

# Predictors of severe kidney disease in long-term lithium treatment

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i Hjärtats Aula, Sahlgrenska Universitetssjukhuset, Vita Stråket 12, Göteborg, den 15de maj 2024, klockan 13:00.

av Mihaela Golic

Fakultetsopponent:

Ursula Werneke, Docent, Institutet för klinisk vetenskap, Umeå Universitet, Umeå

## Avhandlingen baseras på följande delarbeten

- I. Golic M, Aiff H, Attman PO, Ramsauer B, Schön S, Svedlund J. Compliance with the safety guidelines for long-term lithium treatment in Sweden. J Psychopharmacol. 2018 Oct;32(10):1104-1109.
- II. Golic M, Aiff H, Attman PO, Ramsauer B, Schön S, Steingrimsson S, Svedlund J. Starting lithium in patients with compromised renal function - is it wise? J Psychopharmacol. 2021 Feb;35(2):190-197.
- III. Golic M, Aiff H, Attman PO, Ramsauer B, Schön S, Steingrimsson S, Svedlund J. The low risk for early renal damage during lithium treatment has not changed over time. J Psychopharmacol. 2023 Mar;37(3):318-324.
- IV. Golic M, Aiff H, Attman PO, Ramsauer B, Schön S, Steingrimsson S, Svedlund J. Lifetime risk of severe kidney disease in lithium-treated patients: a retrospective study. Int J Bipolar Disord. 2023 Dec 9;11(1):39. <https://doi.org/10.1186/s40345-023-00319-2>

**SAHLGRENKA AKADEMIN  
INSTITUTIONEN FÖR NEUROVETENSKAP OCH  
FYSIOLOGY**



# Predictors of severe kidney disease in long-term lithium treatment

**Mihaela Golic**

Sektionen för psykiatri och neurokemi, Institutionen för neurovetenskap och fysiologi, Sahlgrenska akademien, Göteborgs universitet, Sverige, 24.

## Abstract

The thesis aims to advance the understanding of severe chronic kidney disease in lithium-treated patients through four observational studies in which subjects were recruited from the Sahlgrenska University Hospital laboratory database.

The findings of **Paper I** revealed a gradual increase in adherence to lithium monitoring guidelines over 30 years, with mean lithium levels decreasing over time, within the recommended range. **Paper II** showed an almost sevenfold increased risk of severe chronic kidney disease in patients with moderately elevated serum creatinine, indicating pre-existent renal damage, prior to lithium initiation, compared to matched controls. **Paper III** indicated that a low (1%) risk of severe chronic kidney disease during the first ten years of lithium treatment remained unchanged over a time span of three decades. **Paper IV** highlighted age-dependent variations in the lifetime risk of severe chronic kidney disease, with the highest risk in patients starting lithium at age 65-74 years. Patients below 55 years of age at lithium start had negligible 10-year risk. Prolonged lithium exposure, especially over 20 years, was a significant risk factor.

The findings corroborate the notion that lithium treatment per se poses a certain risk of severe chronic kidney disease. While pretreatment renal impairment markedly elevates the risk, a normal serum creatinine level is associated with moderate excess risk and should not preclude lithium use in patients who could benefit from it. Key predictors of severe renal impairment include age, baseline creatinine and duration of lithium exposure, with no significant influence of sex.

**Keywords:** Lithium; Chronic Kidney Disease; Renal Insufficiency chronic; Guideline adherence

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