

Clozapine Safety in Pregnancy – A Clinical Study

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BACKGROUND

Pregnant women with persistent schizophrenia and related disorders may require ongoing antipsychotic treatment, including clozapine. However, the potential risks of using clozapine during pregnancy and the postnatal period remain uncertain.

Our study was an analysis of a subset of data from our prospective cohort study (2005-2019), called the National Register of Antipsychotic Medication in Pregnancy (NRAMP) (ClinicalTrials.gov identifier NCT00686946).

METHOD

Study design: A nested case-control study using the National Register of Antipsychotic Medication in Pregnancy (NRAMP) database

Groups of interest: Women who took quetiapine (N= 53), clozapine (N= 14) or no antipsychotic medication (N = 24) for at least the first trimester of pregnancy

Primary outcomes:

- Pregnancy outcomes (live birth or miscarriages)
- Delivery mode (vaginal or caesarean)
- Gestational diabetes mellitus (GDM) status
- Weight gained

Secondary outcomes:

- Baby anomalies (fetal/neonatal respiratory distress)
- Gestational age at birth
- Birth weight
- Apgar scores
- Critical care/special care requirements

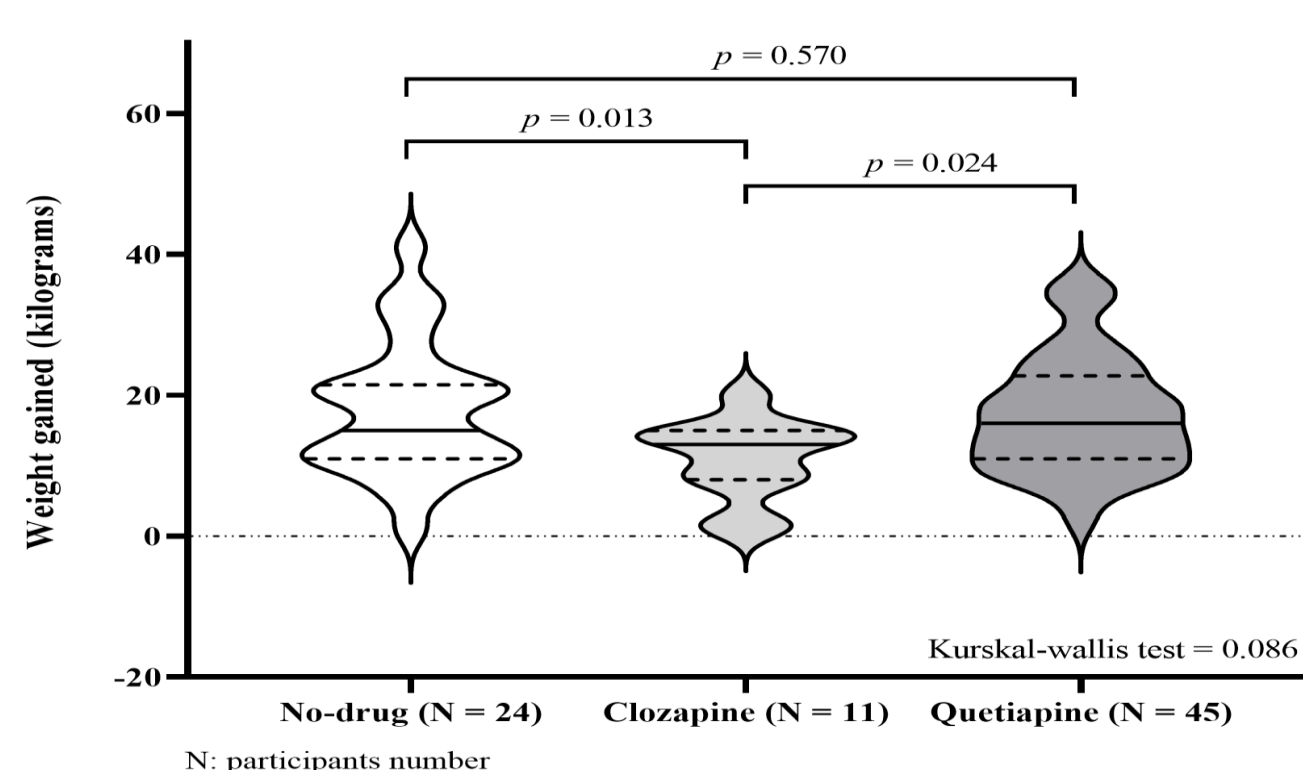
OBSTETRIC OUTCOMES

- Pregnancy outcomes (live birth vs miscarriage/stillbirth) were significantly different between clozapine-exposed vs no-drug ($p = 0.043$) and clozapine-exposed vs quetiapine-exposed groups ($p = 0.033$)
- Weight gained was significantly lower among clozapine vs quetiapine and no-drug groups
- Diagnosis of GDM was over 70% in the clozapine group, which was significantly higher than the no-drug group (8.3%) and the quetiapine group (23.9%)

Table 1. Obstetric outcomes of no-drug, clozapine and quetiapine

	No-drug (N = 24)	Clozapine (N = 14)	Quetiapine (N = 53)	p
Pregnancy outcome				Not applicable
Livebirth	24/24(100%)	11/14(78.6%)	47/48(97.9%)	
Miscarriage	0/24(0%)	3/14(21.4%)	1/48(2.1%)	
Delivery mode				0.194
Vaginal delivery	14/23(60.9%)	8/11(72.7%)	20/44(45.5%)	
Caesarean delivery	9/23(39.1%)	3/11(27.3%)	24/44(54.5%)	
GDM*				<0.001
Yes	2/24(8.3%)	8/11(72.7%)	11/46(23.9%)	

Figure 1. Comparison of weight gained from pre-pregnancy to baby delivery between no-drug, clozapine and quetiapine



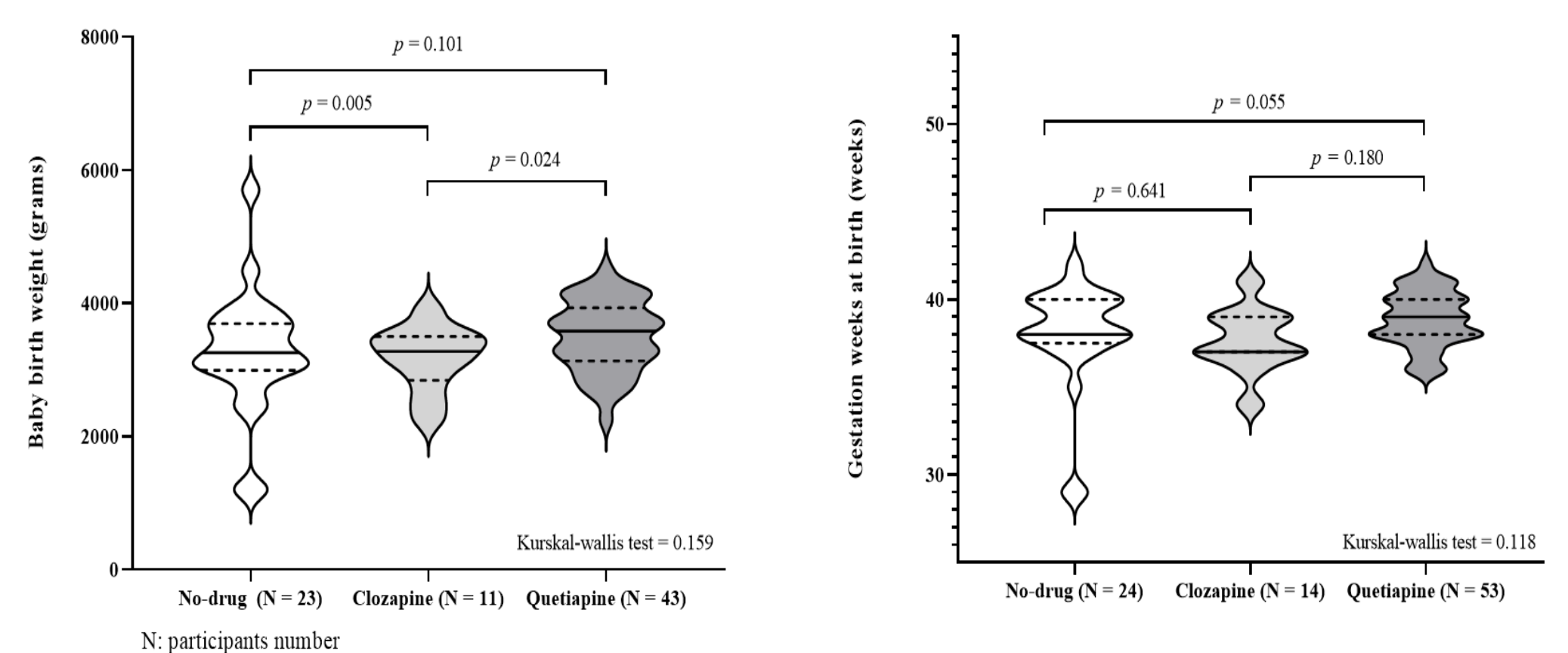
NEONATAL OUTCOMES

- Fetal/neonatal respiratory distress was higher among quetiapine (40.91%), followed by the clozapine group (27.3%), than the no-drug (0%)
- Gestation age appeared to be relatively similar between groups ranging from around 37-38 weeks without any significant differences
- The baby birth weight was significantly lower in the clozapine-exposed babies than in the other groups
- Birth weight was significantly higher in the quetiapine-exposed group compared to the clozapine-exposed group

Table 2. Neonatal outcomes of no-drug, clozapine and quetiapine

	No-drug (N=24)	Clozapine (N = 14)	Quetiapine (N = 53)	p
Fetal/neonatal respiratory distress				Not applicable
Yes	0/24(0%)	3/11(27.3%)	18/44(40.91%)	
Gestational age at birth (weeks, Mean \pm SD)	38.39 \pm 2.40	37.64 \pm 1.77	38.82 \pm 1.54 (N = 44)	0.118
Birth weight (grams, Mean \pm SD)	N = 23 3317.21 \pm 804.29	N = 11 3177.27 \pm 458.76	N = 43 3452.60 \pm 561.48	0.159
Apgar score (Mean \pm SD)	N = 21	N = 8	N = 40	
1 minute*	8.33 \pm 0.94	7.75 \pm 1.71	8.08 \pm 1.49	0.867
5 minute*	8.93 \pm 0.39	9.00 \pm 0	8.99 \pm 0	0.556
NICU/SCN admission				0.171
Yes	9/23(39.1%)	8/11(72.7%)	20/44(45.5%)	
No	14/23(60.9%)	3/11(27.3%)	24/44(54.5%)	

Figure 2. Comparison of baby birth weight and gestation weeks at birth between no-drug, clozapine and quetiapine



CONCLUSIONS

- This study is an important prospective, observational study to evaluate the pregnancy outcomes of a cohort of women specifically taking clozapine
- This study suggests that pregnant women taking clozapine and their babies have greater adverse outcomes compared to other groups
- Clozapine appears to be associated with a greater risk of miscarriages, maternal gestational diabetes and lower birth weight
- However, the gestational age, Apgar scores, and admission to NICU/SCN were comparable between all groups
- The risks and benefits of taking clozapine during pregnancy should be discussed with the woman and her nominated caregivers to promote a better understanding of the need for good antenatal care and excellent obstetric involvement in the birthing process