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The safety of isoniazid tuberculosis preventive treatment in pregnant and postpartum women: systematic review and meta-analysis

Yohhei Hamada ¹, Carmen Figueroa ², Mario Martín-Sánchez ³,
Dennis Falzon² and Avinash Kanchar²

Affiliations: ¹Research Institute of Tuberculosis, Japan Anti-tuberculosis Association, Tokyo, Japan. ²Global TB Program (GTB), World Health Organization, Geneva, Switzerland. ³Preventive Medicine and Public Health Training Unit, Parc de Salut Mar-Pompeu Fabra University-Agència de Salut Pública de Barcelona (PSMar-UPF-ASPB), Barcelona, Spain.

Correspondence: Yohhei Hamada, Research Institute of Tuberculosis, Japan Anti-tuberculosis Association, Matsuyama 3-1-24, Kiyose, Tokyo 204-8533, Japan. E-mail: yohei.hamada0@gmail.com



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Studies report conflicting links between isoniazid preventive therapy (IPT) and adverse pregnancy outcomes. Given known harms of active TB in pregnancy, the findings do not support systematic deferral of IPT until postpartum. We need more safety research. <http://bit.ly/2R0Wc3G>

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ABSTRACT

Background: The World Health Organization (WHO) recommends tuberculosis (TB) preventive treatment for high-risk groups. Isoniazid preventive therapy (IPT) has been used globally for this purpose for many years, including in pregnancy. This review assessed current knowledge about the safety of IPT in pregnancy.

Methods: We searched PubMed, Embase, CENTRAL, Global Health Library and HIV and TB-related conference abstracts, until May 15, 2019, for randomised controlled trials (RCTs) and non-randomised studies (NRS) where IPT was administered to pregnant women. Outcomes of interest were: 1) maternal outcomes, including permanent drug discontinuation due to adverse drug reactions, any grade 3 or 4 drug-related toxic effects, death from any cause and hepatotoxicity; and 2) pregnancy outcomes, including *in utero* fetal death, neonatal death or stillbirth, preterm delivery/prematurity, intrauterine growth restriction, low birth weight and congenital anomalies. Meta-analyses were conducted using a random-effects model.

Results: After screening 1342 citations, nine studies (of 34 to 51 942 participants) met inclusion criteria. We found an increased likelihood of hepatotoxicity among pregnant women given IPT (risk ratio 1.64, 95% CI 0.78–3.44) compared with no IPT exposure in one RCT. Four studies reported on pregnancy outcomes comparing IPT exposure to no exposure among pregnant women with HIV. In one RCT, adverse pregnancy outcomes were associated with IPT exposure during pregnancy (odds ratio (OR) 1.51, 95% CI 1.09–2.10), but three NRS showed a protective effect.

Conclusions: We found inconsistent associations between IPT and adverse pregnancy outcomes. Considering the grave consequences of active TB in pregnancy, current evidence does not support systematic deferral of IPT until postpartum. Research on safety is needed.