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Risk Factors for Congenital Anomalies of the Kidney and Urinary Tract: A Systematic Review and Meta-Analysis with Frequentist and Bayesian Approaches

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ADMINISTRATIVE INFORMATION

Support - No any financial support in this study.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 January 2026 and was last updated on 16 January 2026.

INTRODUCTION

Review question / Objective This review will identify potential novel risks beyond currently recognized factors and will validate the effects of established variables.

Primary Research Question: What will be the modifiable and non-modifiable maternal and neonatal risk factors associated with the development of CAKUTs?

Condition being studied This review will specifically target distinct anomalies including renal agenesis, renal dysplasia, renal hypoplasia, horseshoe kidney, vesicoureteral reflux, posterior urethral valves, ureteropelvic junction obstruction, and ureterovesical junction obstruction. The condition will be studied in the context of various maternal exposures (e.g., diabetes mellitus [Type 1, Type 2, gestational], hypertension, pre-eclampsia, RAG, uremia, and medications).

METHODS

Search strategy This systematic review and meta-analysis will be conducted in accordance with the Meta-Analyses of Observational Studies in Epidemiology (MOOSE) and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A systematic search of PubMed, EMBASE, and Scopus will be performed from database inception to September 2025.

Participant or population The study population will include pregnant women (maternal exposures) exposed to gestational and non-gestational diabetes (Type 1 and Type 2 diabetes, chronic and gestational hypertension), and specific exposures (smoking, alcohol consumption, and RASi use). Offspring: Neonates or infants will be assessed for the presence of Congenital Anomalies of the Kidney and Urinary Tract (CAKUT). Subgroups will include those with specific characteristics such as preterm birth, low birth weight, or small for gestational age.

Intervention Not applicable in this study.

Comparator Not applicable in this study.

Study designs to be included Case-control study or Cohort study.

Eligibility criteria Studies published in peer-reviewed journals that involve human participants will be considered, with no language restrictions to be applied. Eligible studies will be observational in design, including cohort and case-control studies, that will compare exposed and unexposed groups and will report effect estimates or provide sufficient information for calculating effect estimates. Exposure of interest will be maternal characteristics and/or exposures. Primary outcomes will be CAKUT.

Information sources The required information will be extracted from full texts of each study, using a prespecified extraction form adapted for this review. Extracted information will include study design, study setting and enrollment periods, sample size, population characteristics, exposure assessment methods, outcome definitions, statistical models, adjusted covariates, and effect estimates, as well as Newcastle-Ottawa Scale scores for quality appraisal.

Main outcome(s) The primary outcome will be the occurrence of Congenital Anomalies of the Kidney and Urinary Tract (CAKUT) in offspring. Outcomes will be defined based on International Classification of Diseases (ICD) codes, postnatal ultrasound findings, medical records, or surgical reports.

Quality assessment / Risk of bias analysis The quality of included studies will be evaluated using the Newcastle-Ottawa Scale (NOS) of appropriate version for cohort and case-control studies.

Strategy of data synthesis A meta-analysis will be conducted when at least two studies report on the same risk factor and outcome. We will employ a dual-framework approach integrating both frequentist and Bayesian methods to ensure robust estimation.

Subgroup analysis Subgroup analyses will be performed, restricted to high-quality studies (NOS > 6) and those providing adjusted ORs. Studies with high quality (NOS > 6) and those providing adjusted ORs will be analyzed separately.

Sensitivity analysis We will use Bayesians analysis and restrict studies in high-quality studies (NOS > 6) and those providing adjusted ORs for sensitivity analysis.

Country(ies) involved Taiwan.

Keywords CAKUT; congenital anomalies; diabetes; BMI.

Contributions of each author

Author 1 - Chih-Chia Chen - Data extraction and curation, Writing – original draft, Formal analysis.
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