

# Recognising and managing diabetes insipidus in pregnancy: a clinical challenge

## Reconhecimento e abordagem da diabetes insípida na gravidez: um desafio clínico

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### Abstract

Diabetes insipidus in pregnancy is an uncommon condition that requires a high index of suspicion due to the significant overlap with normal pregnancy physiological changes. It may have different causes, including a pre-existing disease unmasked by gestation or forms that develop *de novo* as pregnancy-related complications. We present a clinical case that illustrates the diagnostic and management challenges in this context, particularly when the clinical presentation mimicked the gestational form, but was ultimately found to have a different etiology.

**Keywords:** Diabetes insipidus; Pregnancy; Neurogenic diabetes insipidus; Gestational diabetes insipidus; Desmopressin.

### Resumo

A diabetes insípida na gravidez é uma condição rara que requer um elevado grau de suspeição, dada a sobreposição clínica com as adaptações fisiológicas maternas. Pode ter diversas causas, desde doenças pré-existentes descompensadas pela gravidez, até complicações específicas deste período. Apresentamos um caso clínico que ilustra os desafios diagnósticos e terapêuticos neste contexto, inicialmente interpretado como uma forma gestacional, mas que revelou posteriormente uma etiologia distinta.

**Palavras-chave:** Diabetes insípida; Gravidez; Diabetes insípida central; Diabetes insípida gestacional; Desmopressina.

### INTRODUCTION

Diabetes insipidus (DI) is a rare endocrine condition affecting about 1 per 25,000 individuals<sup>1</sup>. It is characterised by the inability to concentrate urine, due either to a deficiency of antidiuretic hormone (ADH) or renal resistance to its effects<sup>1-3</sup>.

Clinically, it manifests as polyuria (>3 L/day) and polydipsia, often presenting a challenge in differential diagnosis with the physiological changes of pregnancy<sup>4-6</sup>. In-

creased glomerular filtration rate and plasma volume, a lower threshold for thirst, and mild polyuria are expected adaptations during gestation<sup>7</sup>. These overlapping features may delay recognition and treatment, increasing the risk of adverse maternal and fetal outcomes. Since the water deprivation test is contraindicated in pregnancy due to the risk of dehydration, the diagnosis relies on clinical suspicion supported by plasma and urine osmolalities, as well as serum sodium levels<sup>3,8</sup>.

Although uncommon, DI identified during pregnancy may reflect the exacerbation or unmasking of pre-existing central or nephrogenic disease, or most

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often occur as a gestational form developing *de novo*<sup>9</sup>.

In central DI, there is deficient production or secretion of ADH resulting from damage to the hypothalamic-neurohypophyseal axis. The condition is often acquired, usually following head trauma or neurosurgical procedures, and less commonly associated with infiltrative lesions that impair posterior pituitary function<sup>1,3,10-11</sup>. In contrast, nephrogenic DI results from renal resistance to ADH, leading to an inability to concentrate urine despite normal hormone levels. It is typically secondary to kidney disease or medication use, though rare hereditary forms have been described<sup>1,3,11</sup>. Unlike these primary forms, a transient and pregnancy-specific type, known as gestational diabetes insipidus (GDI), may also occur. It usually develops in the late second or third trimester and can persist for a few weeks postpartum. This condition results from the degradation of ADH by vasopressinase, an enzyme produced by placental trophoblasts whose activity is proportional to the placental mass<sup>8-9,12</sup>. Since both neurogenic and gestational forms result from a deficiency of circulating ADH, they respond to treatment with desmopressin, a synthetic analogue resistant to vasopressinase degradation<sup>1,10,13</sup>.

Although GDI is the most frequently identified form during pregnancy, overlapping clinical features may obscure alternative diagnoses. We report a case of central DI first presenting in pregnancy, initially mistaken for the gestational form, underscoring the importance of diagnostic vigilance in such settings.

## CLINICAL CASE

A 32-year-old pregnant woman (G2P1) presented for a routine prenatal visit at 27 weeks and 5 days of gestation, after being diagnosed with gestational diabetes (fasting blood glucose of 99 mg/dL) at 17 weeks. The pregnancy had not been followed up until that point. Her personal medical history included class II obesity (BMI=35.5 kg/m<sup>2</sup>) and a childhood tonsillectomy. She denied alcohol consumption and smoking and was only taking prenatal vitamins. Her maternal grandparents had type 2 diabetes mellitus, but there was no family history of other endocrinopathies or liver disease.

Despite implementing dietary changes about a month earlier, her fasting glucose levels remained per-

sistently elevated, according to her self-monitoring records. In response, metformin was initiated at a maximum dose of 1500 mg/day.

At 30 weeks and 6 days, a third-trimester ultrasound revealed an estimated fetal weight at the 99.8<sup>th</sup> percentile with normal amniotic fluid volume.

Due to continued values above the target range, insulin glargine (26 units/day) was started at 32 weeks. During this period, she developed gestational hypertension, treated with methyldopa 250 mg, without meeting the criteria for preeclampsia.

An obstetric ultrasound performed at 35 weeks and 5 days estimated the fetal weight at 4127 g, remaining above the 99<sup>th</sup> percentile, consistent with suspected fetal macrosomia.

Due to poor metabolic and blood pressure control, the patient was electively admitted at 36 weeks. During hospitalisation, the patient was evaluated by the Endocrinology team. Postprandial glucose values remained mostly within the target range; however, given the persistence of elevated fasting glucose levels despite ongoing insulin therapy, the dose was increased to 28 units/day.

At this point, and considering the suspicion of fetal macrosomia, the overall clinical picture, and the suboptimal control of both glycemic and blood pressure levels, an elective cesarean section was scheduled for around 38 weeks of gestation.

At 37 weeks, the patient reported marked polydipsia (>6 L/day), characterised by intense and persistent thirst, particularly during nighttime, along with significant polyuria, confirmed by urine output exceeding 9 L over 24 hours.

There was no history of head trauma, febrile illness, skin rash, or respiratory symptoms.

Laboratory evaluation revealed mild hyponatremia (146 mEq/L), elevated serum osmolality (306 mOsm/kg) and low urine osmolality (116 mOsm/kg). Renal, hepatic and thyroid function, serum calcium, and other electrolytes were within normal limits. Proteinuria was also present, with a 24-hour urine protein of 0.9 g, meeting the diagnostic threshold for preeclampsia. No evidence of hemolysis or thrombocytopenia was observed.

Following recognition of the new symptoms and supporting biochemical findings, GDI was suspected and

the Endocrinology team reassessed the patient. As the cesarean section was already imminent, their recommendations included liberal water intake until 2 hours before surgery, proceeding as close as possible to the scheduled time, intravenous fluid therapy and close monitoring of serum sodium levels and fluid balance.

Although desmopressin therapy was considered, it was not initiated due to the proximity of surgery and the expected resolution of symptoms following delivery.

The cesarean section was performed without complications. A male newborn was delivered, weighing 4150 g, with Apgar scores of 9/10/10 at 1, 5, and 10 minutes, respectively.

During the postoperative period, the patient reported progressive relief of thirst, with a marked decrease in fluid intake (3 L/day), and diuresis (2.5 L/day). Bloodwork showed normalisation of serum sodium levels (140 mEq/L), supporting the probable diagnosis of a pregnancy-related condition.

She was discharged on postoperative day 4, clinically stable and without pharmacological therapy. Out-patient Endocrinology follow-up was arranged, with recommendations to maintain a daily record of fluid intake and diuresis.

Two weeks postpartum, the patient reported recurrence of symptoms, with daily water consumption of 6–10 litres, associated with polyuria and nocturia. She denied hypotension, visual disturbances, headaches, nausea, vomiting or dizziness. Laboratory tests revealed a normal electrolyte profile (serum sodium 143 mEq/L) and preserved renal function. Evaluation of anterior pituitary function (ACTH, morning cortisol, GH, IGF-1, prolactin, thyroid panel) and an urgent pituitary MRI were scheduled, both of which proved unremarkable. Desmopressin was initiated in the evening as a single dose; however, given only partial improvement of nocturnal symptoms, the regimen was subsequently adjusted to two administrations per day.

At the most recent follow-up, six months postpartum, the patient was asymptomatic, with complete resolution of polyuria and polydipsia and a notable improvement in quality of life. Biochemical parameters remained stable, and she continues on maintenance therapy with oral desmopressin, under regular evaluations in the Endocrinology Department.

## DISCUSSION

This case highlights the diagnostic and management challenges of DI in pregnancy, given the overlap between its symptoms and the physiological adaptations of gestation.

Although the patient first mentioned polydipsia and polyuria during hospitalisation, a detailed history revealed that these had been present since mid-pregnancy but had not previously been reported. This timing coincided with the progressive rise in placental vasopressinase levels, which typically increase throughout gestation<sup>4,7-8,12</sup>; however, in this case, the overlap was coincidental rather than causal.

The development of superimposed preeclampsia added complexity to the diagnostic process, as it can mimic and exacerbate GDI by altering vasopressinase metabolism<sup>4,6,8,12</sup>. Although the initial resolution of symptoms following placental expulsion supported a presumptive diagnosis of this transient form<sup>14</sup>, the recurrence of postpartum polyuria and polydipsia in the absence of hepatic dysfunction or other pregnancy-related factors, ultimately favored a central origin. The diagnosis was supported by biochemical findings, including hypernatremia, elevated serum osmolality, and inappropriately low urine osmolality<sup>7,15</sup>. The favorable clinical evolution after desmopressin therapy provided additional evidence for this interpretation, consistent with preserved renal responsiveness and impaired vasopressin release.

Hormonal evaluation confirmed normal pituitary function (with prolactin levels appropriate for the non-lactating postpartum state) and pituitary MRI demonstrated preservation of the neurohypophyseal T1-bright spot without structural abnormalities<sup>6,10</sup>. These findings, however, do not exclude central DI, as the condition may occur even in the presence of normal pituitary imaging.

The timing of clinical recognition, which occurred close to the scheduled cesarean section, significantly influenced the therapeutic approach. Although desmopressin remains the first-line treatment, it was not initiated due to the imminence of delivery and the expectation of symptom resolution following placental removal. Instead, a conservative strategy was adopted, including liberal oral intake, intravenous fluids, and

close monitoring of serum sodium and fluid balance<sup>14</sup>. Given that water homeostasis is tightly regulated by serum osmolality through thirst and ADH secretion, these supportive measures aimed to restore fluid balance and minimize complications<sup>9</sup>. This approach proved effective in the short term, with marked symptomatic improvement and biochemical normalisation.

This case reinforces the need to include DI in the differential diagnosis of apparently benign pregnancy symptoms. These are often considered physiological, however their persistence, especially when accompanied by biochemical abnormalities should prompt further investigation. Distinguishing the different types and underlying causes of DI can be challenging and requires careful integration of medical history, biochemical evaluation and imaging findings.

## REFERENCES

1. Flynn K, Hatfield J, Brown K, Vietor N, Hoang T. Central and nephrogenic diabetes insipidus: updates on diagnosis and management. *Front Endocrinol (Lausanne)*. 2025 Jan 8;15:1479764. doi: 10.3389/fendo.2024.1479764. PMID: 39845881; PMCID: PMC11750692.
2. Christ-Crain M, Winzeler B, Refardt J. Diagnosis and management of diabetes insipidus for the internist: an update. *J Intern Med*. 2021 Jul;290(1):73-87. doi: 10.1111/joim.13261. Epub 2021 Mar 13. PMID: 33713498.
3. Mutter CM, Smith T, Menze O, Zakharia M, Nguyen H. Diabetes Insipidus: Pathogenesis, Diagnosis, and Clinical Management. *Cureus*. 2021 Feb 23;13(2):e13523. doi: 10.7759/cureus.13523. PMID: 33786230; PMCID: PMC7996474
4. Goldrich A, Yuan J, Stohl H. Postpartum gestational diabetes insipidus related to preeclampsia: A case report. *Case Rep Womens Health*. 2023 Feb 14;37:e00487. doi: 10.1016/j.crwh.2023.e00487. PMID: 36852008; PMCID: PMC9958416.
5. Aleksandrov N, Audibert F, Bedard MJ, Mahone M, Goffinet F, Kadoch IJ. Gestational diabetes insipidus: a review of an underdiagnosed condition. *J Obstet Gynaecol Can*. 2010 Mar;32(3):225-31. doi: 10.1016/s1701-2163(16)34448-6. PMID: 20500966.
6. Kalelioglu, I., Kubat Uzum, A., Yildirim, A. et al. Transient gestational diabetes insipidus diagnosed in successive pregnancies: review of pathophysiology, diagnosis, treatment, and management of delivery. *Pituitary* 10, 87-93 (2007). <https://doi.org/10.1007/s11102-007-0006-1>
7. González MB, Silveiras EA, Pérez GR. Gestational diabetes insipidus. A systematic review of case reports. *J Perinat Med*. 2025 May 28;53(7):885-899. doi: 10.1515/jpm-2024-0499. PMID: 40440645.
8. Marques P, Gunawardana K, Grossman A. Transient diabetes insipidus in pregnancy. *Endocrinol Diabetes Metab Case Rep*. 2015;2015:150078. doi: 10.1530/EDM-15-0078. Epub 2015 Sep 23. PMID: 26524979; PMCID: PMC4626653.
9. Chanson P, Salenave S. Diabetes insipidus and pregnancy. *Ann Endocrinol (Paris)*. 2016 Jun;77(2):135-8. doi: 10.1016/j.ando.2016.04.005. Epub 2016 May 9. PMID: 27172867.
10. Tomkins M, Lawless S, Martin-Grace J, Sherlock M, Thompson CJ. Diagnosis and Management of Central Diabetes Insipidus in Adults. *J Clin Endocrinol Metab*. 2022 Sep 28;107(10):2701-2715. doi: 10.1210/clinem/dgac381. PMID: 35771962; PMCID: PMC9516129.
11. Quigley J, Shelton C, Issa B, Sripada S. Diabetes insipidus in pregnancy. *The Obstetrician & Gynaecologist* 2018;20:41-8. DOI:10.1111/tog.12450
12. Gambito R, Chan M, Sheta M, Ramirez-Arao P, Gurm H, Tunnel A, et al. Gestational Diabetes Insipidus Associated with HELLP Syndrome: A Case Report. *Case Rep Nephrol*. 2012;2012:640365. doi: 10.1155/2012/640365. Epub 2012 Jul 9. PMID: 24555139; PMCID: PMC3914197
13. Ananthakrishnan S. Diabetes insipidus in pregnancy: etiology, evaluation, and management. *Endocr Pract*. 2009 May-Jun;15(4):377-82. doi: 10.4158/EP09090.RA. PMID: 19454377.
14. Aragón-Charris J, Reyna-Villasmil E, De Nobrega-Correa H, Torres-Cepeda D. Diabetes insipidus induced by pregnancy. A case report. *Endocrinol Nutr*. 2013;60(2):105-106. doi:10.1016/j.endoen.2012.01.012.
15. El-Hennawy AS, Bassi T, Koradia N, Bocirnea A. Transient gestational diabetes insipidus: report of two cases and review of pathophysiology and treatment. *J Matern Fetal Neonatal Med*. 2003 Nov;14(5):349-52. doi: 10.1080/jmfm.14.5.349.352. PMID: 14986811.

## AUTHORS' CONTRIBUTIONS

Conception of the article (ARM), literature review (ARM, AM, MDC, ARC) and data acquisition (ARM, MDC, AM), patient care (ARM, ARC) e revising the article critically (MDC, AM, ARC, JPS). All authors approved the final submitted manuscript.

## CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for the publication of this case report.

## COMPETING INTERESTS

The authors declare that they have no competing interests.

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