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Epilepsy: Addressing Management Hurdles in Pregnancy and Lactation with Emphasis on Patient Well-Being

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ABSTRACT

Epilepsy is one of the conditions involving defects in the electrical activity of neurons. This condition mostly affects the adult population, particularly women in their reproductive age. During the treatment of epilepsy with antiepileptic drugs (AEDs) in pregnant women, major congenital malformations were recorded in the born babies. Some of the babies had malformations in their cardiovascular and nervous systems. Among all the AEDs under study, valproate has been found to affect IQ and cause cardiovascular malformations in infants. Phenytoin has been contraindicated for women who are planning for pregnancy. Hence, the physician must discuss the risks and benefits of the designed treatment plan and initiate the same after obtaining the consent of the patient/caretaker. Deficiency of certain vitamins like folate, vitamin – D, and K must be corrected to avoid hemorrhage, and growth retardation in neonates using supplements in recommended doses. These vitamins should be maintained in the normal range in both mother and fetus to also support their brain development and immunity. The importance of patient care at every stage of pregnancy must be educated to both the patient and her family members to promote healthy growth of the fetus and birth of the same. The steps like regular obstetrician visits and undergoing ultrasound of better quality must be informed to the patient/guardian to monitor any possible malformations in the developing fetus. It is important to educate the spouse and children on producing a proper response the sleep deficit conditions, epilepsy episodes, and so on in the pregnant female patient.

Keywords – Anti-epileptic drugs, Pregnancy, Fetus, Infants, Neonates, Valproate, Phenytoin, Neonatal tube defects, Patient care, Folic acid, Levetiracetam, Major Congenital Malformations.

I. INTRODUCTION

Epilepsy is one of the common neurological conditions that affects the general population. It is characterized by recurrent, unprovoked seizures. It can be managed by either life-long intake of antiepileptic drugs of different classes or surgery [8]. It is estimated that there are lakhs of women suffering from epilepsy in India, most of them being in the reproductive age group [3]. Babies born to mothers with epilepsy have a higher chance of congenital malformations, especially when exposed to antiepileptic drugs[5]. Apart from concerns about fetal exposure to AEDs, maternal epilepsy, and stress also pose potential risks to the developing fetus. While the fetus exhibits some resilience to brief hypoxic episodes, extended convulsive seizures can lead to enduring fetal hypoxia. Although the fetus can withstand brief seizures, prolonged convulsions can cause long-lasting hypoxia in the fetus. Infants born to women with epilepsy (WWE) face an approximately four-fold higher risk of developing epilepsy themselves [6]. Ensuring the safety of the fetus during maternal seizures is crucial, as potential risks encompass harm to the unborn child and an increased likelihood of miscarriage resulting from maternal trauma during a seizure. Consequently, advocating for the continued use of AEDs during pregnancy becomes a persuasive argument for safeguarding the well-being of the developing fetus.

Complications in Pregnant women with epilepsy

A recent study of 643 pregnancies in women with epilepsy revealed significant complications compared to those without epilepsy. While spontaneous abortions, ovarian cysts, fibroid uterus, and anemia did not show significant

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differences, generalized seizures at term were linked to transient fetal asphyxia evident in Cardiography. Grand mal seizures were associated with fetal bradycardia, reduced variability, and declarations approximately 15 minutes post seizures [2]. Despite most of these women having 90% of their children born healthy, maternal epilepsy presents fetal risks such as stillbirth, neonatal hypoglycemia, infections, respiratory distress syndrome, adverse effects on congenital and behavioral development, and major congenital malfunctions [1]. Seizures can occur in some women, with a frequency ranging from 8% to 46%. Various factors can contribute to this, such as poor compliance with the prescribed anti-epileptic drugs (sometimes due to vomiting), inappropriate reduction of the dosage and frequency of the medication, lower levels of the drug in the bloodstream during pregnancy, and sleep deprivation[10]. This underscores the importance of rational treatment with the appropriate AED, monitoring drug concentration along with associated effects, and providing proper patient care along with awareness of the treatment.

A. Management of Epilepsy in Pregnant and Breast-feeding women

1. Anti-epileptic drug therapy

1.1 Introduction

Managing epilepsy in pregnant women using anti-epileptic drugs (AEDs) is a significant challenge for healthcare providers. The risk of major congenital malformations (MCMs) is higher in pregnant women who take AEDs than in women of the same reproductive age who do not take AEDs, especially in high-income countries. TheprocessofidentificationoftheseMCMsbystudyingtheteratogenicpotential of the AEDs in a comparative way followed by rational prescribing will not only help the clinicians in generating a better therapeutic outcome but also aid in the birth of a healthy infant with little to no incidenceofmalformations duetothetherapy.Recent studies have shown that the new antiepileptic drugs (AEDs) are safer for pregnant and lactating women due to their low risk of teratogenic effects.

1.2 Monotherapy

In this part of the study, AEDs, their associated major congenital malformations (MCMs), and pharmacokinetics in breastfeeding women have been discussed.

1.2.1 Old-generationAnti-epileptics Phenytoin

Phenytoin is one of the most used anti-seizure medications for the management and treatment of tonic- clonic seizures, focal seizures, and status epilepticus. In pregnancies on phenytoin (PHT), an increased risk of incidence of cleft lip and palate as well as dysmorphic features such as nail and distal phalangeal hypoplasia and craniofacial abnormalities in the fetus were recorded [4, 10]. Relatively, minute amounts of phenytoin were found in the breast milk given to the infant i.e., about 18 – 20% of concentration in plasma and serum levels of PHT in these infants were considerably below the therapeutic level of phenytoin [10].

Valproate

Valproateisthesecond-mostfrequentlyuseddrugtotreatepilepsy,especiallyduringchildhood,whichis later continued till adulthood in most cases. It was found that Valproate (VPA) monotherapy was associated with a higher risk of MCMs.The MCM rates for VPA increased in a dose-dependent manner, keeping Cardiac malformations higher in number compared to that of the new AEDs and polytherapy without VPA [11]. It was also associated with a 1–2% risk of neural tube defects, particularly an open lumbosacral myelocoele [10] in the fetus. Some studies have proven that daily doses of valproate greater than1,000mg/daymightalsocauseahigherriskofspinabifidaandothertypesofmalformations,possibly due to high peak serum concentrations of valproate [4]. If a fetus gets exposed to valproate in the womb, there is a significant dose-dependent risk associated with child cognition and neurodevelopmental disorderssuchasautisticspectrumdisorder[9].Inthepr ospectivestudy,IQatage6waslower(onaverage 8–11points)invalproate-exposedchildrencomparedwithchildrenexposedtootherAEDslikephenytoin, carbamazepine, and lamotrigine. These reductions in IQ were considered to be sufficient to affect the educationandoccupationaloutcomes ofchildrenin thefuture[14].Sodiumvalproatelevelsinbreast-fed babies were found to be as low as 1–10% of plasma concentration [10].

Carbamazepine

Carbamazepine is an anti-epileptic drug used in the treatment of different types of seizures like partial seizures, grand-mal seizures, etc. Carbamazepine was once considered the least

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teratogenic AED among theolderAEDs,butrecentstudieshavefoundalinkbetweencarbamazepineandcongenitalmalformations in the same order of magnitude as barbiturates and phenytoin [10]. However, the MCM frequencies with carbamazepinearelowerwhencomparedtovalproate[14].Ithasadose-dependentincreaseintheriskof MCM[11].Inonestudy,about0.9%riskofneuraltubedefectswasrecordedintheinfantsborntomothers who took carbamazepine during pregnancy. There were also reports of reduced head circumference at birth, delay in development, and dysmorphic features [4]. In a comparative study, only one major renal congenitalmalformationandminorcongenitalheartmalformations(in3 fetuses)weredetectedinachild exposedtoCBZ[15].Itdoesnotappeartobeamajorneuro-behavioralteratogenicagent[9].Theplasma concentrationsofcarbamazepineinbreast-fedbabiesareusuallylow(39–40%)andbelowthelevelwhere pharmacological effects might be expected [10].

Phenobarbitone

Phenobarbitone shows a dose-dependent increase in risk of MCMs [11]. Phenobarbital treatment was associated with craniofacial anomalies, congenital heart defects, and minor dysmorphic features [4].Duetotheslowеliminationrate,accumulationofphenobarbitoneinplasma in the breast-fed baby can occur [10].

Ethosuximide

Ethosuximide can transfer into infants via breast milk in relatively higher daily doses (79–100% of the plasma concentration) and these concentrations in breast-fed babies can be close to therapeutic levels of ethosuximide [10].

1.2.2 New-generationAEDs Oxcarbazepine

AccordingtotheKeralaRegistryobservationalstudy,Oxcarbazepine(OXC)wasassociatedwithahigher MCM rate compared to other new AEDs. It shows a dose-dependent increase in the risk of MCMs [11]. As per recent reviews, oxcarbazepine does not appear to show any specific pattern of malformations [4].

Lamotrigine

As per Kerala Registry data, Lamotrigine (LTG) had the lowest rate of MCMs amongst the new AEDs [11].Inastudyconsistingofdatafromseveralregistrieslikethe UK,Ireland,etc.,nomalformationswere found in fetuses exposed to lamotrigine [15].A few other studies states that LTG might have a similar MCM frequency to that of carbamazepine but less than valproate [14]. Althoughit is considered to be a safe option in pregnancy, it may worsen the myoclonic epilepsies and requires complex titration schedules to maintain its levels that continue to drop drastically during pregnancy which concludes that Levetiracetam can be the best choice to treat myoclonic seizures compared to lamotrigine [16]. It can accumulateinplasma inthebreast-fedbabyduetoslowelimination.

However,Preliminary datain afew cases indicates that lamotrigine gets transferred into fetus plasma via breast milk at 40–45% of the level but there were no adverse effects recorded in any of such infants [10].

Levetiracetam

Uponanalysis,levetiracetam(LEV)wasfoundtobeassociatedwiththelowestriskofmalformations[10]. Thedoseof levetiracetamin the monotherapy group ofpregnantwomendidnotinfluence the mean birth weight or mean gestational age. LEV is an excellent AED to use in myoclonic epilepsies, where the lamotriginemay worsen it. TheLiverpooland Manchester Neurodevelopmentgroup has reported asafer neurodevelopment profile of levetiracetam compared to valproate [17]. A meaningful number of pregnanciesinastudyshowedthatLEVmonotherapycanbeconsidered asasaferalternativeforwomen with epilepsy of childbearing age and potential. Moreover, the LEV effect on neuropsychological and cognitive development remains unidentified [16].

Primidone

Infants who are breastfed can accumulate Primidone in their plasma due to its slow elimination rate[10].

Zonisamide

Zonisamidewasfoundtobeteratogenicinanimalstudies[4].TheNorthAmericanAEDregistrydata has provided information about a lower rate of MCM and reported that zonisamide increases the risk of low birth weight [18].

OtherAEDs

Thereislimitedinformationaboutvigabatrin, gabapentin,topiramate,andtiagabine'sassociationwithhe riskoffetalabnormalitiesinhumans.It is known that Vigabatrin and Gabapentin are excreted

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unchanged in the urine, indicating a low possibility of accumulation. Therefore, infants born to women with epilepsy using these drugs have fully developed renal function. [10].Topiramateisfoundtobe teratogenic in animal studies [4].

1.3 PolytherapyandassociatedMCMs

Polytherapy in the absence of valproate was associated with an increased risk of cardiovascular, genitourinary, and musculoskeletal abnormalities [11].

Valproatepolytherapy

Polytherapy with high-dose valproic acid (VPA) was significantly associated with an increased risk of major congenital malformations (MCM). Neural, cardiac, urinary, and skeletal malformations were recorded at a higher incidence [11].

Levetiracetampolytherapy

The risk of MCM (major congenital malformations) increases when LEV (Levetiracetam) is taken alongside other medications in a polytherapy regimen [16].

Zonisamidepolytherapy

ZonisamideinpolytherapyhasshownalowerMCMrat ecomparedtoitsmonotherapy.Thesame polytherapyregimenshowed4to5casesofMCMswhe nvalproateand/ortopiramatewereincluded[18].

1.4 PrescribingGuidelinesforAEDs

1. The use of low and effective doses of antiepileptic drugs during monotherapy during pregnancy can decrease the risk of congenital abnormalities in the child [12].
2. Optimisethetreatmentbefore conception[13].
3. ChoosethemosteffectiveAnti-epilepticdrugfortheseizuretypeorsyndromediag nosed [13].
4. Therapeutic drug monitoring (TDM)-based dose adjustments help to better control seizures and maintain stable blood levels of AEDs during pregnancy [11].
5. FrequentmonitoringofplasmaconcentrationsofL TGandOXC(atleastmonthly)willbeveryhelpful, especially for dose adjustment before, during, and after pregnancy. Use the strategy of individual approach to all pregnant woman as inter-individual variations in the pharmacokinetics of these drugs have been observed in different studies [12].
6. It is important to provide pre-conception information to all females of childbearing age.
7. If any changes need to be made to AED medications, they should be completed before conception.
8. If a person needs AED treatment, it is recommended to use a single agent rather than multiple ones.
9. Most major congenital malformations (MCMs) occur during the early stages of pregnancy, often before a woman is aware of her pregnancy. Therefore, adequate attention to the patient, proper monitoring of AED effects, and plasma concentration should be considered [10].
10. During the process of making decisions regarding treatment, it is important to follow the principle of shared decision-making between the physician and patient. In cases where the patient cannot fully comprehend the context due to age or a learning disability, discussions should also include the patient's representatives such as caretakers or guardians.
11. It is the physician's responsibility to discuss the available range of treatment options based on epilepsy type and to explain the risks and benefits of the chosen treatment [14].
12. In the case of newly diagnosed epilepsy in females, it is recommended to avoid using valproate unless other treatments are unlikely to provide adequate seizure control [14].
13. Eslicarbazepine (ESL) should not be prescribed to pregnant women unless the benefits outweigh the risks.During ESL therapy, women planning for pregnancy should have their maintenance of ESL evaluated, and high attention should be given during the maintenance of polytherapy [19].
14. According to preclinical studies, the use of perampanel during pregnancy may lead to complications such as intestinal diverticulum, delay in physical development, and pregnancy loss. Therefore, pregnant women taking perampanel should be closely monitored. It is recommended that drug plasma levels be monitored, if possible, and that women be encouraged to participate in a pregnancy registry to gather more data about the effects of perampanel on pregnant women [20].

1.4.1 AED-specificguidelinestoreduceMCMsPhenytoin

Phenytoinshould beavoided in womenof reproductive age, specifically inadolescenceperiod,

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as it has many unwanted side effects [10].
Valproate

1. The risk-benefit ratioshouldbe taken into consideration anddiscussedwiththepatient/caretaker beforeimplementingthevalproate therapy [4].
2. When valproate is chosen for the management of epilepsy, the patient and caregiver must receive comprehensive information on the risks associated with the use of valproate during pregnancy. The risks associated with seizures to both the mother and fetus should be minimized or delayed to achieve proper seizure control and discuss the effectiveness of valproate compared to alternatives for treatment of the patient's seizure type [14].
3. It is important to ensure that both the patient and caregiver have a complete understanding of the potential risks associated with valproate. If valproate is determined to be the most effective treatment, a woman with the potential to become pregnant, or her guardian, may express a strong preference to begin valproate treatment. This preference should be taken seriously when planningthe treatment. In most cases, it may be appropriate to begin valproate treatment during these circumstances [14].
4. After completion of the discussion on risk-benefit, initiate the valproate therapy in cases where a patient who is not planning for pregnancy wants to prefer it as a treatment option [14].
5. For patients already on VPA therapy, consider their preference regarding the continuation of the therapy [14].
6. When it comes to generalized epilepsies, where other treatments may not be as effective as valproate, and in situations where fetal exposure to valproate cannot be avoided, valproate can be considered as the first-line treatment option. Such situations mostly involve young girls with self-limiting epilepsy who are likely to stop treatment before they reach puberty, or girls and women with disabilities that make it unlikely for them to become pregnant [14].
7. Preconceptionguidelinesforvalproate include [14]–

a. In patients suffering from focal epilepsy, valproate therapy should be withdrawn or a change to an alternative treatment must be considered.
b. Valproate therapy should not be withdrawn from a pregnant woman with good seizure control unless the risks of withdrawal are acceptable to the patient, and after carefully analyzing the risks to both the mother and fetus.
c. If seizure control is good, continue with the VPA therapy.
d. It is important to ensure that any changes in the treatment plan are fully assessed and evaluated before conception.
e. During the pre-conception stage, prescribe a low but effective dose of Valproate or other AEDs.
f. TheVPA treatment canbe continuedforwomenwho,

- Show goodcontrolonalow doseofvalproatei.e.,upto500–600 mg/day.
- are aware of the risks upon withdrawal.
- Do not accept a switch of treatment.

g. The women who fall under point (c) and those who require valproate treatment at higher dosages must be informed of the associated teratogenic risks and the limitations of prenatal screening beforehand.

II. VITAMINS ANDMINERAL SUPPLEMENTATION

2.1 InNon-epileptic PregnantWomen.
Micronutrientsasvitaminsandmineralsareessentialduringpregnancyforthegrowthofthe fetus along with a mother's functioning. During pregnancy micronutrient deficiency results in unwanted effects on maternal and birth outcomes.Ironsupplementationhelpsinreducingtheriskofanemia by improving maternal mean hemoglobin concentration. Zinc supplementation showed a significant preterm birth reduction. Folic acid supplementation aids brain development and prevents neural tube defects.
Vitamin D supplements are essential for maintaining good skeletal health and reducing neonatal hypocalcemia.Iodinesupplementationreducestheperinatalandinfant mortality risk. Calcium supplementation helps in reducing the threat of preeclampsia in women. Magnesium supplementation is linked to a reduced incidence of preterm birth and lower risks of negative neurodevelopmental outcomes in infants. Alongwith these,othervitamins such as vitaminsB,C,E, and minerals such ascopper, and selenium are affiliated with fetal development [21].
2.1.1 Inepilepticpregnantwomen

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2.1.1.1 Folicacidsupplementation

Vitamin B9 (Folic acid) deficiency has been strongly linked to an increased risk of neural tube defects (NTDs) in women with epilepsy (WWE) who are taking anti-epileptic medications. Some AEDs, such as phenytoin, carbamazepine, and barbiturates might reduce the absorption of folate [22], however, there seem no studies showing the outcome after the folic acid supplementation is used by WWE on these AEDs. According to certain research, there is a higher chance that a woman taking medications like valproate and carbamazepine for epilepsy would give birth to a child who has a neural tube defect (NTD) [22]. Low Vitamin B9 concentrations have been reported in nonpregnant epilepsy population who are on valproate, oxcarbazepine,topiramate,andlamotriginetreatment whencomparedtononpregnantepilepsypopulation without Anti-Seizure Medication (ASM) use [24].

2.1.1.1.1 As stated by, The Centres for Disease Control and Prevention, a dose of 0.4 mg/day of dietary folic acidsupplementationforallreproductive-age womenisrecommended[22]whichisefficientinth e primary avoidance ofNTDsinthegeneralpopulation.Forsecondaryp revention,High doses,upto 5 mg/day, are advised [22].

2.1.1.1.2 During the pre-conception stage and in the first trimester, a vitamin B9 of dose 4 mg/day is recommended for patientswhohavebeen affected by NTD inapriorpregnancy,andalsostudiesstatethatan identicaldose that is 4 mg/day seems to be befitting for women receiving AEDs [23].

Because folic acid supplementation during pregnancy has been linked to higher IQs in offspring of mothers on lamotrigine or carbamazepine therapy [24], it is advised to take folic acid supplements for the full recommended time to prevent difficulties.

2.1.1.2 VitaminB/Riboflavinsupplementation

In nonpregnant epilepsy populations, patients using carbamazepine, phenobarbital, phenytoin, and primidone have been reported with low riboflavin concentrations. Comparatively, a smaller number of reports have been made with low pyridoxine concentrations during ASM use. [24]. For optimal folate metabolic function in one-carbon metabolism, an adequate amount of riboflavin and pyridoxine is important for normal fetal brain development during pregnancy [24]. Therefore, Riboflavin supplementation should be initiated and maintained until prescribed.

2.1.1.3 VitaminKsupplementation

Deficiency of Vitamin K is seen in neonates of AEDs-taking women, cause of depleted clotting factors dependent on vitamin K neonatal hemorrhage has developed in infants of mothers on AEDs. The coagulationfactors which are vitaminK-dependent exist asdecarboxylated forms, the proteinsinducedbytheabsenceof vitamin K (PIVKAs), when there is Vitamin K deficiency [23]. Hemorrhagic complicationswereobservedandconsideredashemorr hagewithinthe dayofbirth.InAED-exposed newborns, hemorrhages have been majorly considered for premature birth (34 weeks) [25].

To prevent neonatal hemorrhage, Antenatal supplementation of vitamin K has been recommended [23]. Newborns susceptible to AEDs-inducing release of enzymes in the uterus are typically administered vitamin K upon delivery to control their vitamin K levels. [25]. If clotting factors are deficient then, fresh frozen plasma administration may be required for neonates. [23].

a. In the last month of pregnancy, 10mg/day of Vitamin-K in the oral route has been recommended to reduce the presence or appearance of some PIVKAs and neonatal deficiency of vitamin K [23].

b. Giving a baby one milligram of vitamin K is the treatment for vitamin K insufficiency in the baby [23].

There is insufficient data to say whether prenatal vitamin K supplementation lowers the risk of newborn hemorrhagic problems in WWE. To find out if vitamin K supplementation during late pregnancy can lower the risk of hemorrhagic illness in newborns born to WWE users of AEDs, more research must be conducted [25].

2.1.1.4 Mineralsupplementation

Toreducetheriskofmalformations,ithasbeensuggeste dtotakeselenium,0.1mg/day[26].

3 Patientcareandfamilyeducation

3.1 Women suffering fromepilepsywhoareplanningforconceptionare tobeinstructedregardingtherisks of pregnancy and the effects of the use of AEDs on the fetus, reassurance that the outcomes of pregnancy are good must be given to WWE[23].

3.2 Epileptic mothers, as well as mothers who have not experienced a seizure attack in a while, should be urged to take precautions because puberty-related weariness, lack of sleep, and stress can all contribute to the

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recurrence of seizures or an increase in their frequency [10].

3.3 Extensive counseling should be given to the patient if a Neuro tube defect (NTD) is detected. At the time of amniocentesis, analysis of karyotype must be carried out. The patient should be reviewed for pregnancy management and prognosis of neonate along with the risks of recurrence and prevention strategies. Patients should consult with surgeons and physicians who treat NTD children, as well as the families of NTD children.
Nondirectivecounselingshouldbeperformedwith the patients and the choice of termination of pregnancy should be conveyed. [23].

Although most epileptic women have normal deliveries, childbirth management is suggestedin patientswithNTDstooptimizefutureneurologicfunction. Forpatientswhose fetushas an NTD, cesarean delivery should be taken into consideration, although the cesarean delivery benefits are unproven [23].

3.4 Forwomenwithepilepsyespeciallybeforeconception,healthproviders mustencouragethemto talk abouttheir medical conditionandplausible adverse eventsoftherapyinaregularmanner andprepare the latest and up-to-the-minute information. “Having epilepsy should not be a limiting factor to having a child”. Women-centered clinics should be established as they help improve the current situation by offering preconception counseling and treatment and follow-up during and after pregnancy [27].

3.5 Itisadvisedtoassessthecharacteristicsofthe seizures in awoman[10]asitwillhelpinaccuratediagnosis and treatment.

3.6 It is advised that moms of children with uncontrolled juvenile myoclonic epilepsy throughout the puerperium designate a caregiver to take care of the child in the early morning [10].

3.7 Safety precautions to be followed before birth are very important in pregnant women with epilepsy. Hencea skilled health visitor and an epilepsy nurse are tomake ahomevisitshortly before the birth and provide adequate information for better care in the home [10].

3.8 Educate the kids and make sure they know what to do from a young age if their mother experiences a seizure attack inside or outside the house. Because the child won't become afraid while witnessing their mother's condition, this procedure will be beneficial [10].

3.9 Femalepatientsandtheircaretakers are also to be briefed regarding the constraintsofprenatalscreening methods,asitisimpossibletoidentifyvalproate'seffectsonintelligencequotient(IQ)andneurological development of children, and some malformations using these screening methods [14].

4 Stage-specificpatientcareguidelines

4.1 Preconceptionstage

Proper evaluation before conception is crucial for managing epilepsy and pregnancy effectively. Counseling with essential information should be given to all Females with childbearing potential.

a. Every woman intending to become pregnant needs to take folic acid, at least 5 MG per day [3].
b. To enable any potential changes to the current treatment plan and to ensure proper monitoring of the revised treatment, schedule a consultation with the epilepsy specialist well in advance of the intended pregnancy. It is best to start this process a year or more in advance of the anticipated time of conception [14].
c. Because exposure to AEDs, especially those that induce hemorrhagic disease in newborns,increases the risk of hemorrhagic disease, vitamin K should be given to the mother during the finalmonth of her pregnancy and to the newborn after birth [4].

4.2 Pregnantstage

a. Patients should be reassured that most of the women with epilepsy give birth without incident[21].
b. If the patient isn't taking folic acid, medical professionals should talk to them about how important it is to start. They should also explain that regular obstetrician visits can be used to monitor the patient's antiseizure medication concentrations during pregnancy.
c. A strategy for managing epilepsy should be devised for pregnant women who experience seizures.
d. AED dosage adjustments should be made appropriately, and the patient's seizures should be tracked and documented.
e. Pregnantwomenshouldbereferredtoaspecialistcenterforgood-quality ultrasound by their obstetric/gynecological consultant [21].
f. An obstetric unit equipped with resources for both maternal and newborn resuscitation should always be the site of delivery.
g. After the delivery, review the ideal AED

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maintenance dose [21].

h. If a baby delivered to a phenobarbitone-using mother exhibits signs of sleepiness, breastfeeding and bottle-feeding can be alternated [10].

4.3 Postpartumstage

Up until the eighth postpartum week, maternal plasma levels of AEDs may vary, and during this time, plasma AED levels may need to be monitored. Specifically, it might be necessary to lower the dosages of lamotrigine and oxcarbazepine in postpartum[6].

4.4 Breast-feeding/Lactatingmothers

Both mothers and their children can benefit much from breastfeeding. Benefits include improved nutrition, boosted immunity, and enhanced social development. Additionally, it lowers a child's risk of developing dose-dependent epilepsy at one year of age. A longer breastfeeding history has decreased the risk [7]. The risks of infections, diabetes, asthma, childhood leukemia, obesity, and sudden infant death syndrome are all lower in breastfed babies [1].

a. Encouragewomenwithepilepsytobreastfeedtheirbabies[10].
b. All AEDs enter the mother's milk. When compared to that of older AEDs, new AEDs have been found in higher concentrations in breast milk [6]. Hence proper monitoring and continuous assessment of AED concentrations in the mother are necessary.
c. Due to longer half-lives of drugs, Phenobarbital, Benzodiazepines can accumulate in the mother, which leads to poor weight gain and dizziness, so careful monitoring of plasma concentrations of AEDs must be done [7].
d. Women who are breastfeeding every 2-4 hours encounter fatigue and fragmented sleep in the postpartum period. The risk of seizures is known to increase due to missed medications and sleepdeprivationduringthepostpartumperiod.Thus, it is important to encourage patients to ask family members to feed their infants and give them uninterrupted stretches of sleep [1]. To allow the mother to get some rest, the spouse should be urged to help with feeding the infant, particularly at night (by, for example, using a breast pump to provide breast milk at night) [10].
e.

III. CONCLUSION

Valproate, phenobarbitone, carbamazepine, and oxcarbazepine have shown a dose-dependent increase in the risk of MCMs. In the old AEDs, Valproate showed a higher risk of MCMs, particularly cardiac malformations,intelligencequotientinthechildren,etc.Therefore,itisbettertoavoidvalproatetreatment, whenever possible, in patients with childbearing capacity, who are planning to become pregnant or are pregnantduringconsultation.IncaseswhereotherAEDshavefailedtocontrolseizures,valproatecanbe chosen.Insuchcases,theMCMrisksassociatedwithvalproatecanbepacifiedbyathorough analysisof the risk-benefit ratio and shared discussion between clinicians and women with childbearing potential. Withdrawal of valproate treatment must be done after knowing the preference of the patient and/or the patient'srepresentatives,and analysisofrisks.Phenytointreatmentshouldbeavoided inwomenwhoare planning for conception. Carbamazepine shows a lower risk of MCMs and does not show a teratogenic effectonneuro-behavioralaspectsofinfantswhencomparedwithotheroldAEDs.New-generationAED monotherapieshaveshownarelativelylowerincidenceofcongenitalmalformations(MCMs)when compared to Old-generation anti-epileptic drugs. Among new AEDs, Lamotrigine and Levetiracetam monotherapiesshowabetterprofileintreating epilepsy conditions in pregnant women. Levetiracetamisthe best choice to treat myoclonic epilepsies than lamotrigine.

A treatmentwith thelowesteffectivedoses ofAEDs helps to minimizetheMCM rate. Monitor the plasma concentrations of AEDs to detect any undesirable effects. Prescribe folate, vitamin K, and riboflavin supplementation to manage deficiencies before, during, and after pregnancy. Proper patient counseling and care help for the greater treatment of epilepsy during the pregnancy phase. Encourage thepatienttoscheduleandattendobstetricianconsultationsregularly.Familyeducation,particularlychild education, is very important for appropriate timely action during seizure attacks in mothers. It also helps inmonitoringtheseizurecharacteristicsandensurestha tthemotherdoesn'texperiencesleepdeprivation. Women in the post-partum phase must be encouraged to breastfeed their babies.

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