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# Acute Neurological disorders in pregnancy and postpartum period – Systematic review

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**Abstract:**
**Objective:** Stroke among young and elderly people is frequently caused by cervical artery dissection (CeAD). A rupture in any one or more blood vessel layers of tissue results in cervical artery detachment. Information for the causative factor of one-fifth of ischemic stroke patients is available from case reports and case reviews. CeAD is rare during pregnancy and in the early postpartum period. In addition, other risk factors have been suggested, such as infection, migraine, hyperhomocysteinaemia, and the 677TT genotype of the 5,10-methylenetetrahydrofolate reductase gene (*MTHFR* 677TT).
**Limitation:** A lack of neurological diseases during pregnancy and the postpartum period provides major obstacles for both the mother and child. The restricted therapeutic choices might impair care and complicate management. Multidisciplinary care is frequently required to achieve a delicate equilibrium between the health of the mother and the risk of foetal hazards.
**Method:** This systematic review with a systematically registered protocol was the strategy to study the clinical presentation, management, and outcome of this situation. For inclusion, 40 studies were found through language-free searches on Google Scholar and PubMed.
**Results:** The key factors of the greatest incidence found were migraine, hyperlipidemia, connective tissue diseases, HELLP syndrome, preeclampsia or eclampsia, and the protracted second phase of labor. The most frequent complaint was a headache with soreness in the neck. Anticoagulant medication, anti-platelet agents, and endovascular procedures were among the acute medical interventions.
**Conclusion:** This research emphasizes the value of efficient, all-encompassing care and raised knowledge to optimize results in pregnant women.

***Key words: Pregnancy, Postpartum, Neck Pain, Stroke, Cervical Artery Dissection (CeAD)***

## 1. Introduction

The international obstetrics field has exposed that headaches and other neurological symptoms are preeclampsia's individual features [1]. Acute ischemic stroke (AIS) is the potential fatal condition that is an incomparable and developed at pregnancy and the initial postpartum period [2]. Patient having illness in prenatal hypertension are more probable for the occurrence in high blood pressure (BP) in the postpartum time and it occurs after pregnancy [3]. Pregnant women and younger people have an increase in the probability of stroke during pregnancy, because of the hemodynamic changes, the hypercoagulable state, and other factors that have yet to be identified likely contribute to the increased risk of cardiovascular events. The increasing prevalence of traditional cardiovascular risk factors such as hypertension, diabetes, and obesity among younger adults, as well as the advancing maternal age at the time of birth, may contribute to increase the risk of acute stroke during pregnancy [4]. The treatment of preeclampsia and eclampsia requires an in-depth understanding of neurological auto-regulation, endothelial function, and angiogenic balance [5]. Vascular events, such as stroke and cervical artery classification are associated to hypertensive disorders of pregnancy (HDP) [6]. Pregnancy-related sickle cell disease (SCD) care is becoming increasingly significant as most people with this disorder reach reproductive age and beyond [7]. The central nervous system

(CNS) autoimmune disease recognized as neuro-myelitis optica (NMO) primarily affects the spinal cord and optic nerves, causing myelitis and optic neuritis. It is highly serious [8]. The pattern of endothelial cell damage in cases with hyperhomocyesteinemia describes thrombotic micro-angiopathy (TMA), a potentially fatal condition. It is established that there is an increased probability of developing various types of TMA during pregnancy and the postpartum phase [9]. Training and directing healthcare providers in making treatment decisions for female stroke patients is the objective [10]. The suggestions emphasize the necessity of obtaining information for preventing strokes and immediate treatment for women who are at greater risk of stroke in their entire lives. The objective of the study is to analyze and provide more explanation about acute neurological disorders in pregnancy and postpartum period by demonstrating factors, clinical characteristics and treatment for the disorders.

## 2. Methodology

The purpose of the systematic review is to improve the comprehensiveness and ease of use of the review process by following to the recommendations established by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA).

### 2.1 Source of data and searching

The PRISMA indicating standard was observed by this investigation (Figure 1). The total number of 2010 studies was obtained from a language-free search in Google Scholar, PubMed, and other sources. Research discovered a total of 2010 studies that covered 40 studies. The most common causes of the highest prevalence were hyperlipidemia, migraine, HELLP syndrome, connective tissue illnesses, preeclampsia, eclampsia, and a prolonged second phase of labor and the (Table 1) shows that Records included and PRISMA steps.

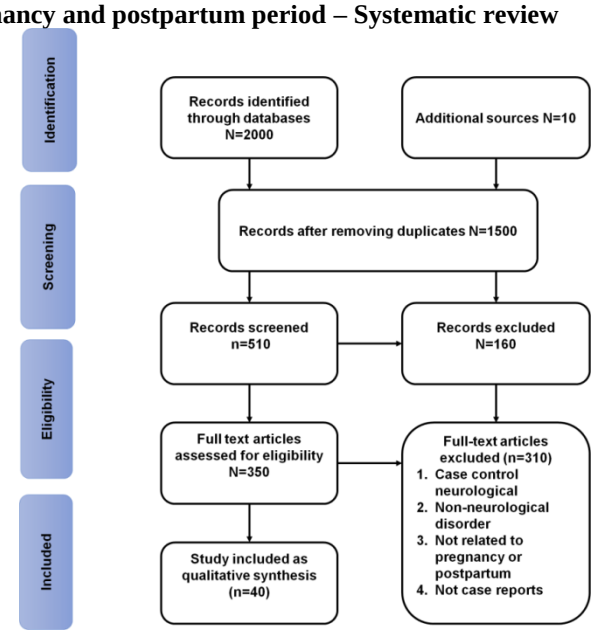


**Figure 1:** PRISMA Framework

**Table 1:** Records Identified from Additional Sources

| Step | Number of Records |
|---|---|
| Records identifies through databases | 2000 |
| Additional sources | 10 |
| Records after removing duplicates | 1500 |
| Records screened | 510 |
| Records excluded | 160 |
| Full-text articles assessed for eligibility | 350 |
| Full-text articles excluded | 310 |
| Studies included in quantitative synthesis | 40 |

### 2.2 Study Selection Criteria

We included human-driven, English-language research investigations. Studies involving case-control, non-neurological disorder, systematic reviews were excluded. Papers that failed to meet the objectives of the investigation (unrelated pregnancy or postpartum and not case reports) were eliminated. We only included studies that exceeded all of the following criteria after reviewing the research: headache along with neck discomfort, extended second phase of labor, migraine, hyperlipidemia, vascular disorders, HELLP syndrome, and preeclampsia and eclampsia.

### 2.3 Eligibility Criteria

1500 duplicate studies were excluded from the 2010 studies and 510 screened studies were

obtained. From the screened studies, we excluded 160 studies, and full-text articles determined for eligibility were 350 studies. Full-text articles were excluded with 310 studies for case-control, unrelated pregnancy or postpartum and not case reports. Finally, 40 neurological patient reports were considered for the research.

### 2.4 Inclusion Criteria

The human-conducted assessment, reports from neurological patients, and English-language writing are evaluated based on the inclusion criteria. Twenty English-language papers were chosen for the study's human-performed evaluation.

### 2.5 Exclusion Criteria

The entire number of reports and exclusion were conducted with 310studies of neurological disorders in pregnant women. Case-control studies have 90studiesand non-neurological disorders (20 studies) were not included. Articles reporting on no case report data with 175studies were similarly excluded. The study or case reports lacked information on the exact prevalence of the postpartum period (25 studies) and were also excluded.

### 2.6 Data Description

Articles that were certainly unnecessary were eliminated. Data on the following variables was retrieved from eligible studies after implementing inclusion and exclusion criteria: hyperlipidemia, migraine, HELLP syndrome, connective tissue illnesses, preeclampsia, eclampsia, and an extended second phase of labor. Headache, frequently accompanied by neck pain was the most prevalent concern. Within the acute medical treatments were endovascular operations, anticoagulant medicines, and ant platelet medications.

### 2.7 Data Extraction

The processes, including dosage, length of time, mode of administration, participant number, and the research design and patient selection, have been gathered from each publication. The outcomes and primary criteria of every observational research were also obtained.

### 2.8 Data Synthesis

The research performed a narrative synthesis of the data using basic statistics and percentages and mainly estimated a small number of suitable case studies. There were tables with descriptive reviews. Comparing the outcomes of the selected case reports with those of the non-postpartum control group.

## 3. Results

2010 studies from all databases were found by the search, and ten extra studies were found using PubMed and a Google Scholar search. There were 40 studies remaining after duplicates were eliminated and inclusion and exclusion criteria were applied.

### 3.1 Pregnancy and postpartum period

Anti-N-methyl-d-aspartate (Anti-NMDA) [11] receptor encephalitis during pregnancy and post-recovery pregnancy has been reported in several instances. Over a female's lifetime, hormonal changes have a substantial impact on her risk of neuromyelitis optica spectrum disorder (NMOSD). Postpartum psychosis [12] commonly emerges in three to ten days following pregnancy. Similar to postpartum psychosis, physical ailments can also manifest with these kinds of symptoms. Assessment is necessary for autoimmune diseases, postpartum hemorrhage, and fever infections [13]. Treatment with a neurology specialist is necessary for patients experiencing changes in consciousness to exclude neurological disorders.

### 3.2 Factors for treatments

Preeclampsia or, migraines, hyperlipidemia, connective tissue illnesses, HELLP syndrome, and extended second phase of labor were the primary factors of the highest prevalence that were identified. Table 2 provides an evaluation of the patient's medical characteristics and concerns related to pregnancy and delivery.

**Table 2:** Primary factors of patients and issues in pregnancy and delivery

| Factors | Percentage of issues (%) |
|---|---|
| Preeclampsia or eclampsia | 14/70 (20%) |
| Hyperlipidemia | 9/70 (12.9%) |
| Extended second phase of labor | 10/70 (14.3%) |
| HELLP syndrome | 7/70 (10%) |
| Migraines | 4/70 (5.71%) |
| Connective tissue illnesses | 8/70 (11.42%) |

### 3.2.1 Preeclampsia or Eclampsia

With decades of research, it is rather unidentified that pregnancy either increases or decreases hypertension, and hypertensive disorders continue to be a significant cause of morbidity and death among mothers globally. Preeclampsia [14] is more probable to occur in nulliparous women, which occur first as an interaction between having *chorionic villi* and being disposed genetically to increase conditions as hypertensive during pregnancy with previously existing conditions like diabetes, heart disease or nephrological illness, immune system conditions and females who are susceptible to an increased number of *chorionic villi* or who have other conditions related to the induction of endothelial cells or inflammation.

It has been determined that there is a relationship among the increase in bacteria quantity at pre-eclamptic placentas and women in normotensive condition. Eclampsia conditions are associated with an extensive number of bacterial species that indicate the several infectious agents' occurrence than a single infection. The development in inflammatory and anti-angiogenic activity that contributes to reduce endothelial and trophoblastic functions or elevated pressure of blood is the basis for the relationship between poly-microbial communities and preeclampsia [15]. Figure 2 depicts the eclampsia effects.

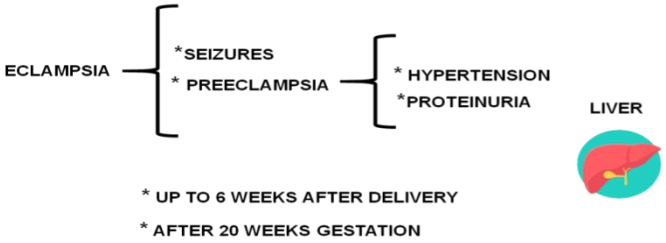


**Figure 2:** Effects of Eclampsia

Individuals with preeclampsia who have altered maternal immune systems are more likely to have low levels of chronic inflammation that promotes the cycle of damage to endothelial cells. Angiogenic and anti-angiogenic factor abnormalities could result from the factors [16]. Placental disease, inflammation, and angiogenesis alterations interact intricately to produce preeclampsia, a clinical disease that negatively impacts a patient's health during and after pregnancy [17].

### 3.2.2 Migraines

The sex prevalence ratio for migraine is around 3:1, with an increased frequency in women. Longer headaches, concomitant symptoms, impairment related to migraine, an increased risk of dual diagnosis, and a decrease in age are all prevalent in women compared to males with migraine. The introduction of non-pharmacologic treatments and lifestyle factor adjustments are the first-line treatments for managing migraine during pregnancy [18]. Improving sleep time and quality, eating regularly, staying hydrated, and keeping up a regular exercise routine are practices that can reduce the impact of migraines during pregnancy. Regular utilization of non-pharmacologic treatments [19], such as biofeedback and relaxation training, has been demonstrated to be beneficial in preventing migraines. Migraine impacts during the pregnancy period are determined in Figure 3.

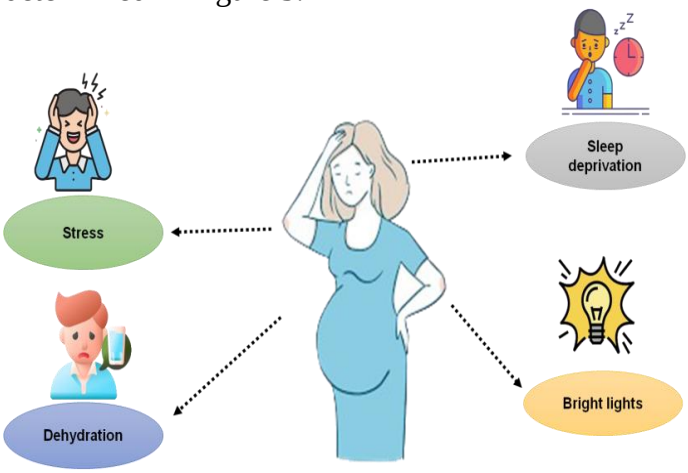


**Figure 3:** Impacts of migraines during pregnancy time

### 3.2.3 Hyperlipidemia

The primary complex factor of CAD that remains the most common cause of mortality is hyperlipidemia [20]. "Low density lipoprotein (LDL)" contents have been identified as an effective predictor of heart disease and stroke by prospective research, and it has been demonstrated that "high density lipoprotein (HDL)" levels are an effective cardiac protective factor. It is an abnormal HDL and "triglyceride (TG)" [21] at postpartum period than LDL or full cholesterol that is connected with prognostic variables during pregnancy. This research indicates that alterations in lipid profiles could appear in multiple forms postpartum [22]. Some variables or complex pregnancies have been strongly linked to HDL or TG implementing the condition of the pregnancy. The possibility of lipid management during pregnancy time is demonstrated in Figure 4.

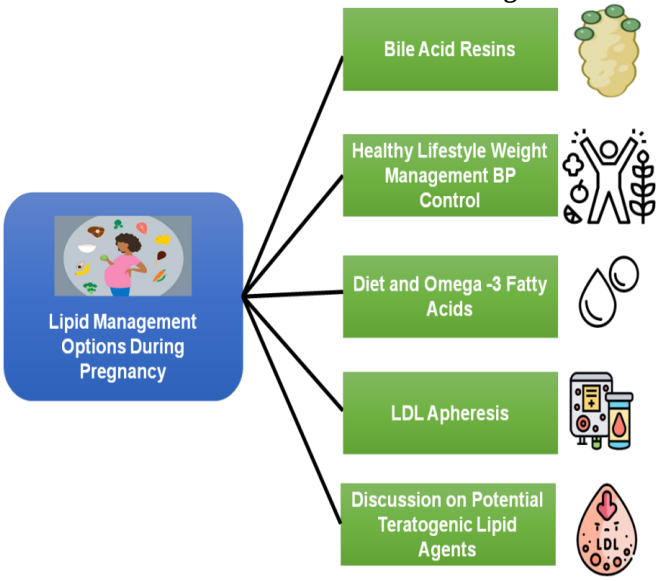


**Figure 4:** Lipid management during pregnancy

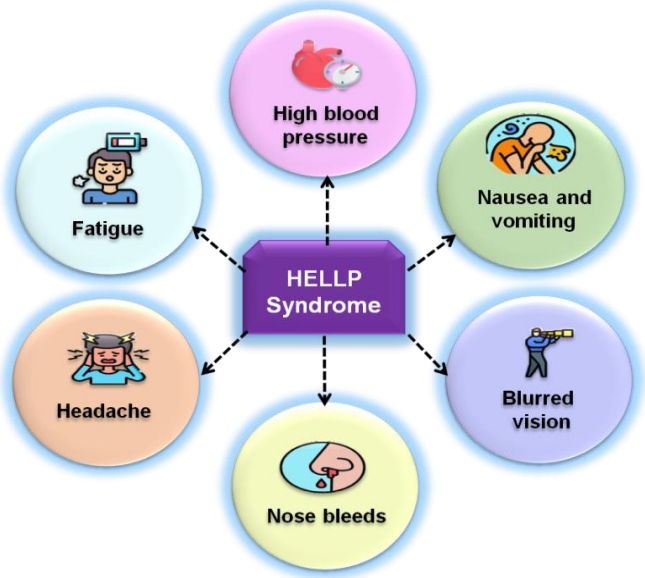


**Figure 5:** HELLP Syndrome

### 3.2.4 Connective Tissue Illnesses

Many organs and tissues, such as the joints, skin, kidneys, circulatory system, and blood are impacted by connective tissue illnesses [23]. Women with these illnesses frequently report to maternal medicine clinics, as the majorities are caused by autoimmune pathophysiology, are mostly female, and start during their pregnancy. Whereas there is a tendency for many inflammatory connective tissue illnesses to occur in children, these illnesses cannot be transmitted directly from parent to child [24]. Similar to cardiovascular and atherosclerotic illnesses in non-pregnant individuals, preeclampsia is considered to be caused by underlying processes that lead to vascular dysfunction [25].

### 3.2.5 Syndrome of Hemolysis elevated liver enzymes and low platelets (HELLP)

Following hospitalization requirements for mothers and infants were established, patients with HELLP syndrome [26] identified at external centers that had been referred to the clinic were selected. A major pregnancy complication is HELLP syndrome [27]. Severe preeclampsia, characterized by hemolysis, there are significant clinical consequences associated with low platelets syndrome and elevated liver enzymes. Postpartum bleeding is a serious clinical consequence of HELLP syndrome that can connected to a terrible prognosis [28]. Figure 5 shows the HELLP syndromes.

### 3.2.6 Second phase of labor

During the second stage of labor, the mother's pelvic shape and size are crucial. Anthropoid (oval with larger anterior-posterior axis), android (more triangle), and platypelloid (oval with greater transverse diameter), Gynaecoid (heart-shaped) are the various shapes of the pelvic inlet [29]. Experience of the range of processes that can be involved in the second phase of labor is crucial for birth attendants. Clinical characteristics of the reporting headache in patients arriving at the emergency room with subarachnoid hemorrhage were assessed in a prospective observational research.

### 3.3 Clinical characteristics of cervical artery dissection (CeAD)

It is critical that the clinical practice [30] perceive the effects of the findings. Significant value can be obtained from improving treatment options by the integration of endometrial micro-biota investigation into routine clinical evaluations, particularly in the framework of assisted reproductive technology (ART) methods [31]. In reproductive medicine, healthcare providers can become more adept at developing treatments to provide improved patient care. There is a significant overlap in the clinical characteristics of CeAD between pregnant and postpartum women, and many illnesses could potentially occur [32].

**Table 3:** Clinical characteristics

| Clinical characteristics | Number of effects (%) |
|---|---|
| Seizures | 6/80 (7.5%) |
| Hemiparesis | 30/80 (37.5%) |
| Neck pain | 41/80 (51.25%) |
| Headache | 69/80 (86.25%) |
| Tinnitus | 2/80 (2.5%) |
| Paresthesia | 14/80 (17.5%) |
| Facial palsy | 9/80 (11.25%) |

Various symptoms of neurological disease were identified like CAD with different rates in a clinical trial including eighty participants. 69 people (86.25%) reported having headaches, which were the most prevalent condition. Neck discomfort occurred in 41 participants (51.25%), and hemiparesis of 30 individuals (37.5%). 9 individuals (11.25%) reported having facial palsy, whereas fourteen people (17.5%) had paresthesia. Six people (7.5%) experienced seizures, whereas two people (2.5%) reported tinnitus as the least prevalent symptom. This information demonstrates the distinct way it affected people with neurological symptoms. Table 3 illustrates the clinical characteristics and impact percentages.

### 3.4 Radiological Characteristics of cervical artery dissection (CeAD)

Radiological features [33] associated with pregnancy include uterine expansion, enhanced vascularity, and abdominal organ displacement. Because ultrasound is safe and can indicate placental placement and fetal development, it is chosen. Magnetic Resonance Imaging (MRI) is a non-ionizing radiation method of detailed imaging [34]. With radiation hazards, radiography and computed tomography (CT) are restricted and can be performed as the benefits exceed the risks.

### 3.5 Fetal Women with Cerebral venous thrombosis (CVT)

Pregnant women with cerebral venous thrombosis (CVT) [35] have an uncommon and dangerous illness where blood clots develop in the venous sinuses of the brain, potentially leading to strokes. Neurological deficiencies, seizures, eyesight issues, and excruciating migraines are among the symptoms. Preeclampsia, postpartum infections, and pregnancy-related hypercoagulability are risk factors [36]. Improving outcomes for the mother and fetus depends on early detection using imaging and timely anticoagulant therapy.

**Table 4:** Conditions in thrombotic events

| Conditions | Diagnosis | Clinical Symptoms | Control |
|---|---|---|---|
| Thrombophilias | Counting of Platelet, Protein Mutation and Prothrombin | Thrombosis in the family and migraines thrombotic events. | Long-term anticoagulant therapy, such as vitamin K antagonist is utilized for treating recurrent thrombosis (except during pregnancy). |
| Pregnancy | Beta-HCG tests | Delay in Menstruation, vomiting, and others | Pregnancy interruption during CVT is not suggested except the mother constitutes serious risks to her life. |
| Infection and Sepsis | Laboratory tests and imaging are necessary for medical assessments based on system signals and symptoms. | Fever, hypertension, neutrophilia and lymphocytosis | Appropriate treatment in instances of severe illness or sepsis. |
| Oral Contraception usage | History of Clinical Research | - | Utilizing CVT can be prevented if there have been prior issues. |

Certain conditions can make thrombotic events occur more frequently (Table 4) [37]. Thrombophilias that are frequently suggested with familial thrombosis and headaches are identified by platelet counts, protein mutation, and prothrombin testing. The treatment for recurrent thrombosis is long-term anticoagulant medication, barring pregnancy. Beta-HCG testing establishes pregnancy, and unless the mother's life is in danger, CVT intervention is avoided. Lab testing and imaging are used to determine infection and sepsis, with treatment necessary for severe cases. Clinical history informs the management of oral contraception.

To treat vascular diseases such as CVT, caution must be taken while using clotting agents during pregnancy and after delivery. Low-molecular-weight-heparin (LMWH) is one of treatment [38]. As it is safe for both the mother and the fetus, LMWH is suggested. Since there is a chance of teratogenicity, antagonists to vitamin K are

usually avoided. To effectively manage thrombosis while decreasing bleed risks during and after delivery, postpartum therapy involves continuing with LMWH or switching to oral coagulants depending on clinical assessment. In the initial phase, parenteral anticoagulant with LMWH was the basis of therapy for both patient groups. There have been a few cases of direct oral anticoagulants (DOACs) such as rivaroxaban being used for long-term oral anticoagulation [39]. Decompressive operations and endovascular treatments were not performed. Acute neurological diseases [40] during the pregnancy and after delivery phase provide distinct difficulties that can affect both the mother and the infant. To reduce risks, conditions such as cerebral venous thrombosis, eclampsia, and intracranial hemorrhage need to be identified and treated quickly. Table 5 demonstrates the treatments for neuromyelitis optica spectrum with pregnancy issues.

**Table 5:** Treatment for women with Neuromyelitis Optica Spectrum Disorder during pregnancy

| References | Treatment | Pregnancy Issues | |
|---|---|---|---|
| | | Congenital defect | Other issues |
| [41] | Rituximab | An increased risk of congenital defects. | There were no anatomical abnormalities associated with rituximab in any human live birth and all were healthy. |
| [42] | Eculizumab | Reduced risk of congenital defects. | There is no higher risk of pregnancy or neonatal loss |
| [43] | Tacrolimus | Animal research indicates dose-related persistence, whereas human studies point to a modest incidence of congenital defects. | Three species were shown to have abortifacient qualities in animal research, and this was not observed in human trials. Research on humans indicates a potential correlation with hypertension, hyperkalemia, and premature birth. |
| [44] | Mycophenolate mofetil | Mycophenolate mofetil usage early in a pregnancy's course is connected to serious birth abnormalities that can be predictive of a certain phenotype. | Connected to miscarriages occurring spontaneously. |
| [45] | Mitoxantrone | Teratogenicity is not suggested by animal research. Its usage is prohibited during the first trimester as it has its cytocidal action on human cells that are multiplying and those that are not. | Harmful to certain cases indicates an increased probability of premature deliveries and development restriction. |
| [46] | Methotrexate | The embryopathy of | Fetal toxicity and death can |

| | | | |
|---|---|---|---|
| | | methotrexate | be connected to exposure during the second and third trimesters. |
| [47] | Cyclophosphamide | Congenital abnormalities resulting from exposure during organogenesis | A possible hazard is prenatal bone marrow suppression when treatment occurs later in pregnancy. |
| [48] | Amitriptyline | A few congenital defect cases are reported occasionally, and pregnancy is generally thought to be safe. | No greater risk of fetal miscarriage or other fetal injury is indicated by research on humans and animals. |
| [49] | Azathioprine | Birth defects are not more prevalent in the newborns of pregnant women receiving Azathioprine medication compared to the general population. | Reducing the dosage during the third trimester appears to lessen the possibility of the toxicity, exposure at that stage has been associated with immunosuppressive and suppression of bone marrow in the baby. |
| [50] | Corticosteroids | The human record indicates that congenital defects, such as orofacial clefts, are not significantly more frequent. | The human record indicates a potential correlation between underweight baby born prematurely and with any higher risk of foetal loss. |

## 4. Discussion

That research recurrence rates for multiple sclerosis (MS) are decreased during the pregnancy, especially in the 3rd pregnancy. However, rates of recurrence and MRI-detected lesions increased significantly in after delivery. Remarkably, new MRI lesions were presented in 31% of patients who did not experience postnatal relapses. Relapse prevention appears to be aided by exclusively nursing for at least three months. Those results emphasize the significance of early postpartum psychological and radiologic surveillance in direct care [51].

The influence of pregnancy on neuromuscular illnesses was reviewed in that article, which also notes that pregnancy can change the course or severity of a disease by revealing hidden inherited problems. The text underscores the difficulties associated with delivered and administered care for patients with skeletal muscular disorders and emphasizes the necessity of customized anesthetic and delivery techniques. Many illnesses are included in that overview, ranging from simple problems like amyotrophic lateral sclerosis to more sophisticated ones like focal neurological disorders. The ambiguity surrounding the toxicity of certain therapies to humans was also highlighted, which choosed preventive measures and treatment alternatives during pregnancy more difficult [52].

In that study assesses the effect of natalizumab (NTZ) and rituximab (RTX) suspensions on condition responsiveness in multiple sclerosis-afflicted pregnant women both during and after pregnancy. Results showed that postpartum recurrence rates were considerably lower in RTX-suspended patients than in NTZ-treated patients, and considerably lower in untreated women. It seems that RTX provided long-term illness management during pregnancy and the postpartum phase. That highlights RTX's possible advantages in controlling MS throughout pregnancy and implies it may have longer-lasting effects on MS activation than NTZ [53].

The study examined the effects of endocrine disrupting chemicals (EDCs) on neurodevelopment and their role in the formation of adult neurological diseases. Research on EDCs in growing babies was highlighted, which may have connections to conditions like schizophrenia, autism, and despair. Emphasizing the susceptibility of early brain development to these

chemicals and the necessity for further investigation, the highlights the impact of EDCs on gene connections and signaling networks [54].

Our study examines the difficulties and complications of managing cervical artery dissection (CeAD), which is a cause of stroke in pregnant and postpartum women. Even though CeAD is uncommon at these times, there are serious hazards for both the mother and the kid. After reviewing forty papers, the review determined that high-risk variables were preeclampsia, high cholesterol levels, and migraines. Complaints including headaches and neck pain were frequent. Anticoagulants, antiplatelet medicines, and endovascular surgeries were examples of acute interventions. In order to balance fetal safety and maternal health, the study emphasizes the value of multidisciplinary care. It also calls for more awareness and all-encompassing management to enhance results for this vulnerable population.

## 5. Conclusion

The research emphasizes that pregnancy-related disorders, migraine headaches, and hyperlipidemia are major risk factors for cervical artery dissection (CeAD), and a significant contributing factor to strokes in pregnant people. The standard symptom of headache, frequently accompanied by neck stiffness, is highlighted by the research, which examined 150 patient reports. Endovascular treatments and anticoagulant medicines are examples of acute treatments. It emphasizes the significance of quick, comprehensive treatment and increased consciousness to maximize results, especially for expectant mothers. The outcomes emphasize the need for a multidisciplinary approach that includes neurologists, obstetricians, and other researchers to effectively manage the issues associated with stroke during pregnancy and the postpartum period. The lack of attempt to investigate possible causes of confusion or interactions among risk factors makes it harder to determine the cause of occurrences. Several areas should be explored in future studies to improve information and treatment for pregnancy-related stroke and cervical artery dissection (CeAD). Enhancing early identification and risk classification through the incorporation of information and advanced imaging methods into algorithmic diagnostics.

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