

# The Risk of Withdrawal Seizures & Other Adverse Events in Newborns Associated with Levetiracetam Use as Monotherapy or in Combination Therapy for Seizures During Pregnancy - A Systematic Review

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## Abstract

**Introduction:** Epilepsy is a neurological disorder that can affect pregnant women, and the use of anti-epileptic drugs during pregnancy must be carefully evaluated. This systematic review aims to assess the risk of withdrawal seizures and other adverse events in newborns when pregnant women with seizures are treated with levetiracetam compared to other treatments.

**Methods:** Multiple online scientific databases including PubMed, PubMed Central, Ovid MEDLINE, CINAHL, the Cochrane Central Register of Controlled Trials, Web of Knowledge, PsycINFO, and Scopus. The studies were chosen based on the developed inclusion and exclusion criteria. The quality of articles retrieved was assessed by the Robins I-tool for non-randomized trials and a standard Excel data extraction sheet was used to extract data from relevant studies.

**Results & Discussion:** Out of the 211 studies obtained from database searches and registers, only 11 met the inclusion criteria and were included in this systematic review. A total of 4726 patients were included in this systematic review. The studies were from different geographical regions and countries. The study found that AED polytherapy increased the risk of adverse pregnancy outcomes, including congenital malformations, intrauterine growth restriction, and preterm delivery, and recommended the use of AED monotherapy whenever possible to minimize these risks. Levetiracetam was found to be a safe alternative to other AEDs during pregnancy. The study also established the safety of AED use during lactation, but monitoring of AED levels is essential.

**Conclusion:** Levetiracetam and other AEDs as monotherapy treatment during pregnancy are generally safe and effective for women with epilepsy. AED polytherapy should be avoided, and treatment choices should be individualized to minimize adverse events.

**Keywords:** Epilepsy, Neurological disorder, AED monotherapy, Levetiracetam

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## Introduction

Epilepsy is a central nervous system disorder characterized by way of abnormally high electric impulses produced by neurons, resulting in involuntary body movements, abnormal behavior, loss of awareness, and altered memory [1]. Various factors can cause epilepsy, including cerebral stroke, brain tumors, head injuries, hypoxic damage, infections, metabolic diseases, storage diseases, hormonal imbalances, and substance abuse [2].

Anti-epileptic medications are available to control unusual impulses and prevent seizure episodes. However, some of these medications can have teratogenic effects on the fetus as they cross the placental barrier. In the 1990s, newer anti-epileptic drugs were discovered that were safer for use during pregnancy. One of these drugs is levetiracetam, a second-generation anti-epileptic drug that binds to the SV2A protein

found in the synaptic vesicles of neurons, preventing the release of neurotransmitters without affecting normal neurotransmission [3].

The use of anti-epileptic tablets during pregnancy is vital, as untreated seizures can damage the mom and the growing fetus. However, it's of paramount importance to weigh the benefits and risks of treatment, specifically when it comes to the protection of the fetus. Therefore, this systematic review aims to evaluate the risk of withdrawal seizures in newborns associated with using levetiracetam as monotherapy or in aggregate remedy for seizures at some point of pregnancy, compared to different anti-epileptic capsules or placebo. Given the potential teratogenic outcomes of some anti-epileptic drugs on the fetus, it's far crucial to evaluate the safety and efficacy of levetiracetam to be used at some stage in pregnancy to guide clinical exercise and improve maternal and fetal effects.



## Objective

To evaluate the risk of withdrawal seizures and other adverse events in newborns of pregnant women with seizures who are treated with levetiracetam as monotherapy or in combination therapy, compared to placebo or other antiepileptic drugs.

## PICO Research Question

- P: Pregnant women with seizures
- I: Levetiracetam monotherapy or combination therapy
- C: Placebo or other antiepileptic drugs
- O: Risk of withdrawal seizures in the newborn and other adverse Events

PICO question: In pregnant women with seizures does the use of levetiracetam as monotherapy or in combination therapy compared to placebo or other antiepileptic drugs, increase the risk of withdrawal seizures in the newborn? What will be the most appropriate topic for my systematic review?

## Methods

The guidelines in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) by [4] were followed. Our methodology and reporting were aligned with the standards established by this source to ensure consistency.

## Inclusion Criteria

- Studies reported on the use of levetiracetam in pregnant women with epilepsy.
- RCTs, cohort studies, observational studies, retrospective studies & studies & other original research published between 2013 & 2023.
- Studies reported on the use of levetiracetam either as monotherapy or in combination with other medications.
- Studies reported on the occurrence of withdrawal seizures in newborns & any other adverse reactions as a result of exposure to AEDs through the mother.
- Studies that used a comparison group (e.g., placebo, other antiepileptic medications, or no treatment).
- Studies published in English.

## Exclusion Criteria

- Studies that did not include pregnant women with seizures/epilepsy.
- Studies that did not use levetiracetam as a treatment.
- Studies that did not report on the occurrence of withdrawal seizures in newborns & other adverse reactions to AED exposure
- Studies that were not published in English.
- Studies that were not published in the research and documentation of this systematic review
- Secondary research was subject to a high degree of bias.

## Search Criteria

The search was conducted across multiple online databases including PubMed, PubMed Central, Embase, CINAHL, the Cochrane Central Register of Controlled Trials, Web of Knowledge, PsycINFO, and Scopus. Google Scholar was utilized as a search engine. The bibliographic databases, especially Medline and CENTRAL, were found to be highly valuable due to their millions of references with Medical Subject Headings (MeSH). The search string used across multiple databases included: ("Levetiracetam" OR "AEDs" OR "Antiepileptic drugs") AND ("pregnancy" OR "pregnant women" OR "maternal exposure" OR "antenatal exposure") AND ("seizures" OR "epilepsy" OR "convulsions") AND ("neonates" OR "newborns" OR "infants" OR "fetus")

## Quality assessment

Quality was assessed using the ROBINS-I tool for non-randomized studies as shown in Table 1.

## Data Extraction

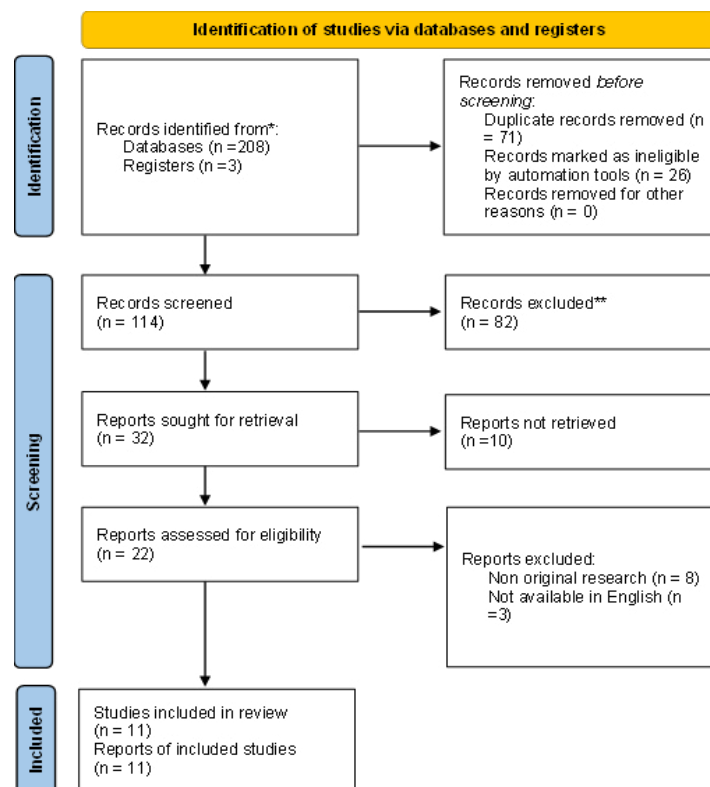
A standard data extraction form was used to extract relevant data from tables, including author and year of publication, study type, research design, number of participants, study aims, and population.

## Search Results

The database search and register search identified a total of 208 studies, out of which 71 duplicates and 26 publications published before 2013 were removed. After screening the abstracts, 82 studies were excluded, leaving 114 studies. Out of these, 32 studies were

**Table 1:** Quality assessment using ROBINS-I tool for non-randomized studies ranging from 2018 to 2022.

Year	Bias due to confounding	Bias in the selection of participants for the study	Bias in Classification of interventions	Bias due to deviation from intended interventions	Bias due to missing data	Bias due to measurements of outcomes	Bias in selection of reported result	Low/moderate/serious/critical
2022	Moderate	Low	Moderate	Low	Serious	Low	Low	Moderate
2022	Low	Moderate	Moderate	Moderate	Low	Moderate	Serious	Moderate
2018	Moderate	Moderate	Low	Moderate	Moderate	Low	Low	Moderate
2019	Low	Low	Low	Low	Low	Low	Low	Low
2013	Moderate	Serious	Low	Low	Moderate	Moderate	Serious	Moderate
2018	Low	Serious	Low	Serious	Low	Low	Moderate	Moderate
2022	Moderate	Low	Serious	Low	Low	Serious	Moderate	Moderate
2018	Low	Low	Low	Moderate	Serious	Moderate	Moderate	Moderate
2021	Moderate	Serious	Moderate	Moderate	Low	Low	Moderate	Moderate
2020	Low	Serious	Low	Moderate	Low	Moderate	Moderate	Moderate
2021	Low	Serious	Low	Moderate	Moderate	Moderate	Serious	Moderate



**Figure 1:** Prisma Flow Diagram.

selected for retrieval, but only 22 were retrieved. Among these, 8 studies were removed because they were non-original research, mainly consisting of case reports and literature reviews. Additionally, 3 studies were published in Russian without an English translation, and

hence removed. Finally, 11 studies met the inclusion criteria and were included in the systematic review.

## Results

The results are described in table 2.

**Table 2:** Showing results of the studies (n=11) included in the review.

Author & year	Study design	Study aims	Population	Country	Intervention	AEDs Used	Conclusion
(Shi et al., 2022) [5]	Observational study	to investigate the effect of antiepileptic drug (AED) polytherapy on pregnancy outcomes in women with epilepsy.	123 pregnancies	China	The study investigates the effects of AED polytherapy on pregnancy outcomes.	phenobarbital, topiramate, valproate, lamotrigine, and levetiracetam	The study showed that AED polytherapy in pregnant women with epilepsy increases the risk of adverse pregnancy outcomes, and recommends using AED monotherapy whenever possible to minimize risk. Prenatal exposure to phenobarbital and topiramate was associated with an increased risk of congenital malformations, while valproate, phenobarbital, and topiramate were correlated with adverse pregnancy outcomes. The combination of lamotrigine and levetiracetam had no adverse outcomes.
(Mari et al., 2022) [6]	Retrospective observational study	to compare the safety and efficacy of levetiracetam, lamotrigine, and carbamazepine monotherapy during pregnancy in women with epilepsy.	185 pregnancies	Italy	Monotherapy	levetiracetam, lamotrigine, and carbamazepine.	The study did not report any information on withdrawal seizures in newborns. However, the study did report that there were no significant differences in the frequency of major congenital malformations or neurodevelopmental disorders among the three groups, which suggests that the use of any of these three AEDs as monotherapy during pregnancy did not result in significant adverse effects on the newborns. The study concluded that all three AEDs, levetiracetam, lamotrigine, and carbamazepine, are effective and safe options for monotherapy during pregnancy in women with epilepsy. The choice of AED should be individualized based on the patient's clinical characteristics and preferences.



(Bansal et al., 2018) [7]	Retrospective observational study	To assess the safety and efficacy of levetiracetam use during pregnancy in women with epilepsy in a tertiary care center in Northern India.	46 pregnant women with epilepsy	Northern India.	Monotherapy or adjunctive therapy	Primary focus was on levetiracetam use during pregnancy.	Researchers did not report any significant differences in the incidence of congenital malformations, intrauterine growth restriction, preterm delivery, or neonatal complications among the study participants and concluded that levetiracetam use during pregnancy appears to be safe and effective for women with epilepsy. Although they recommended further large-scale studies to confirm these findings.
(Ae et al., 2019) [8]	Clinical Trial	Main aim was to assess the safety of levetiracetam use during pregnancy	982 pregnancies	Multiple countries (the Levetiracetam Pregnancy Registry is a multi-center international registry)	Monotherapy or adjunctive therapy.	levetiracetam	According to the results collected during the study, it was noted that the risk of major congenital malformations or developmental outcomes in infants did not increase upon exposure of a pregnant woman to levetiracetam. Prevalence of major congenital malformations was recorded to be 3.2%, similar to the general population. Researchers therefore concluded that levetiracetam use during pregnancy appeared to be safe for both the mother and the developing fetus.
(Mawhinney et al., 2013) [9]	Retrospective study	The study aimed to investigate the safety of levetiracetam use during pregnancy	566 pregnancies	The United Kingdom and Ireland	Monotherapy	levetiracetam	Based on the results collected, levetiracetam was not associated with increased risk of major congenital malformations or developmental delays in infants. In addition, there were no significant difference in birth weight, head circumference, or Apgar scores between infants exposed to levetiracetam Vs other AEDs. Researchers in this study concluded that levetiracetam use during pregnancy was safe and did not result in major complications in infants. The study suggests that levetiracetam may be a safe alternative to other antiepileptic drugs during pregnancy.
(Koc et al., 2018) [10]	Retrospective cohort study	To evaluate the fetal safety of levetiracetam use during pregnancy.	92 pregnancies	Turkey	Monotherapy or Polytherapy	Levetiracetam as monotherapy (n=113) & 36 women with other AEDs (lamotrigine, carbamazepine, valproate, or phenobarbital)	The study concluded that the use of levetiracetam monotherapy during pregnancy did not increase risk of congenital malformations when compared with the general population. Lower doses of levetiracetam were associated with a lower risk of major congenital malformations. the risk increased when it was used as a part of polytherapy
(Thomas et al., 2022) [11]	Prospective cohort study	To evaluate the differential impact of antenatal exposure to antiseizure medications (ASMs) on motor and mental development in infants of women with epilepsy (WWE)	149 infants born to WWE and 90 infants born to women without epilepsy (WWE-free)	France	Antenatal exposure to ASMs	The study included women who were taking either monotherapy or polytherapy with various ASMs, including valproate, lamotrigine, levetiracetam, carbamazepine, oxcarbazepine, and phenobarbital	Infants between 2 and 12 months were evaluated using the Ages and Stages Questionnaires (ASQ). The main outcomes being evaluated were motor and mental development. Results from this study showed that antenatal exposure to ASMs, especially valproate, was associated with a higher risk of delayed motor and mental development in infants of WWE compared to infants of WWE-free. The study also found that the risk of developmental delay was highest among infants exposed to polytherapy with valproate. The authors suggest that careful consideration should be given to the choice of ASMs during pregnancy to minimize the risk of adverse developmental outcomes in infants of WWE.
(Vajda et al., 2018) [12]	Retrospective observational study	To investigate the effects of antiepileptic drug (AED) polytherapy on pregnancy outcomes in pregnant women with epilepsy	1810 pregnancies	Australia	Antiepileptic drug polytherapy	lamotrigine and levetiracetam  valproate and topiramate	Polytherapy increased the risk of fetal malformations experientially in instance where valproate and topiramate were used in the drug combinations. Lamotrigine and levetiracetam offered the chance of seizure control and fetal safety. The study concluded that the use of AEDs during pregnancy had no negative impact on mother or infant except when valproate and topiramate combinations were used. Polytherapy-treated pregnancies were less often seizure-free than monotherapy-treated ones, but drug combinations with dissimilar and similar mechanisms of action achieved similar rates of seizure freedom during pregnancy



(Sharma et al., 2021) [13]	Retrospective study	To assess the efficacy and safety of levetiracetam monotherapy or polytherapy in pregnant women with active epilepsy	111 pregnant women	North Eastern India.	Monotherapy or polytherapy	Levetiracetam	The study found that the use of levetiracetam during pregnancy was associated with a lower risk of adverse pregnancy outcomes such as stillbirth, neonatal death, low birth weight, and preterm delivery. Researchers concluded that levetiracetam monotherapy or polytherapy was an effective and safe treatment option for pregnant women with active epilepsy.
(Birnbaum et al., 2020) [14]	Prospective cohort study	To assess the effect of antiepileptic drug exposure on the neurodevelopment of breastfed infants.	351 pregnancies	The USA	AEDs	carbamazepine, lamotrigine, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, topiramate, and valproic acid.	The results showed that AEDs used by pregnant and breastfeeding mothers was available in breastmilk and infant serum. There was however no significant difference in cognitive development and growth in infants who were exposed to AEDs in breastmilk and those who were not exposed. The researchers concluded that even though AEDs were safe to use during breastfeeding concentrations in breast milk and infant serum is necessary to ensure safety.
(Meador et al., 2021) [15]	Prospective cohort study	To evaluate the cognitive outcomes of children born to pregnant women with epilepsy who were exposed to antiepileptic drugs in utero.	311 mother-infant pairs	The USA	AEDs	carbamazepine, lamotrigine, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, topiramate, and valproic acid.	The results from this study showed that children born to pregnant women with epilepsy who were exposed to antiepileptic drugs in utero had lower cognitive scores compared to children of women without epilepsy. However, there was no significant difference in cognitive outcomes between children who were exposed to different types of antiepileptic drugs.

## Discussion

11 studies were included in this systematic review, the studies investigated the safety and efficacy of levetiracetam an antiepileptic drug (AED) uses during pregnancy with regards to the impact it has on newborn babies. The studies included women who were prescribed levetiracetam as either monotherapy or polytherapy. The results of this systematic review show that AED polytherapy increased the risk of adverse pregnancy outcomes including congenital malformations, intrauterine growth restriction, and preterm delivery. The study recommended AED monotherapy whenever possible to minimize these risks. However, levetiracetam was associated with lower rates of these adverse effects when used in monotherapy or polytherapy as opposed to when valproate and topiramate were used. The use of AED monotherapy during pregnancy appeared to be safe when and effective when levetiracetam, lamotrigine, and carbamazepine as monotherapy. No significant differences in the frequency of major congenital malformations or neurodevelopmental disorders among the three groups. Levetiracetam, in particular, was found to be safe and did not result in major complications in infants.

Results from the 4726 pregnancies indicate that the use of levetiracetam and other AEDs as monotherapy treatment during pregnancy is generally safe and effective for women with epilepsy. However, the choice of which AED to use should be individualized based on the patient's clinical history and presenting characteristics to minimize adverse events. AED use during lactation was also found to be safe, however, the levels of AEDs in breastmilk should be monitored. While polytherapy should be avoided to minimize adverse pregnancy outcomes, levetiracetam appears to be a safe alternative to other AEDs during pregnancy. Further research that includes large samples should be conducted to validate these findings. In addition, no studies reported on withdrawal seizures or the risk of withdrawal seizures in newborns. Research needs to be done that assesses this specific outcome when AEDs are used by pregnant women.

The findings of this systematic review are consistent with research done in this area, one meta-analysis by [16] aimed to compare the risk of congenital malformations and prenatal outcome of infants and

children exposed to AEDs in utero. The study included 58,461 patients from 96 studies and concluded that the newer AEDs (lamotrigine and levetiracetam) were associated with a significantly lesser risk of congenital malformations compared to the control group population. These AEDs were also associated with lesser cardiac malformations compared to the control. This research also reported that other AEDs such as ethosuximide, valproate, topiramate, phenobarbital, phenytoin, carbamazepine, and polytherapy were significantly more harmful than control. Researchers in this study keenly noted that even though infants exposed to lamotrigine and levetiracetam were less likely to experience the adverse reactions reported, it did not mean that these agents were not harmful to infants in utero and thus these treatments should be approached carefully. The study advocated for the switch from polytherapy to monotherapy and avoiding AEDs with recorded high-risk ratios such as valproate.

## Strengths

- The systematic review includes 11 research studies from different countries and regions worldwide, which offers enormous quantity of data for evaluation & covers the safety and efficacy of levetiracetam at some stage in being pregnant, which is a clinically critical subject matter for women with epilepsy.
- The review provides valuable information at the risks associated with AED polytherapy and recommends the use of AED monotherapy to limit these adverse outcomes & additionally provides evidence for the safety and effectiveness of levetiracetam, lamotrigine, and carbamazepine as monotherapy during pregnancy.
- The review includes information on AED use during lactation, which is a crucial consideration for postpartum care.

## Limitations

One major limitation of this systematic review is the failure to include studies that reported on the risk of withdrawal seizures in newborns, which is a significant gap in the literature. Other limitations are the use of majorly retrospective and cohort studies which present a lower level of evidence as opposed to the gold standard RCTs.





## Recommendations

Based on the above findings, this study presents the following implications:

- Healthcare providers should consider AED monotherapy as the first-line treatment option for pregnant women with epilepsy but the choice of which AED is prescribed to a patient should be individualized.
- Patients ought to be informed of the risks related to AED polytherapy and encouraged to discuss treatment options with their healthcare provider.
- Women who're prescribed AEDs in the course of pregnancy ought to be monitored closely for unfavorable effects and the levels of AEDs in their breastmilk.
- Further research needs to be carried out to evaluate the risk of withdrawal seizures in newborns when AEDs are used by pregnant women.

## Conclusion

The use of levetiracetam and other AEDs as monotherapy during pregnancy is generally safe and effective for women with epilepsy. AED polytherapy increased the risk of adverse pregnancy outcomes, and therefore, monotherapy should be the preferred treatment option whenever possible. Levetiracetam was associated with lower rates of adverse effects compared to valproate and topiramate when used as either monotherapy or polytherapy. The review also recommended individualized AED treatment choices based on patient characteristics and clinical history to minimize adverse events. The safety of AED use during lactation was also established, but monitoring of AED levels in breast milk is crucial. Finally, further research with larger samples is needed to validate these findings, and research should be conducted to assess the risk of withdrawal seizures in newborns when AEDs are used by pregnant women.

## References

1. Beghi E (2020) The epidemiology of epilepsy. *Neuroepidemiology* 54: 185–191. <https://doi.org/10.1159/000503831>
2. Annegers JF, Rocca WA, Hauser WA (1996) Causes of epilepsy: contributions of the Rochester epidemiology project. *Mayo Clin Proc* 71: 570–575. <https://doi.org/10.4065/71.6.570>
3. Kośmider K, Kamieniak M, Czuczwar SJ, Miziak B (2023) Second generation of antiepileptic drugs and oxidative stress. *Int J Mol Sci* 24: 3873. <https://doi.org/10.3390/ijms24043873>
4. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, et al. (2015) Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 350: g7647. <https://doi.org/10.1136/bmj.g7647>
5. Shi X, Wang Y, Zhang Y, Song C, Jiang Y, et al. (2022) Effects of antiepileptic drugs polytherapy on pregnancy outcomes in women with epilepsy: an observation study in northwest China. *Epilepsy Behav* 135: 108904. <https://doi.org/10.1016/j.yebeh.2022.108904>
6. Mari L, Placidi F, Romigi A, Tombini M, Del Bianco C, et al. (2022) Levetiracetam, lamotrigine and carbamazepine: which monotherapy during pregnancy? *Neurol Sci* 43: 1993–2001. <https://doi.org/10.1007/s10072-021-05542-2>
7. Bansal R, Suri V, Chopra S, Aggarwal N, Sikka P, et al. (2018) Levetiracetam use during pregnancy in women with epilepsy: preliminary observations from a tertiary care center in Northern India. *Indian J Pharmacol* 50: 39–43. [https://doi.org/10.4103/ijp.IJP\\_692\\_17](https://doi.org/10.4103/ijp.IJP_692_17)
8. Scheuerle AE, Holmes LB, Albano JD, Badalamenti V, Battino D, et al. (2019) Levetiracetam pregnancy registry: final results and a review of the impact of registry methodology and definitions on the prevalence of major congenital malformations. *Birth Defects Res* 111: 872–887. <https://doi.org/10.1002/bdr2.1526>
9. Mawhinney E, Craig J, Morrow J, Russell A, Smithson WH, et al. (2013) Levetiracetam in pregnancy: results from the UK and Ireland epilepsy and pregnancy registers. *Neurology* 80: 400–405. <https://doi.org/10.1212/WNL.0b013e31827f0874>
10. Koc G, Guler SK, Karadas O, Yoldas T, Gokcil Z (2018) Fetal safety of levetiracetam use during pregnancy. *Acta Neurol Belg* 118: 503–508. <https://doi.org/10.1007/s13760-018-0996-7>
11. Thomas SV, Jeemon P, Jose M, Amrithum LM, Bhaskar D, et al. (2022) Differential impact of antenatal exposure to antiseizure medications on motor and mental development in infants of women with epilepsy. *Epileptic Disord* 24: 531–540. <https://doi.org/10.1684/epd.2022.1414>
12. Vajda FJE, O'Brien TJ, Graham JE, Hitchcock AA, Lander CM, et al. (2018) Antiepileptic drug polytherapy in pregnant women with epilepsy. *Acta Neurol Scand* 138: 115–121. <https://doi.org/10.1111/ane.12965>
13. Sharma SR, Sharma N, Hussain M, Mobing H, Hynniewta Y (2021) Levetiracetam use during pregnancy in women with active epilepsy: a hospital-based, retrospective study from a tertiary care hospital in North Eastern INDIA. *Neurology India* 69: 692–697. <https://doi.org/10.4103/0028-3886.319234>
14. Birnbaum AK, Meador KJ, Karanam A, Brown C, May RC, et al. (2020) Antiepileptic drug exposure in infants of breastfeeding mothers with epilepsy. *JAMA Neurol* 77: 441–450. <https://doi.org/10.1001/jamaneurol.2019.4443>
15. Meador KJ, Cohen MJ, Loring DW, May RC, Brown C, Ret al. (2021) Two-year-old cognitive outcomes in children of pregnant women with epilepsy in the maternal outcomes and neurodevelopmental effects of antiepileptic drugs study. *JAMA Neurol* 78: 927–936. <https://doi.org/10.1001/jamaneurol.2021.1583>
16. Veroniki AA, Cogo E, Rios P, Straus SE, Finkelstein Y, et al. (2017) Comparative safety of anti-epileptic drugs during pregnancy: a systematic review and network meta-analysis of congenital malformations and prenatal outcomes. *BMC Med* 15: 95. <https://doi.org/10.1186/s12916-017-0845-1>