Review Article

Traversing Antepartum Wernicke's Encephalopathy: In-Depth Insights and Strategies

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Abstract

Antepartum Wernicke's encephalopathy (WE) is a severe neurological disorder caused by a deficiency of thiamine (Vitamin B1), essential for glucose metabolism, and neuronal function. This review aims to provide an in-depth analysis of WE during pregnancy, highlighting its pathophysiology, risk factors, clinical presentation, diagnostic challenges, and management strategies. Thiamine is critical in the Krebs cycle and neurotransmitter production, and its deficiency leads to substantial biochemical disruptions and neuronal damage. Pregnant women are particularly susceptible due to their increased nutritional demands to support fetal growth and maternal metabolic changes, making them prone to thiamine deficiency and its severe neurological consequences. The clinical manifestations of WE include ophthalmoplegia, ataxia, confusion or altered mental state, peripheral neuropathy, and cardiovascular issues. Diagnosing WE during pregnancy is challenging due to its atypical presentation, requiring a high degree of clinical suspicion and awareness of risk factors. Diagnostic limitations include variable clinical symptoms and challenges in interpreting serum thiamine levels and neuroimaging findings. While neuroimaging can show characteristic brain lesions, its utility is limited by variability. Managing WE during pregnancy requires prompt recognition, immediate thiamine supplementation, continued supportive measures, and careful monitoring. Severe or refractory cases may require advanced management strategies. Pharmacological treatments include standardized thiamine administration protocols, guided by clinical guidelines and recommendations. Early detection and management of WE in pregnant women are vital to prevent irreversible neurological damage and improve maternal and fetal outcomes. Adherence to clinical guidelines is crucial to mitigate the impact of this condition.

Keywords: Antepartum Wernicke's encephalopathy, clinical management of we, neurological disorders in pregnancy, prenatal nutritional requirements, thiamine deficiency

Introduction to Antepartum Wernicke's Encephalopathy (WE)

Antepartum WE is a devastating neurological disorder resulting from a deficiency of thiamine (Vitamin B1), a crucial nutrient for glucose metabolism and neuronal function.

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Thiamine plays a key role in the Krebs cycle and the production of neurotransmitters; thus, its deficiency leads to significant biochemical disruptions and neuronal damage.[1] This condition predominantly affects individuals suffering from malnutrition, with pregnant women being particularly vulnerable due to their increased nutritional requirements. As pregnancy progresses, the demand for thiamine rises to support the growing fetus and the metabolic changes in the mother's body, making pregnant women susceptible to thiamine deficiency and its severe consequences.[2]

Historically, WE was first described by Carl Wernicke in 1881, who noted a triad of symptoms: ophthalmoplegia, ataxia, and confusion. Although traditionally associated with chronic alcoholism, WE can occur in any condition that leads to malnutrition or impaired thiamine absorption. In the context of pregnancy, hyperemesis gravidarum — a

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condition characterized by severe and persistent vomiting — can precipitate WE by causing prolonged nutritional deprivation. Other risk factors include bariatric surgery, dietary restrictions, and conditions that increase metabolic demand or impair thiamine absorption.[3] Despite its known etiology, antepartum WE remains underdiagnosed due to its varied clinical presentation, which can differ significantly from the classic symptoms.

The clinical presentation of WE in pregnant women often poses diagnostic challenges. Symptoms such as confusion, ataxia, and nystagmus may be subtle or overshadowed by other pregnancy-related conditions, leading to delays in diagnosis and treatment.[4] Neuroimaging, particularly magnetic resonance imaging (MRI), can reveal characteristic lesions; yet, these findings may not always be present in the early stages. Early intervention with high-dose thiamine is critical to prevent permanent neurological damage and improve maternal and fetal outcomes.[3,4] Thus, heightened clinical awareness and prompt recognition of WE symptoms in pregnant patients are imperative for timely management.

The selection of this topic for review is driven by the need to increase awareness among healthcare providers about the importance of recognizing and managing WE in pregnant women. Despite its potential for severe outcomes, antepartum WE is often overlooked or misdiagnosed, leading to significant morbidity. This review aims to consolidate current knowledge on the pathophysiology, risk factors, clinical presentation, diagnostic challenges, neuroimaging findings, and management strategies of antepartum WE. By doing so, it seeks to provide a comprehensive resource that highlights the importance of early diagnosis and intervention, ultimately contributing to better health-care practices and improved outcomes for both mothers and their babies.

Pathophysiology and Risk Factors

The underlying mechanisms of WE focus on how thiamine deficiency disrupts key biochemical pathways, leading to neuronal injury and brain lesions. Thiamine is essential for the function of enzymes involved in energy metabolism, and its deficiency can cause cell death and lesions in regions such as the mammillary bodies, thalamus, and brainstem.[5] Thiamine acts as a coenzyme for several key enzymes, including pyruvate dehydrogenase, alpha-ketoglutarate dehydrogenase, and transketolase, which are critical in the Krebs cycle and the pentose phosphate pathway. When thiamine is deficient, these enzymes' activities are impaired, resulting in reduced ATP production and increased oxidative stress, ultimately causing neuronal injury and death.[6]

Risk factors for antepartum WE will be discussed in detail, including hyperemesis gravidarum, which leads to prolonged vomiting and subsequent malnutrition; chronic alcoholism; bariatric surgery; and dietary restrictions that are common in pregnancy.[7] Hyperemesis gravidarum, characterized by severe nausea and vomiting, can result in significant thiamine depletion due to persistent vomiting and poor dietary intake. Chronic alcoholism is another well-known risk factor, as alcohol interferes with thiamine absorption and storage, exacerbating the deficiency. In addition, individuals who have undergone bariatric surgery may be at risk due to altered gastrointestinal anatomy and nutrient absorption, leading to inadequate thiamine levels. Dietary restrictions during pregnancy, whether due to nausea, food aversions, or cultural practices, can further reduce thiamine intake, increasing the risk of WE.[8]

Another critical aspect to consider is the interaction between thiamine deficiency and other nutritional deficiencies, which may co-occur and complicate the clinical picture. For instance, deficiencies in other B vitamins, such as B12 and folate, can exacerbate neurological symptoms and delay diagnosis. The presence of multiple deficiencies can lead to a more complex clinical presentation, making it challenging to identify and treat WE promptly.[9] In addition, conditions like hyperemesis gravidarum and bariatric surgery not only cause thiamine deficiency but also lead to deficits in other essential nutrients, further aggravating the patient's condition.

Finally, genetic predispositions and underlying health conditions may play a role in the susceptibility to WE. Variations in genes involved in thiamine transport and metabolism could affect individual thiamine requirements and risk of deficiency. Chronic health conditions such as gastrointestinal disorders, which impair nutrient absorption, can also increase the risk of developing WE. Understanding these genetic and health-related factors is crucial for identifying at-risk populations and implementing preventive measures effectively.[10] This multifaceted approach to examining the pathophysiology and risk factors of WE highlights the complexity of this condition and the importance of comprehensive clinical assessment and intervention.

Clinical Presentation and Diagnosis Challenges

WE often presents with a classic triad of symptoms: ophthalmoplegia (eye movement abnormalities), ataxia (loss of coordination), and confusion or altered mental state. However, in pregnant women, the presentation can be atypical or incomplete, complicating diagnosis. This section will detail the various clinical manifestations of WE, including less common symptoms such as peripheral neuropathy and cardiovascular issues.[11]

Clinical manifestations

Ophthalmoplegia

This symptom involves paralysis or weakness of the eye muscles, leading to issues such as nystagmus (rapid, involuntary eye movements), double vision, or drooping of the eyelids (ptosis). In pregnant women, these symptoms might be subtle or mistaken for other pregnancy-related issues, thereby delaying diagnosis.[12]

Ataxia

Ataxia refers to a loss of coordination and balance, making it difficult for individuals to walk or perform tasks requiring fine motor skills. In the context of pregnancy, ataxia might be

attributed to general weakness or other neurological conditions, which can further obscure the underlying cause.[13]

Confusion or altered mental state

This encompasses a range of cognitive impairments, from mild confusion and memory problems to severe disorientation and psychosis. Pregnant women may experience mood swings and cognitive changes due to hormonal fluctuations, complicating the recognition of WE symptoms.[14]

Peripheral neuropathy

WE can also present with symptoms of peripheral neuropathy, such as numbness, tingling, or pain in the extremities. These symptoms are often less emphasized in the classic presentation but are significant in a comprehensive assessment of WE, especially in the pregnant population.[15]

Cardiovascular issues

Cardiovascular manifestations may include tachycardia (rapid heartbeat), low blood pressure, and heart failure. These symptoms might overlap with common pregnancy complications, making it crucial to distinguish them through a thorough clinical evaluation.[16]

Diagnosis challenges

Atypical presentation in pregnancy

Pregnant women may present with an incomplete or atypical manifestation of WE, which makes diagnosis challenging. The classic triad is not always present, and symptoms like nausea, vomiting, and fatigue can overlap with common pregnancy experiences, masking the underlying condition.[17]

Clinical suspicion and risk factors

A high index of clinical suspicion is essential, particularly in patients with risk factors such as hyperemesis gravidarum, which can lead to prolonged vomiting and malnutrition. Recognizing these risk factors early can prompt further investigation and timely intervention.[18]

Limitations of clinical diagnosis

Clinical diagnosis of WE is challenging due to the non-specific nature of symptoms and their overlap with other conditions. The limitations of relying solely on clinical presentation necessitate the use of additional diagnostic tools to confirm the diagnosis.[3]

Serum thiamine levels

Measurement of serum thiamine levels can aid in diagnosing WE, although normal levels do not exclude the diagnosis due to the difficulty in accurately reflecting tissue thiamine stores. Low levels strongly support the diagnosis, especially in symptomatic individuals.[19]

Neuroimaging

Neuroimaging techniques, such as MRI, play a crucial role in diagnosing WE. Typical findings include symmetrical lesions in the thalamus, mammillary bodies, and periaqueductal area. However, these findings might not be present in all cases, and a normal MRI does not rule out WE.[20]

Challenges in Interpretation

The interpretation of diagnostic tests can be challenging. For instance, MRI findings might be subtle or delayed, and thiamine levels might not accurately reflect deficiency due to assay limitations or concurrent illnesses.

Early recognition and diagnosis of WE in pregnant women are critical to preventing severe neurological damage and adverse pregnancy outcomes. By understanding the diverse clinical manifestations and employing a high index of suspicion, healthcare providers can improve diagnostic accuracy and outcomes for affected individuals. This requires a comprehensive approach, integrating clinical assessment with diagnostic tools and considering the unique challenges posed by pregnancy.

Neuroimaging Findings

Neuroimaging plays a crucial role in the diagnosis of WE, particularly MRI, which is the preferred modality due to its superior ability to detect characteristic brain lesions. In WE, MRI typically reveals symmetrical hyperintense lesions on T2-weighted and fluid-attenuated inversion recovery sequences in specific brain regions. These regions include the thalamus, mammillary bodies, periaqueductal area, and midbrain. Lesions may also appear in the cerebellum and medulla. These findings are considered pathognomonic for WE, significantly aiding in the diagnosis when the clinical presentation is ambiguous or incomplete.[21]

MRI's advantage over other imaging modalities, such as computed tomography (CT), lies in its high sensitivity to early and subtle changes in brain tissue. CT scans often fail to detect the characteristic lesions of WE until the disease is advanced. MRI, on the other hand, can identify abnormalities even in the early stages, allowing for prompt intervention. This early detection is particularly vital in antepartum WE, where rapid diagnosis and treatment are crucial to prevent irreversible damage to both the mother and fetus. In addition, MRI does not involve ionizing radiation, making it safer for pregnant patients.[20]

However, interpreting MRI results in WE can present challenges. Not all patients will show the classic lesions, and the absence of abnormalities on MRI does not exclude the diagnosis. Furthermore, lesions may be subtle or atypical, necessitating a high degree of expertise in reading the scans. In some cases, other conditions such as multiple sclerosis or metabolic disorders can mimic the imaging appearance of WE, potentially leading to misdiagnosis. Including case studies or examples of neuroimaging in antepartum WE within this section would illustrate these key points and provide concrete examples of how MRI findings correlate with clinical presentation and patient outcomes.[22]

Management Strategies during Pregnancy

Prompt recognition and immediate thiamine supplementation

Management of WE during pregnancy necessitates prompt recognition and immediate initiation of treatment with thiamine

supplementation. Given the urgency of the condition and its potential to cause severe and irreversible neurological damage, rapid clinical assessment is critical. On suspicion of WE, particularly in pregnant women with hyperemesis gravidarum or other risk factors, high-dose intravenous thiamine should be administered without delay. The initial recommended dosage typically involves 500 mg of thiamine hydrochloride intravenously 3 times daily for the first 2–3 days. This aggressive approach ensures rapid replenishment of thiamine levels, aiming to halt the progression of neurological damage.[23]

Continuing thiamine supplementation and supportive measures

Following the acute phase, it is essential to continue thiamine supplementation throughout the remainder of the pregnancy and into the postpartum period to prevent recurrence. Once the initial critical period has passed and the patient shows signs of improvement, the regimen can be adjusted to oral thiamine, typically at doses of 100–250 mg/day. Alongside thiamine, comprehensive nutritional support is crucial. This includes rehydration with appropriate electrolyte solutions to correct any fluid and electrolyte imbalances caused by prolonged vomiting or malnutrition. Ensuring a well-balanced diet rich in essential nutrients helps in overall recovery and supports both maternal and fetal health. Regular monitoring of thiamine levels and overall nutritional status is necessary to adjust the supplementation as needed.[24]

Managing severe or refractory cases and monitoring

In cases where the response to initial thiamine supplementation is inadequate or if the condition is particularly severe, more intensive management may be required. This might involve prolonged intravenous administration of thiamine or increased dosages tailored to the patient's clinical response. Close maternal and fetal monitoring is imperative to detect any complications early and to adjust the treatment plan accordingly. Monitoring should include regular neurological assessments, nutritional evaluations, and fetal well-being checks through appropriate obstetric monitoring techniques. In certain instances, coordination with a multidisciplinary team, including neurologists, obstetricians, and nutritionists, ensures comprehensive care for the patient. Management of severe cases might also necessitate additional imaging studies or adjustments in the supportive care regimen to address any concurrent issues effectively.[23]

Overall, the goal of these management strategies is to ensure timely and adequate thiamine repletion, provide supportive care to address nutritional deficiencies, and closely monitor both maternal and fetal health to mitigate the risks associated with WE during pregnancy.

Pharmacological Treatments and Guidelines

Thiamine administration protocols

A cornerstone of pharmacological treatment for WE is thiamine supplementation. This section will delve into the recommended thiamine administration protocols, emphasizing the importance of high-dose intravenous thiamine during the acute phase of the condition. Guidelines typically advocate for the administration of 500 mg of thiamine hydrochloride intravenously 3 times daily for the initial 2–3 days to rapidly replenish thiamine stores and prevent further neurological damage. Once the acute phase is managed, guidelines suggest transitioning to lower maintenance doses, usually administered orally, to sustain thiamine levels and prevent recurrence.[25] The efficacy and safety profiles of various thiamine formulations, including oral, intravenous, and intramuscular routes, will be critically compared to provide clinicians with evidence-based insights into optimal thiamine delivery methods.

Guidelines and recommendations

In addition to discussing thiamine administration protocols, this section will comprehensively review guidelines from major health organizations regarding the prevention and treatment of WE in pregnant women. These guidelines often stress the importance of routine thiamine supplementation in high-risk populations, such as pregnant women with hyperemesis gravidarum or those with a history of chronic alcoholism. By adhering to these guidelines, health-care providers can effectively identify at-risk individuals and implement preventive measures to mitigate the risk of WE development during pregnancy. Furthermore, potential side effects and contraindications of thiamine therapy will be meticulously examined to ensure a thorough understanding of pharmacological management. By delineating these guidelines and recommendations, this section aims to equip clinicians with the necessary knowledge and tools to optimize thiamine supplementation strategies and improve clinical outcomes in pregnant women at risk of WE.[26]

While current guidelines provide valuable insights into the pharmacological management of WE during pregnancy, ongoing research efforts continue to explore novel therapeutic approaches and refine existing treatment protocols. This section will briefly highlight promising avenues for future research, including investigations into alternative thiamine formulations, adjunctive therapies to enhance thiamine absorption and utilization, and potential biomarkers for early detection and monitoring of WE. By staying abreast of these developments, health-care providers can anticipate advancements in pharmacological treatments for WE and adapt their clinical practices accordingly, ultimately enhancing patient care and outcomes.[27]

Conclusion and Summary

The review will conclude by summarizing the key points discussed, emphasizing the critical importance of early diagnosis and prompt treatment of antepartum WE to prevent serious complications. It will reiterate the need for heightened awareness among health-care providers about the risk factors and clinical presentation of WE in pregnant women. The

summary will also highlight areas for future research, such as the development of better diagnostic tools and strategies for prevention in high-risk groups. This section will aim to leave the reader with a clear understanding of antepartum WE and the steps necessary to manage and prevent this serious condition effectively.

Conflicts of interest

None.

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References

1. Ott M, Werneke U. Wernicke's encephalopathy - from basic science to clinical practice. Part 1: Understanding the role of thiamine. Ther Adv Psychopharmacol 2020;10:204512532097810.
2. Fernandes LM, Bezerra FR, Monteiro MC, Silva ML, de Oliveira FR, Lima RR, *et al*. Thiamine deficiency, oxidative metabolic pathways and ethanol-induced neurotoxicity: How poor nutrition contributes to the alcoholic syndrome, as Marchiafava-Bignami disease. Eur J Clin Nutr 2017;71:580-6.
3. Elzouki AN, Habas E, Farfar K, Errayes N, Rayani A. Wernicke encephalopathy: An updated narrative review. Saudi J Med Med Sci 2023;11:193.
4. Berdai MA, Labib S, Harandou M. Wernicke's encephalopathy complicating hyperemesis during pregnancy. Case Rep Crit Care 2016;2016:8783932.
5. Ota Y, Capizzano AA, Moritani T, Naganawa S, Kurokawa R, Srinivasan A. Comprehensive review of Wernicke encephalopathy: Pathophysiology, clinical symptoms and imaging findings. Jpn J Radiol 2020;38:809-20.
6. Martin PR, Singleton CK, Hiller-Sturmhöfel S. The role of thiamine deficiency in alcoholic brain disease. Alcohol Res Health 2003;27:134-42.
7. Jennings LK, Mahdy H. Hyperemesis gravidarum. In: StatPearls. Treasure Island, FL: StatPearlsPublishing; 2023.
8. Nagarajan E, Rupareliya C, Bollu PC. Wernicke's encephalopathy as a rare complication of hyperemesis gravidarum: A case report and review of literature. Cureus 2018;10:e2597.
9. Whitfield KC, Bourassa MW, Adamolekun B, Bergeron G, Bettendorff L, Brown KH, *et al*. Thiamine deficiency disorders: Diagnosis, prevalence, and a roadmap for global control programs. Ann N Y Acad Sci 2018;1430:3-43.
10. Marcé-Grau A, Martí-Sánchez L, Baide-Mairena H, Ortigoza-Escobar JD, Pérez-Dueñas B. Genetic defects of thiamine transport and metabolism: A review of clinical phenotypes, genetics, and functional studies. J Inherit Metab Dis 2019;42:581-97.
11. Vasan S, Kumar A. Wernicke encephalopathy. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2023.
12. Feroze KB, Wang J. Internuclear ophthalmoplegia. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2023.
13. Rothblum-Oviatt C, Wright J, Lefton-Greif MA, McGrath-Morrow SA, Crawford TO, Lederman HM. Ataxia telangiectasia: A review. Orphanet J Rare Dis 2016;11:159.
14. Kassaw C, Wale T, Negash M, Temesgen K, Mekuriaw B, Tolessa O, *et al*. Cognitive disorder and associated factors among pregnant women attending antenatal service at Dilla University Referral Hospital, 2022. Front Glob Womens Health 2023;4:1061626.
15. Misra UK, Kalita J, Nair PP. Diagnostic approach to peripheral neuropathy. Ann Indian Acad Neurol 2008;11:89-97.
16. Coad F, Frise C. Tachycardia in pregnancy: When to worry? Clin Med 2021;21:e434-7.
17. Chung J, Berryman RP. An atypical case of a common pregnancy issue: Appendicitis-like hyperemesis gravidarum. Case Rep Med 2020;2020:6959605.
18. Borgemenke R, Borgemenke S, Mall S, Pagur P. Wernicke encephalopathy secondary to hyperemesis gravidarum in a 22-year-old female patient: A case report. Cureus 2023;15:e45172.
19. Dhir S, Tarasenko M, Napoli E, Giulivi C. Neurological, psychiatric, and biochemical aspects of thiamine deficiency in children and adults. Front Psychiatry 2019;10:207.
20. Sullivan EV, Pfefferbaum A. Neuroimaging of the Wernicke-korsakoff syndrome. Alcohol Alcohol 2009;44:155-65.
21. Jung YC, Chanraud S, Sullivan EV. Neuroimaging of Wernicke's encephalopathy and Korsakoff's syndrome. Neuropsychol Rev 2012;22:170-80.
22. Richter RH, Byerly D, Schultz D, Mansfield LT. Challenges in the interpretation of MRI examinations without radiographic correlation: Pearls and pitfalls to avoid. Cureus 2021;13:e16419.
23. Chandwani J, Kantor S, Sarma K, Albahrani MJ. Wernicke's encephalopathy following hyperemesis gravidarum. Indian J Crit Care Med 2014;18:164-6.
24. Nisar S, Kareem O, Muzaffer U, Tanvir M, Ganaie MA, Ahmed RN. Descriptive spectrum of thiamine deficiency in pregnancy: A potentially preventable condition. Int J Gynaecol Obstet 2024;164:157-65.
25. Latt N, Dore G. Thiamine in the treatment of Wernicke encephalopathy in patients with alcohol use disorders: Thiamine in Wernicke's encephalopathy. Intern Med J 2014;44:911-5.
26. Kareem O, Nisar S, Tanvir M, Muzaffer U, Bader GN. Thiamine deficiency in pregnancy and lactation: Implications and present perspectives. Front Nutr 2023;10:1080611.
27. Dathe K, Schaefer C. The use of medication in pregnancy. Dtsch Arztebl Int 2019;116:783-90.

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