

Czeizel AE et al. A population-based case-control study of oral griseofulvin treatment during pregnancy. *Acta Obstet Gynecol Scand* 83, 827-31, 2004

Type of study	Population-based case-control (Hungarian Case-Control Surveillance of Congenital Abnormalities-HCCSCA and Hungarian Congenital Abnormality Registry-HCAR)
Where	Hungary
When	1980-1996 (HCCSCA) and 1970-2002 (HCAR)
Cases	22,843 newborns or fetuses with congenital abnormalities (CAs) (HCCSCA). Cases with isolated CAs and multiple CAs of the HCCSCA were identified from the data set of the HCAR reported in the first 3 months after births or termination of pregnancies. These cases comprised 77% of the HCAR. Three mild CAs (such as congenital dislocation of the hip based on the Ortolani click, congenital inguinal hernia, and hemangiomas), minor variants (eg umbilical hernia), and CA syndromes of Mendelian and chromosomal origin were excluded. 55 conjoined twins (HCAR)
Case prevalence among the population	The total recorded prevalence of cases with CA diagnosed from the second trimester of pregnancy through to the age of one year was 35 per 1,000 informative offspring (liveborn infants, stillborn fetuses and malformed fetuses after elective termination of pregnancy). Approximately 90% of major CAs were reported to the Hungarian Congenital Abnormality Registry during the study period
Controls	38,151 newborns without any defects. Controls without CA were selected from the National Birth Registry of the Central Statistical Office, followed by 1-2 months of case notification. Two newborns were matched to every case according to sex, week of birth and district of parents' residence
Exposure definition	- Oral griseofulvin in the second and third months of pregnancy (in general the treatment was stopped after the diagnosis of pregnancy in the second, but mainly in the third month) - Most pregnant women used daily 500mg once/two parts - Duration of treatment: 3-8 weeks
Ascertainment of drug exposure	Exposure data were obtained from three different sources: - a structured questionnaire and a list of drugs and diseases mailed to the mothers immediately after the selection of cases and controls (information on pregnancy complications, maternal diseases and drugs and supplements during pregnancy according to gestational months and family history of CAs) - mothers were asked to send the antenatal care logbook and other medical records - regional nurses were asked to visit and question all non-respondents All conjoined twins were evaluated on the basis of surgical and/or autopsy records, their mothers visited at home, the data regarding drugs, maternal disorders, etc collected through a personal interview
Prevalence of exposure among controls	0.06%
Analysis	- Crude and adjusted OR and 95% CI were estimated (logistic regression to control for potential confounders: maternal age, birth order, employment status of mothers, acute maternal infectious diseases, chronic maternal diseases, other drugs) - Comparison of the expected and observed number of different CAs
Strengths	- Large, racially homogenous, population-based data set

	<ul style="list-style-type: none"> - Standardized answers (structured questionnaire, list of drugs and diseases) - Thorough search of exposure data - Good characterization of cases
Weaknesses	<ul style="list-style-type: none"> - Control infants with no birth defects (risk of recall bias) - Information available for a total of 96.3% cases, 82.6% controls: the response rate was somewhat lower in the controls than in the cases (risk of selection bias) - Active follow up for all non respondents in the case group, but only 200 families in the control group (risk of selection bias) - Despite the size of the population-based data set there were no cases or only a limited number of cases in some CA groups - The number of drug users was limited - The mean time between birth and return of the questionnaire was different in the two groups (1.6 vs 3.5 months)
Main results	<p>Data do not indicate a detectable teratogenic risk of oral griseofulvin treatment during pregnancy. There was no significant difference in any CA group, adjusted OR 1.1, 95%CI 0.2-6.4 for all CAs during the second and third months of pregnancy. Of 55 conjoined twins, no conjoined twins had mother with griseofulvin treatment during pregnancy. A higher mean birthweight was found in infants born to mother with griseofulvin treatment compared with the control infants</p>