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Diabetes during pregnancy and congenital genitourinary malformations: A systematic review and meta-analysis

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Congenital Abnormalities of the Kidney and the Urinary Tract (CAKUT) are responsible for up to 50% of paediatric chronic kidney disease cases. Diabetes is accepted as a risk factor for congenital abnormalities (CA) generally, but, evidence of diabetes as risk factor specifically for CAKUT is sparse. This systematic review aimed to understand the association between diabetes during pregnancy and CAKUT in the offspring, and to estimate the number of CAKUT cases in the general population that may be attributed to diabetic pregnancies.

CINAHL Plus, EMBASE, MEDLINE, PubMed, Popline databases and Cochrane library were searched from inception to April 12, 2017 with a thorough search strategy combining any form of diabetes and any form of CA. Articles were included if they were from peer reviewed journals, identified diabetes during pregnancy as a risk factor, and CA as an outcome. 6,962 articles were screened, and 26 studies were included in the review. Random effects meta-analysis was performed to estimate the association of offspring's CAKUT with the mother's pre-existing, gestational or any diabetes during pregnancy.

Included studies identified CAKUT at birth or shortly after birth, and varying case-definitions, leading to heterogeneity in study results. Overall, offspring born to mothers who suffered from any form of diabetes in pregnancy had a 50% increase in risk of having CAKUT compared to offspring of mothers without diabetes (RR 1.51; 95 CI: 1.36-1.67). Compared to offspring with non-diabetic mothers, offspring of mothers who had pre-existing diabetes had an almost two-fold rate of CAKUT (Rate Ratio (RR) 1.97; 95 CI 1.52 to 2.54). Offspring born to mothers with gestational diabetes compared to offspring of mothers with no diabetes had a smaller risk (RR 1.39; 95 CI:1.26 -1.55). Sensitivity analyses suggest that the results are robust to confounding from BMI. Population attributable risks for gestational diabetes were estimated to be 3.7% of cases of CAKUT in the USA, 4% of CAKUT cases in the UK, with up to 14.4% CAKUT cases in the South Asian population in the UK.

This systematic review and meta-analysis provides evidence of a potential link between diabetes during pregnancy and CAKUT. Finding suggests that up to 14% of CAKUT cases in some populations could be eliminated if gestational diabetes was prevented in pregnant women. It remains unknown whether later cases of CAKUT are linked to maternal diabetes. This study shows that there are implications for maternal care during pregnancy and supports enforcing policies targeting improvement of glycaemic control during early weeks of pregnancy, during foetal kidney development.