigations include a bedside dipstick urinalysis which showed colourless urine with a pH of 6.5 and a S.G of 1.005 without glycosuria or proteinuria. Random plasma glucose was 5.2mmol/L. Serum electrolytes, urea and creatinine were all within the reference range. Serum Osmolality was 292.6mOsm/kg. Serum-corrected calcium was within the reference limit. Full blood count with differentials and ESR were within the reference ranges. Urine microscopy and culture showed no significant growth. Urine test for drug of abuse was negative

Abdominal ultrasonography findings were essentially normal.

A 24-hour urine collection was 9.6 liters, random serum osmolality was found to be 293mOmo/kg with corresponding urine osmolality of 292.6mOsm/kg

A water deprivation test was conducted using Fishberg concentration technique as shown in the table 3.

The observed results showed serum osmolality slightly above the upper limit of the reference interval at the beginning of the procedure. The values continued to rise with increasing dehydration induced by fluid deprivation. The corresponding urinary osmolality values before DDVAP administration were within the reference intervals but were all below 750mosmol/kg despite fluid deprivation. However, with subsequent administration of DDVAP, the urinary osmolality values appreciated to above 750mOsmol/kg (less than 50% increase) from the values before drug administration.

Brain Imaging and ADH assay could not be done due to financial constraints.

A Provisional diagnosis of Partial cranial diabetes insipidus was made. He was placed on intranasal vasopressin and improved significantly. He was able to return to school after 3months of treatment.

Table 3. Result summary for case 2

TIME	Na mmol/L	K mmol/L	Urea mmol/L	Glucose. mmol/L	Osmolality mOsmol/kg
Plasma					
8:21am	133	3.8	3.1	5.4	282.1
9:21am	140	3.8	1.8	5.4	294.8
10:21am	138	3.4	1.8	6.4	291
12:07pm	144	3.8	2.1	5.8	303.5
1:07pm	142	3.6	2.4	6.3	299.9
2:07pm	139	3.6	3.1	5.5	293.8
Urine					
8:37am	151	24	1.8	N/A	351.8
9:37am	246	23	51.6	N/A	589.6
10:37am	298	23	62.8	N/A	704.4
12:07pm	388	33.9	71.5	N/A	915.3
1:07pm	489	25.9	84.8	N/A	1,114.6
2:07pm	485	19	48.8	N/A	1,056.8

NB: 2ug of DDVAP was administered at 12:07 pm

2.3 Case 3

Patient SS is a ten-year-old female referred from the pediatric outpatient clinic with complaints of excessive intake of water and urination of two months duration. The onset of symptoms started with excessive intake of water which increased from about 2.5 litres to 9-12 litres per day and this usually disturbs her sleep. She also noticed excessive urination both during the day and at night. There was no history of body swelling, polyphagia, fever, chronic cough, weight loss, trauma to the head, seizures and use of nephrotoxic drugs or surgery prior to the onset of symptoms. There was also no history of hearing loss and visual disturbances Pregnancy, birth, neonatal and developmental histories were essentially uneventful. She is the fifth of seven children (3 males and 4 females) in a monogamous setting. Mother is a 38-year-old nurse and her father is a 42-year-old businessman with tertiary education. There was no history of similar symptoms in the parents, siblings or close relatives.

Examination findings were essentially normal. Her Random plasma glucose (RPG) was 6.1mmol/l, urinalysis showed a low specific gravity (S.G) of 1.005 while other parameters were normal. Serum electrolytes, urea and creatinine were within the reference range. Corrected serum calcium was 2.2mmol/l which was also within the reference range. Full blood count (FBC) and differentials were also within the reference range and her Erythrocyte sedimentation rate (ESR) was normal. Urine microscopy, culture and sensitivity showed no significant growth of organisms. Abdominal ultrasound showed normal findings, no renal calculi were reported. Radiograph of the skull showed normal skull vault, sutures and sella. No evidence of lucency and calcification.

24h urine collection was 6.9 litres, random serum Osmolality was 290mOsm/kg while the corresponding urinary osmolality was 250mOsmol/kg.

The following differential diagnosis was considered; Diabetes Insipidus and primary polydipsia.

A water deprivation test was conducted using Fishberg concentration technique as shown in Table 4.

The result showed serum osmolality within the reference range at the beginning of the procedure and all subsequent serum osmolality values remained below 300mOsmol/Kg, despite fluid restriction. The corresponding urinary osmolality values continued to increase throughout the test period. The third-hour urine osmolality was well above 750mOsmol/Kg.

The result was suggestive of Primary polydipsia and the patient was referred to the Psychiatrist for further review. She responded to psychotherapy and has no symptoms now.

3. DISCUSSION

Diabetes insipidus is a form of polyuric, polydipsic disorder which occurs mainly due to lesions of the neurohypophysis or the hypothalamic median eminence resulting in the deficiency of synthesis or release of AVP. It could also result from defect or destruction of AVP receptor on the ascending loops of the nephron which usually results in non–concentration of the water reaching the ascending loop of Henle and collecting duct [6]. The clinical manifestation of DI is variable, depending on the magnitude of neuronal affectation. Usually, about 80 to 90% damage of the magnocellular neurons will occur before symptoms of DI arise [8].

Table 4. Result summary of case 3

TIME	Na mmol/L	K mmol/L	Urea mmol/L	Glucose mmol/L	Osmolality mOsmol/kg
Plasma					
8:33am	137	3.9	2.5	5.0	289
9:33am	140	4.8	3.9	4.3	298
10:33am	139	3.9	3.5	4.0	293
Urine					
8:33am	106	47	40	N/A	346
9:33am	165	128	98	N/A	687
10:33am	283	228	101	N/A	1123

Polyuria occurs if a patient passes more than 3000mls of urine a day and it could be a symptom of numerous illnesses. In such a case, renal status must be assessed, since diuresis may result either from uraemia or the polyuric phase of acute renal failure. Moreover, hyperglycemia should also be excluded because glycosuria leads to osmotic diuresis. Polyuria also accompanies hypercalcaemia and psychogenic polydipsia. Lastly, polyuria may result from central diabetes insipidus or nephrogenic diabetes insipidus and this was the main presenting complaint in all three cases reported in this study.

Twenty-four-hour urinary volumes for the three patients were 18.6, 9.6 and 6.9 litres respectively. Other causes of polyuria were clinically excluded. There was a history of head injury in one of the patients but the cause of DI in the other patient with cranial diabetes insipidus was not clear. All the patient's histories were abrupt in nature and progressed gradually. The age range of the patient was between 10 years to 21years, this was different from Okpere et.al [5] who reported a case of 2 years and 6-month-old baby with central diabetes insipidus. Maghnie et.al [9] in Italy in a study of children with Central DI reported that the mean age at presentation was 6.4 years, 7.5 years and 14 years for the idiopathic, secondary form due to an intracranial tumor and the familial forms respectively.

The age at presentation varies depending on the underlying cause. Severe neonatal forms are rarely described in children. While hereditary Nephrogenic DI manifests in early infancy, often before the age of 1 week. The familial autosomal recessive form may manifest in infancy while due to developmental, defects of midline brain structure may present early [10].

For the first and second cases, partial Central DI was confirmed based on the absence of urine concentration on water deprivation followed by increased urine and serum osmolality following the administration of desmopressin. Both the first and second patients were managed with desmopressin nasal spray and they both improved significantly and were able to return to their normal day-to-day activities. The third case was referred to the paediatric mental health clinic and she improved tremendously.

The main limitation was the inability to perform brain imaging for the second patient due to financial constraints and we also couldn't conduct genetic studies on two of the patients due to a lack of appropriate facilities in this environment.

4. CONCLUSION

DI occurs among Nigerian patients who respond well to intranasal desmopressin. We recommend a high index of suspicion in children and young adult with polyuria and polydipsia as early recognition and accurate diagnosis is crucial to both safe and effective disease treatment.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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