

## Genetski faktori rizika za razvoj posttransplantacijskog dijabetesa kod pacijenata nakon transplantacije bubrega

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KLJUČNE RIJEČI: dijabetes; faktori rizika; genetski polimorfizmi; transplantacija bubrega

UVOD: Posttransplantacijski dijabetes (PTDM) ozbiljna je komplikacija transplantacije bubrega i imunosupresivne terapije. Bolest izravno utječe na morbiditet, uzrokujući metaboličku neravnotežu, što pogoduje nastanku kardiovaskularnih bolesti, infekcija te povećanom riziku za kronično odbacivanje organa. Nove studije bave se istraživanjem genetske podloge ovog stanja s ciljem razvoja pouzdanih metoda probira. Stoga je cilj ovog istraživanja bio pronaći dosadašnje spoznaje o genetskoj podlozi PTDM-a.

MATERIJALI I METODE: Baza PubMed je bila pretražena koristeći ključne riječi „posttransplantacijski dijabetes“ i „genetski faktori“ u periodu od 2018. do 2023. Pretraga je pronašla 76 rezultata, od kojih su se razmotrile studije i analize pacijenata nakon transplantacije bubrega. Analizirano je 10 radova s ukupno 3702 PTDM pacijenta.

REZULTATI: Sistematskom analizom radova utvrđeni su geni u kojima određeni polimorfizmi jednog nukleotida predstavljaju statistički značajno povećanje prevalencije PTDM-a. Riječ je o genima uključenima u homeostazu glukoze te metabolizam imunosupresivnih lijekova. Navedeni geni su: *TCF7L2*, *SLC30A8*, *KCNQ1*, *IL-7R*, *MBL2*, *POR*, *ABCB1*, *CYP3A5*, *LEPR*, *CDKAL1* te *HNF1β*. Od odabranih 10 studija, 6 ih je uočilo povezanost između farmakogenomskog profila PTDM pacijenata na terapiji takrolimusom i PTDM-a. Povećani rizik je uočen kod pacijenata koji su vrlo slabi ili slabi metabolizatori lijeka, dok kod pacijenata s urednom metabolizacijom takrolimusa nije uočena veća prevalencija. Konačno, jedna studija istovjetno povezuje rizik od razvoja PTDM-a s terapijom ciklosporinom.

ZAKLJUČAK: Određene genetske varijante identificirane su kao faktori rizika za razvoj PTDM-a. Ovi rezultati ukazuju kako bi ciljano genetsko testiranje pacijenata s transplantiranim bubregom moglo biti vrijedno sredstvo u predviđanju ishoda i omogućiti personaliziraniji pristup posttransplantacijskom liječenju.

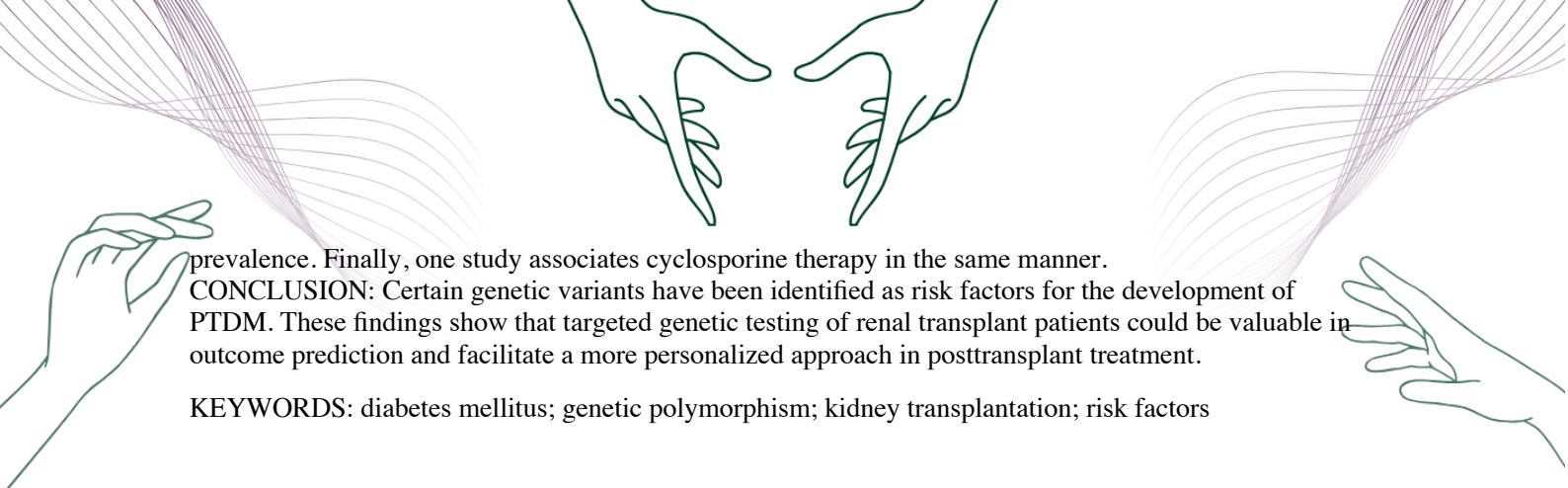
### Genetic risk factors for the development of posttransplant diabetes mellitus in renal transplant patients

INTRODUCTION: Posttransplant diabetes mellitus (PTDM) is a severe complication of renal transplantation and immunosuppressive therapy. Its onset is associated with increased morbidity due to metabolic disequilibrium, which facilitates the development of cardiovascular diseases, infections and chronic transplant rejection. Recent studies have investigated its genetic background to develop proper screening and the goal of this review is to present this currently available data.

MATERIALS AND METHODS: The PubMed database was searched using the keywords “posttransplant diabetes” and “genetic factors” in 2018.-2023. The search yielded 76 results, of which studies and analyses regarding renal transplant patients were selected. Ten papers were analyzed with a total of 3702 PTDM patients.

RESULTS: A systematic research analysis revealed genes in which certain single nucleotide polymorphisms lead to a statistically significant increase in PTDM prevalence. The genes are associated with glucose homeostasis and immunosuppressive drug metabolism, and are listed as follows: *TCF7L2*, *SLC30A8*, *KCNQ1*, *IL-7R*, *MBL2*, *POR*, *ABCB1*, *CYP3A5*, *LEPR*, *CDKAL1*, and *HNF1β*. Six studies observed a link between the pharmacogenetic profile of patients on tacrolimus therapy and PTDM. An increased risk was noted in very slow and slow metabolizers, while normal metabolizers had no greater



The top of the page features a stylized illustration. At the top center, two hands are shown with fingers slightly curled, as if holding something. From the left and right sides, several thin, purple, wavy lines flow towards the center, resembling genetic strands or data paths. Below these lines, on the left and right, are two more hands, one on each side, with fingers spread out.

prevalence. Finally, one study associates cyclosporine therapy in the same manner.

**CONCLUSION:** Certain genetic variants have been identified as risk factors for the development of PTDM. These findings show that targeted genetic testing of renal transplant patients could be valuable in outcome prediction and facilitate a more personalized approach in posttransplant treatment.

**KEYWORDS:** diabetes mellitus; genetic polymorphism; kidney transplantation; risk factors

