# Diabetes Insipidus: An Unusual Cause of Urinary Frequency During Pregnancy

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Urinary frequency during pregnancy is common. The most common causes are compression of the urinary bladder by the gravid uterus, urinary tract infections, and hyperglycemia. Diabetes insipidus is an unusual cause of urinary frequency during pregnancy but should be considered when patients frequently void large volumes of urine. Diabetes insipidus can be a preexisting disease (clinically overt or subclinical) or can be associated with pregnancy as a result of excessive placental vasopressinase activity. We describe a case of diabetes insipidus that was not diagnosed until the postpartum period and review the pertinent literature.

## **Case Report:**

A 17-year-old woman was involved in a motor vehicle accident that resulted in closed-head trauma, intracerebral hemorrhage, and coma. At the same time she was found to be 16-weeks pregnant. Her mental status improved, and she underwent extensive rehabilitation. Her prenatal course was unremarkable, though she complained of polydipsia, polyuria, and nocturia. Her glucose tolerance test and urinalysis were both normal, and these symptoms were attributed to her pregnancy.

At 33 weeks' gestation the patient complained of nausea and vomiting. Her blood pressure was 150/ 100 mm Hg; she had right upper quadrant tenderness; and her platelet count was 22,000/ $\mu$ L, aspartate aminotransferase 420 U/L, and total bilirubin 1.4 mg/dL. A diagnosis of preeclampsia and possible HELLP syndrome was made, and labor was induced. She was given magnesium sulfate, and she received nothing by mouth but was given intravenous fluids at 125 mL/h. Labor progressed rapidly, and she gave birth to a 2540-g female infant.

During the next 24 hours she continued with intravenous magnesium and fluid restriction. Her liver function tests and platelet counts began to improve. Her urine output during labor and the postpartum period was 200 mL/h. Laboratory values 15 hours after delivery were sodium 167 mEq/L, potassium 3.6 mEq/L, chloride 134 mEq/L, and bicarbonate 30 mEq/L. Because a laboratory error was suspected, a second sodium determination was requested, which was 171 mEq/L. Her serum osmolality was 366 mOsm/kg, while her urine osmolality was 156 mOsm/kg. She was given 1-desmino-8D-arginine-vasopressin (DDAVP), and her osmolality returned to normal within 24 hours. Serum and urine osmolality determinations were repeated 3 weeks, 6, and 12 months later, which confirmed persistent diabetes insipidus. She did not undergo a formal water-deprivation challenge, and her anterior pituitary function and oxytocin levels remained normal.

## Discussion

We postulate that this patient had posttraumatic diabetes insipidus as a result of her closed-head injury. She had no symptoms predating her injury, and polyuria and polydipsia began after the injury. Traumatic diabetes insipidus has been associated with severe head trauma, as occurred in this patient.<sup>1,2</sup> The injury damages the axons of the pituitary stalk and impairs the transport and release of vasopressin from the posterior pituitary.<sup>3</sup> In a minority of cases there is spontaneous remission of the diabetes insipidus as axonal regeneration within the pituitary stalk occurs.<sup>1,2</sup> Because the anterior pituitary relies on a local endocrine system rather than a direct neural connection, most patients with traumatic diabetes insipidus have preserved anterior pituitary function. Although uncommon, the incidence of posttraumatic diabetes insipidus is well documented. In a series of 196 patients with longstanding central diabetes insipidus, the most common causes are idiopathic (25%) and head trauma

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#### Table 1. Causes of Long-Standing Central Diabetes Insipidus (n - 135).

34 24 20	25 18 15
24 20	18 15
20	15
20	15
12	9
11	8
7	5
5	4
1	1
1	1
	7 5 1 1

Modified, with permission, from: Moses AM Streeten, DH. Disorders of the neurohypophysis. In: Fauci AS, Braunwald E, Illelbacher KJ, et al, editors. Harrison's principles of internal medicine. 14th ed. New York: McGraw-Hill, 1998:2005;Table 330-1.

Note: long-standing refers to longer than 6-months or until death.

(18%) (Table 1).<sup>4</sup> Diabetes insipidus has been associated with postpartum pituitary necrosis (Sheehan syndrome), but this patient had no other peripartum complications, and her anterior pituitary function was intact.<sup>5</sup>

Our patient's thirst mechanisms were intact, and up until the time of delivery, she had free access to water. Under these circumstances it is possible to maintain normal water balance and normal electrolytes because free water losses are replaced. In this setting, distinguishing between diabetes insipidus and psychogenic polydipsia can be difficult. A supervised water-deprivation test and documented response to injected vasopressin will differentiate these conditions. This patient had an informal arater deprivation test when she did not have ready access to water during labor and the postpartim period. Her serum and urine osmolality and her response to vasopressin confirmed the diagnosis of diabetes insipidus (Figure 1).

During the prepartum period, our patient's symptoms were attributed to mechanical irritation of the urinary bladder by the gravid uterus. She had no evidence of gestational diabetes or urinary tract in section. Volume expansion and changes in water balance occur normally during pregnancy and can contribute to polydipsia and polyuria. The changes in were balance are the result of a lowered thirst threshold and a lowered threshold for vasopressin release. As a result, the osmostat is reset, and plasma osmolally decreases by 10 mOsm/kg during the first tringster.<sup>6,7</sup>

An uncommon cause of polyuria during pregnancy is transient diabetes insipidus. These wo conditions occur simultaneously in 2 to 6 of 100,000 pregnancies.<sup>8,9</sup> Transient diabetes inspidus of pregnancy results from increased circulating vasopressinase produced by the placenta. Although its physiologic function is unclear, vasopressinase increases throughout pregnancy. From the 4th to the 38th week there is a 1000-fold increased in vasopressinase activity.<sup>9-11</sup> As a result of increased vasopressinase activity, there are several manifestations of diabetes insipidus during pregnancy. Women with complete diabetes insipidus before en-





ception have normal fertility and can have normal pregnancies.<sup>12</sup> The increased vasopressinase activity usually results in increased vasopressin requirements during pregnancy. This change will be less apparent in women using the synthetic analogue of vasopressin, DDAVP, because substitutions in the synthetic molecule make it resistant to degradation by vasopressinase.<sup>10</sup> Patients with previously undiagnosed subclinical diabetes insipidus could become symptomatic during pregnancy because endogenous vasopressin is degraded by vasopressinase, creating a relative vasopressin deficiency.<sup>13,14</sup> Lastly, a small number of patients will develop transient diabetes insipidus during pregnancy solely on the basis of very high vasopressinase levels. Serum vasopressinase activity is proportional to the weight of the placenta. (In one case a patient was delivered of a placenta 2.5 times the appropriate weight for gestation.) Multiple pregnancies also show increased plasma vasopressinase activity.<sup>15</sup>

There appears to be a relation between preeclampsia and transient diabetes insipidus of pregnancy. In one recent report, all 17 cases of transient diabetes insipidus of pregnancy were associated with abnormal liver function tests; 13 of the 17 patients had hypertension, 13 had elevated uric acid levels, and 7 had proteinuria. Hepatic function decreases in preeclampsia, and this diminished function impairs vasopressinase clearance, resulting in decreased vasopressin levels and large-volume polyuria.<sup>16</sup> This syndrome is transient because vasopressinase levels fall dramatically once the placenta has been delivered. Levels fall approximately 25% per day and become undetectable by 4 weeks.<sup>10</sup> The synthetic vasopressin analog DDAVP, administered subcutaneously or intravenously, is the drug of choice for any form of diabetes insipidus during pregnancy. This syndrome can recur with subsequent pregnancies.<sup>11</sup>

We have described and discussed a case of posttraumatic diabetes insipidus that was overlooked during pregnancy but diagnosed and treated postpartum. This case illustrates that the diagnosis of diabetes insipidus can be difficult to make when the patient has intact thirst mechanisms and access to water. We hope that our case discussion will increase physicians' awareness of posttraumatic diabetes insipidus and broaden their differential diagnosis of urinary frequency to include the unusual diagnosis of transient diabetes insipidus of pregnancy.

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