# Transient Gestational Diabetes Insipidus: Case Report

## Gebelikte Geçici Diabetes İnsipidus

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Geliş Tarihi/*Received:* 05.05.2007
Kabul Tarihi/*Accepted:* 21.06.2007

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**ABSTRACT** Transient diabetes insipidus is an uncommon complication of pregnancy, usually manifesting with polydipsia and polyuria. This condition is considered as a result of excess placental vasopressinase activity and is managed with deamino-D-arginine vasopressin. A 34-year-old woman had an uncomplicated prenatal course until she was admitted to the hospital at 32 weeks of gestation with a one week history of severe polyuria, polydipsia (10-15 L daily), frequent urgency and nocturia. The clinical presentation and abnormalities were considered consistent with transient diabetes insipidus of pregnancy. The patient responded well to administered deamino-D arginine-vasopressin. In conclusion, intense thirst and polyuria in a patient in the third trimester of gestation should raise the suspicion of diabetes insipidus. Measurements of plasma osmolality and sodium, and urine osmolality should be warranted. When urine osmolality is less than serum osmolality, diabetes insipidus is probably present.

**Key Words:** Diabetes insipidus, pregnancy, polyuria

**ÖZET** Poliüri ve polidipsi semptomları ile ortaya çıkan geçici diabetes insipidus gebeliğin çok nadir görülen komplikasyonlarındandır. Plasental vasopresinaz aktivitesinin artmış olması sonucunda meydana geldiği düşünülür. Deamino-D-arginin-vasopresin verilmesi ile tedavi edilebilir. 34 yaşında, prenatal takipleri normal olan hasta, gebeliğinin 32'nci haftasında, yaklaşık bir hafta önce başlayan çok su içme (10-15 litre/gün), çok idrara gitme ve birkaç kez gece idrara çıkma şikayetleri ile kliniğimize başvurdu. Yapılan klinik incelemeler sonucunda gebeliğe bağlı geçici diabetes insipidus tanısı konuldu. Deamino-D-arginin-vasopresin tedavisi başlanan hasta, tedaviye olumlu yanıt verdi. Aşırı su içme ve çok sık idrara gitme şikayetleri ile gelen gebelerde geçici diabetes insipitus ayırıcı tanılar arasında düşünülmelidir. Bu tür hastalarda, plazma sodyum değeri ve osmolalitesi ve de idrar osmolalitesine bakılmalıdır. Elde edilen idrar osmolalitesi değeri serum osmolalite değerinden düşük ise diabetes insipidus tanısı düşünülmelidir.

**Anahtar Kelimeler:** Diabetes insipidus, gebelik, poliüri

**Turkiye Klinikleri J Gynecol Obst 2008, 18:130-133**

Diabetes insipidus (DI) is a disorder in which the abnormal secretion, degradation, or activity of vasopressin causes hypotonic polyuria, polydipsia, and dehydration. A rare complication in pregnancy, its incidence is about 1 per 300.000.[1] DI occurring during pregnancy is generally transient and resolved in the postpartum periods. DI can also be associated with Sheehan's syndrome, acute fatty liver and preeclampsia.[2]

We report a diabetes insipidus patient as a complication of pregnancy

## CASE REPORT

A 34-year-old woman (gravida 2, para 1, abortus 0) had an uncomplicated prenatal course until she was admitted to the hospital at 32 weeks of gestation with a one week history of severe polyuria, polydipsia (10-15 L daily), frequent urgency and nocturia. The patient had no family history of diabetes mellitus, and a normal 1-hour glucose challenge test at 28 weeks' gestation (107 mg/dL).

Her previous pregnancy was uncomplicated. Blood pressure was 110/80 mmHg, pulse 96 beats per minute and physical examination was unremarkable. Urine analysis revealed a specific gravity of 1.005, no protein or glucose, and no cells. Liver function study results and platelet count were normal. Her plasma osmolality was 316 mOsm/kg, while serum sodium and glucose levels were 156 mEq/l and 140 mg/dl respectively. Urine output was 360 ml/h, with an osmolality of 161 mOsm/kg. External and ultrasound examination revealed a normal-size fetus in cephalic position; the nonstress cardiotocogram showed no abnormalities.

Given her clinical condition, the patient was referred to the endocrinology department, which initiated study of the sudden onset of polyuria and polydipsia. The following diagnostic possibilities were considered; psychogenic polydipsia or diabetes insipidus. As gestational DI was suspected, the levels of vasopressin in plasma were also checked (ADH: 11.70 pg/mL; 1-27 pg/ml). The water deprivation test was not performed as it is not indicated during pregnancy. Treatment with deamino-D-arginine vasopressin intranasal 0.005/12 h, was started. She responded well to treatment, with a significant decrease in urine output and an increase in urine osmolality. The patient underwent cesarean section under general anesthesia because of she had a cesarean section on her first delivery. A 3875-g male infant was delivered, with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. In the immediate post-partum period several tests were performed to identify a possible (partial) central cause of the DI.

All clinical findings and abnormal laboratory data returned to normal within two weeks after delivery. Seven days after delivery the water deprivation test was performed and showed a normal increase in urine osmolality from 285 to 730 mosmol/kg, indicating that the DI had disappeared.

Given the clinical presentation of the patient, the results of the tests performed which were associated with 9.40 pg/ml and the spontaneous remittance of the symptoms at the end of the pregnancy, the diagnosis was transient gestational DI.

## DISCUSSION

The syndrome of diabetes insipidus is characterized by polyuria and polydipsia, associated with intense thirst due to the loss of concentrating ability by the kidney. This results in the rapid loss of water and increase in serum sodium. If the patient is conscious and has free access to water, the sensation of thirst often mitigates the rise in the serum osmolality and serum sodium, but the loss of water in urine is obligate. Four pathophysiologic mechanisms related to vasopressin produce large volumes of dilute urine and polydipsia, resulting from the following conditions; a) *Hypothalamic* (central or neurohypophyseal) *diabetes insipidus*, with inability to secrete and usually to synthesize vasopressin in the neurohypophyseal system; b) *Nephrogenic diabetes insipidus*, in which there is an inappropriate renal response to vasopressin; c) *Transient diabetes insipidus* of pregnancy, increased vasopressinase production by the placenta, or decreased breakdown by the liver, usually associated with pre-eclampsia or acute fatty liver; d) *Primary polydipsia*, in which the initial pathophysiology involves the ingestion of fluid rather than the excretion of fluid.[2]

In normal pregnancy, there are many hemodynamic, renal and electrolyte changes that occur during the first trimester. They reach their peak during the second trimester, remain relatively stable during the third trimester and rapidly reverse after delivery. Some of these changes include an

increase in cardiac output and glomerular filtration rate, sodium and water retention leading to blood volume expansion, decreases plasma osmolality.[3,4] There is a decline in the thirst threshold associated with enhanced vasopressinase secretion with reduced vasopressin secretory capacity increased degradation of vasopressin by placenta derived vasopressinase and a substantial increase in the placental clearance of vasopressin may be theoretical predisposing factors for pregnancy associated DI.[5-8] However, in view of the fact that the association of pregnancy with DI is rare (1 per 300.000). This rare incidence might be attributed in part to an increase in antidiuretic hormone (ADH) release to maintain sufficient antidiuretic activity during normal pregnancy. One possible explanation for GDI is the release of vasopressinases from the placenta, leading to an approximately four-fold increased rate of ADH catabolism.[1,2] Since vasopressinase is of placental origin, the clinical course should therefore be self-limiting once the placenta is removed.[1,2]

Barron et al first used the term "transient vasopressin-resistant diabetes insipidus of pregnancy" in 1984 to characterize 3 women with vasopressin-resistance diabetes insipidus that developed in late gestation and remitted postpartum. This term, therefore, excludes patients with central diabetes insipidus that preexisted pregnancy, and those with nephrogenic diabetes insipidus.[9] Transient central diabetes insipidus has been associated with acute fatty liver of pregnancy and eclampsia.[2] A link between transient DI during pregnancy and acute fatty liver associated with raised liver transaminase has been described. The patients with this condition are, in general, vasopressin-resistant and successfully treated with DDAVP, which is resistant to vasopressinase.[10]

Subclinical forms of central diabetes insipidus is another form of transient diabetes insipidus in pregnant women. In this form, water balance is normal when they are not pregnant, the underlying defect in the pituitary gland is unmasked when these women become pregnant. This is due to their inability to match the rate of vasopressin secretion to compensate the rate of degradation of the hormone. As expected, these patients were able to maintain urine-concentrating ability when treated with vasopressin and were not vasopressin resistant.[2,10]

Since patients with GDI usually present with polyuria and polydipsia, the urine should be tested for glucose to rule out glucosuria as the cause of polyuria. Initial evaluation for diabetes insipidus also includes evaluation for preeclampsia and HELLP (hemolysis, elevated liver enzymes and low platelets) syndrome as these entities may coexist. Many tests such as complete blood count, peripheral smear to look for evidence of hemolysis, coagulation studies, urine osmolality, serum electrolytes, serum osmolality, liver enzymes, serum creatinine, bilirubin, fibrinogen, calcium, total protein and uric acid can be performed.[4] In normal pregnancy, the level of serum osmolality is below 280 mOsm/kg and serum sodium is below 140 mEq/L. If the patient has rising serum osmolality with urine osmolality less than 280 mOsm/kg and inappropriately high urinary flow, the diagnosis of diabetes insipidus is established. If the patient has normal serum osmolality and inappropriately high urinary flow and urine osmolality less than 280 mOsm/kg, a water deprivation test could be carried out, but this test may lead to significant dehydration and is not recommended during pregnancy. The test can be used to establish the diagnosis in the postpartum period.[3]

The water deprivation test measures renal concentrating capacity in response to dehydration and is an indirect measurement of the AVP axis. It is usually followed by assessment of renal response to the synthetic AVP analogue DDAVP. Results may be interpreted as; urine osmolality less than 300 mosmol/kg after fluid deprivation and greater than 800 mosmol/kg after desmopressin suggests cranial diabetes insipidus, urine osmolality less than 300 mosmol/kg after fluid deprivation and less than 300 mosmol/kg after desmopressin suggests nephrogenic diabetes insipidus and urine osmolarity greater than 800 mosmol/kg after fluid deprivation and greater than 800 mosmol/kg after desmopressin suggests primary polydipsia.[11]

The treatment of choice for GDI is an early administration of intranasal desmopressin acetate (2-

20 mg of intranasally twice daily). In general, labor and parturition proceed normally, and patients have no trouble with lactation.[2]

In conclusion, intense thirst and polyuria in a patient in the third trimester of gestation should raise the suspicion of diabetes insipidus and warrant measurements of plasma osmolality and sodium, and urine osmolality. When urine osmolality is less than serum osmolality, diabetes insipidus is probably present.

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