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Pregnancy outcome after rheumatologic methotrexate (MTX) treatment prior to or during early pregnancy: A prospective multicenter cohort study.

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Objective: High-dose methotrexate (MTX) exposure in pregnancy is associated with the MTX embryopathy. There is uncertainty about the teratogenic potential of rheumatologic doses of MTX. Methods: Pregnancy outcome of women on MTX (≤30mg/week) either in the post-conception period or within 12 weeks before conception was evaluated in a prospective observational multicenter cohort study. Pregnancy outcomes in the MTX group were compared to a group of disease-matched women and to a group of comparison women without autoimmune disease (non-AD), neither group exposed to MTX. Outcomes evaluated were spontaneous abortion, major birth defects, elective termination of pregnancy (ETOP), gestational age at delivery and birth weight. Results: The sample included 324 MTX-exposed pregnancies (188 post-conception, 136 pre-conception exposed), 459 disease-matched and 1,107 non-AD comparison women. In the post-conception cohort, the cumulative incidence of spontaneous abortion was 42.5% (95% CI 29.2-58.7), significantly higher than both comparison groups. The risk of major birth defects (7/106; 6.6%) was elevated compared to both the cohort of non-AD women (29/1,001; 2.9%; AOR 3.1; 95% CI 1.03-9.5) and the disease-matched cohort (14/393; 3.6%; AOR 1.8; 95% CI 0.6-5.7). No malformations were clearly consistent with the MTX embryopathy. Neither the cumulative incidence of spontaneous abortion (14.4%; 95% CI 8.0-25.3) nor the risk of major birth defects (4/114; 3.5%) was increased in the pre-conception cohort. Rates of ETOPs were increased in both MTX-exposed cohorts. There were no significant differences on other study endpoints. Conclusions: Post-conception use of rheumatologic doses of MTX was associated with an increased risk of major birth defects and spontaneous abortion. Such evidence was not found for pre-conception use.