

# A Review of Awareness of Pregnancy-Related Issues Among Reproductive-Aged Croatian Women with Epilepsy

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**Abstract** - Pregnancy-related epilepsy issues (PREIs) are crucial in managing women with epilepsy (WWE). The main PREIs are reduced compliance and self-discontinuation of antiseizure medications (ASMs), pharmacokinetic alterations during pregnancy, and the teratogenic potential of particular ASMs. According to a recent study, knowledge of PREIs among reproductive-aged WWE in Croatia is unsatisfactory, as are neurologist consultations about PREIs. Two hundred WWE were polled on their knowledge, sources, and needs for information about PREIs and their current ASMs usage. Prior consultation with a neurologist and increased use of books/brochures were the main predictors of knowledge. Forty-five percent of participants had a prior neurologist consultation on PREIs. Most women (61 %) chose their neurologist as their favourite future source of information, and 13 % favoured Internet. The most usually prescribed ASM was levetiracetam (34.5 %). Valproate was utilized by 26 % of respondents, among which 59 % claimed no prior PREIs consultation with a neurologist. A new campaign called Epilepsy and Pregnancy was launched by the International Bureau for Epilepsy in 2021. In February 2021, a poll of nearly 900 women was conducted across Europe as the first stage in this significant project, including 94 respondents from Croatia. Forty-two percent of Croatian WWE were given no information on pregnancy-related risks. In contrast with the aforementioned study, neurologists provided 82 percent of information about the risks of ASMs. Seventy percent reported they were not given contraception information. Providing clear, accurate and timely information on PREIs should become the norm for all neurologists caring for WWE.

**Key words:** awareness; epilepsy; knowledge; pregnancy; women

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## Introduction

With an estimated prevalence of 6.85 cases per 1000 women worldwide, epilepsy is a common disease in women [1]. Women with epilepsy (WWE) encounter particular difficulties throughout their lifespans, such as unique reproductive and general health concerns. Because a woman's lifetime hormonal changes

can impact seizure control and the metabolism of antiseizure medications (ASMs), the disease presents particular management issues in this group of patients [2]. Between 0.3 % and 0.5 % of all pregnancies occur among WWE, which makes pregnancy-related epilepsy issues (PREIs) crucial in managing WWE [3]. The main PREIs are seizure control, reduced compliance and self-discontinuation of antiseizure medications (ASMs), ASM metabolism and pharmacokinetic alterations during pregnancy, teratogenic potential of particular ASMs, and pregnancy complications. Most

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WWE experience a decreased seizure frequency or remain seizure-free during pregnancy [4]. However, some studies have shown higher status epilepticus incidence and increased mortality in pregnancy for WWE compared with those without epilepsy, with sudden unexpected death in epilepsy being the most common cause [3,5,6]. Some studies' findings highlight that WWE are more prone to stop using their ASMs during pregnancy. Additionally, the majority of patients who discontinue ASM do so after conception rather than before it, and the majority of those who do so do not admit it [7]. Pregnancy-related physiological changes impact the absorption, distribution, metabolism, and excretion of ASMs. As the pregnancy continues, circulating levels of lamotrigine, levetiracetam, topiramate, zonisamide, and oxcarbazepine may decrease [8]. Therapeutic drug monitoring can aid ASMs' dose adjustment during pregnancy [9]. ASMs have been linked with congenital malformations, with valproate carrying the highest risk. The risk is dose-related and increases when the daily dosage is increased from 500 mg to 750 mg [10]. Congenital abnormalities may also be caused by genetic factors, such as a family history of neural tube malformations or an individual's predisposition [11]. To effectively counsel a pregnant or potentially pregnant WWE, it is necessary to inform them that most WWE will experience an uncomplicated pregnancy and deliver a healthy child [12]. Several studies on WWE, however, revealed an elevated risk of pregnancy complications, including a higher rate of spontaneous abortion and pregnancy termination, as well as a higher prevalence of pre-eclampsia. Additionally, pregnant WWE are more likely to be obese, which increases their chance of excessive bleeding or needing a caesarean section [8]. Preconceptual counselling for WWE is recommended due to a high rate of unintended pregnancies, up to 55 % [13]. Providing information about adequate contraception is part of managing WWE. The importance of folic acid supplementation is highlighted. Although there is considerable uncertainty about folic acid's ability to prevent

congenital malformations in this population, the supplement is linked to neurodevelopmental benefits [14]. Postnatal care involves peripartum psychiatric comorbidities treatment and breastfeeding support for WWE [8].

Studies have shown that engaging in educational and counselling activities can improve ASMs tolerance and compliance and reduce side effects [15,16]. Specifically, when carried out prior to conception, they can lower the likelihood of congenital malformations and assist WWE in making an educated decision about potential motherhood [18]. Therefore, understanding WWE's level of PREIs knowledge, where their information comes from, and which AEDs they are currently taking, considering their possible teratogenicity, is required to plan for rational, successful, and timely educational interventions.

## Subjects and Methods

Two main sources deal with the awareness of pregnancy-related issues among reproductive-aged Croatian women. The first is the study conducted in 2016 with an online anonymous questionnaire offered to all visitors of the Croatian Association for Epilepsy website [19]. The second source is the results of a questionnaire as a part of a new campaign called Epilepsy and Pregnancy, launched in February 2021 by the International Bureau for Epilepsy (IBE) [20].

## Results

All visitors to the [www.epilepsija.hr](http://www.epilepsija.hr) website of the Croatian Association for Epilepsy was given the option to complete an online anonymous survey between August and September 2016. The target population for the survey was females receiving epilepsy treatment aged between 15 and 45. Two hundred women, with a mean age of  $29 \pm 8.1$  years and a college or university degree held by nearly a third of participants, responded to the study's findings. Thirty-five percent of the individuals have already given birth, and of those, 67 % have had at least one pregnancy while receiving AED treatment. The wish to have children in the future was expressed by 43 % of

respondents, with 24 % remaining undecided. The following factors were linked to higher total knowledge scores: older age, higher education level, prior pregnancy, ASM during past pregnancy or pregnancies, having been counselled by a neurologist, timing of initial consultation prior to/during pregnancy planning as opposed to when already pregnant, higher level of using information sources overall, and higher usage of Internet, books/brochures, neurologist, and other physicians as sources. Less than half (45 %) of WWE reported that they had received advice from their neurologist on pregnancy- and breastfeeding-related issues, with 39 % of those declaring that the advice was inadequate. Most respondents (56 %) felt that their neurologist had not given them all the information they needed about PREIs (not being counselled at all or insufficient despite the personal need for such counselling). Compared to WWE, who do not want children in the future, this occurred more frequently. A neurologist provided counselling before or during pregnancy planning in 75 % of the cases. More than two-thirds (68 %) of the participants stated that they initiated this consultation independently. On a scale of 0 to 3, the participants were asked to rate how much they had previously used various sources on PREIs. Internet received the highest rating, followed by their neurologist, while other WWE had the lowest rating. Older age, a longer history of epilepsy, and receiving neurologist advice were all associated with a better overall score when accessing information sources. Higher education levels and earlier pregnancies were linked to higher ratings for using Internet as a source. In the future, the majority of the women (61 %) want their neurologist to inform them about PREIs directly; 22 % prefer written materials that their neurologist would deliver; 13 % prefer receiving information online; and 3 % have no interest in receiving this information. WWE, who were better informed and used information sources more regularly, reported a preference for receiving future PREIs information online as opposed to their neurologist. The majority

of respondents (58 %) were currently being treated with a single ASM. Levetiracetam was the ASM most frequently used (34.5 %), followed by lamotrigine (33.5 %) and valproate (26 %). In addition, 56.5 % of the individuals had at least one FDA category D AED as their current medication, and 47.5 % currently only used new AEDs. Sixty-nine percent of those receiving valproate medication wanted children in the future or were unsure about it, and 59 % claimed their neurologist did not provide them with PREIs counselling.

The International Bureau for Epilepsy launched a new campaign called Epilepsy and Pregnancy. In February 2021, a poll of nearly 900 women was conducted across Europe as the first stage in this significant project, piloted in Europe, including 94 respondents from Croatia. Demographic data gathered were age, marital status, employment status, education, country of origin, and the respondents' membership in an epilepsy organization. In addition, information about the number of years since diagnosis, whether under the care of an epilepsy specialist, pregnancy history, and history of ASM were included. The majority of participants were in the age range of 20 to 39. Sixty-one percent (61 %) had a college or university education. Sixty percent of people were currently employed, with the majority working in paid positions instead of being self-employed. The question of whether respondents had ever been pregnant was posed. The range of responses was 44 - 74 %, with a mean response of 52 % across the sampled countries, and for Croatia, 72 %. There was a significant variation across the countries in taking ASMs at the time of the pregnancy, with Croatian respondents reporting 68 %. Forty-two percent of Croatian WWE were given no information on risks associated with ASMs before pregnancy. Regarding the information they have received, almost half (48 %) of Croatian respondents answered that information was neither easy nor difficult to access. Forty-five percent of them find this information somewhat or very easy to understand, while 80 % find it helpful. The majority of the respondents

identified that neurologists were likely to be the leading provider (in 82 %), followed by Internet, or they found it in their own research. Epilepsy organizations, in the main, were not a frequent source of information. Seventy percent reported that they were not provided with information in respect of contraception. Seventy-nine percent have not been made aware of the risks of taking ASMs while pregnant, and 43 % have never been asked to plan pregnancy by a medical specialist. The majority of Croatian WWE (82 %) would contact a medical professional before making any decision about whether or not to stop taking medication in a case of pregnancy. Sixty-two percent of respondents would not avoid becoming pregnant if they were on ASMs. More than half (56 %) consider the given information on the issue of epilepsy and the risks associated with pregnancy helpful in deciding whether to become pregnant.

## Discussion

The awareness and knowledge of pregnancy-related issues among Croatian WWE of reproductive age are primarily studied in two sources: a survey carried out in 2016 via the website of the Croatian Association for Epilepsy and a questionnaire completed in 2021 as part of the Epilepsy and Pregnancy campaign [19,20]. The results have shown that WWE in their childbearing age are still not sufficiently informed about the specific issues related to pregnancy.

Despite the recent surge of guidelines about the management of WWE, which focus on counselling about teratogenicity, 42 % of women were still unaware that the teratogenic risk is not the same for all ASMs, and the same percentage was given no information on risks associated with ASMs before pregnancy. The majority of the women (82 %) would speak with a doctor before deciding to change their medication in the case of pregnancy, and the majority (88 %) were aware that they need to discuss their treatment with their neurologist at the latest when they begin

planning their pregnancies. Lack of information about PREIs can have a variety of adverse effects on family planning decisions as well as the health of women and their children. For example, respondents in WWE who do not want to have children in the future were more likely to feel that their neurologist had not fully informed them about PREIs. A prior consultation on PREIs with a neurologist and the time of this consultation prior to the pregnancy rather than while the woman was already pregnant are further predictors of better knowledge, in addition to demographic and epilepsy characteristics. Greater reliance on widely regarded as more credible information sources - such as physicians, Internet, and printed materials - was associated with higher knowledge, whereas receiving a lot of information from the media and other WWE did not. Being advised by a neurologist and using more books and brochures are the two most significant indicators of better knowledge. These findings are substantial to WWE management because they highlight the need to provide credible written materials and counselling from a neurologist to WWE who are of childbearing age, regardless of patient age or educational ability. Although the majority of the respondents in 2021 (82 %) identified neurologists as a leading source of information (82 %), only 45 % of participants in 2016 said they had had a prior neurologist consultation on PREIs. It could be explained as a bias that in the first study, women who did not receive information tended to respond. The same bias may also apply to the fact that the majority received information from neurologists; however, it is disputed that they did not obtain knowledge concerning ASMs. Seventy percent of those surveyed said they didn't get any counsel or information regarding contraception is a very unsettling and disturbing finding, indicating the need for better-planned care. In general, epilepsy organizations were not recognized as a frequent source of information, although most women took part in the surveys via the website of the Croatian Epilepsy Association. This leads to the con-

clusion that the existing educational resources need to be made more noticeable and recognizable and that more efforts should be made in the health and general public to encourage women to contact the association.

WWE face many difficult issues at different life stages, with reproductive-aged women often requiring counselling about contraception, fertility, and pregnancy. WWE report inadequate knowledge and awareness of key pregnancy and birth issues, suggesting that contraceptive and preconception counselling for many WWE could be improved. Providing clear, accurate, and timely information about

PREIs should become the standard of care for all neurologists taking care of women of reproductive age with epilepsy.

### Acknowledgements

None.

### Conflict of interest

None to declare.

### Funding Sources

None.

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