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RESEARCH ARTICLE

HELLP SYNDROME

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ABSTRACT

HELLP syndrome is a life-threatening pregnancy complication usually considered to be a variant of preeclampsia. Both conditions usually occur during the later stages of pregnancy, or sometimes after childbirth. It has been known for a long time that preeclampsia may be associated with haemolysis, elevated liver enzymes and thrombocytopenia. Weinstein regarded signs and symptoms to constitute an entity separated from severe preeclampsia and in 1982 named the condition HELLP (H = Haemolysis, EL = Elevated Liver enzymes, LP = Low Platelets) syndrome. The HELLP is currently regarded as a variant of severe preeclampsia or a complication. Diagnosis of the complete form of the HELLP syndrome requires the presence of all 3 major components, while partial or incomplete HELLP syndrome consists of only 1 or 2 elements of the triad (H or EL or LP).

INTRODUCTION

HELLP syndrome is a life - threatening pregnancy complication usually considered to be a variant or complication of pre eclampsia. Both conditions usually occur during the later stages of pregnancy, or sometimes after child birth. HELLP is an abbreviation of the three main features of the syndrome. Hemolysis, Elevated liver enzymes, and Low platelet count. The syndrome may be associated with serious liver manifestation, including Infarction Hemorrhage, and rupture.[1, 2]

The spectrum of disease resulting from pathophysiology of pre-eclampsia continues to challenge diagnostic accuracy of clinicians out of pre-eclampsia's various manifestations; a specific entity is HELLP syndrome.

The acronym HELLP was coined by Weinstein in 1982 to describe a syndrome consisting of Hemolysis, Elevated liver enzymes and low platelet count.

Definition

It is a syndrome that is characterized by hepatic endothelial disruption followed by platelet activation, aggregation and consumption, ultimately resulting in ischemia and hepatocyte death.

-C Bansal

The term HELLP syndrome is used to describe preeclampsia in association with Hemolytic anemia, Elevated Liver enzyme levels, and Low Platelet count. The diagnosis is not always clear, and the syndrome may be confused with other medical conditions. Any patient diagnosed with HELLP syndrome should be considered to have severe preeclampsia.

Incidence

The incidence of HELLP syndrome is significantly higher in whites and women of European descent.

- HELLP syndrome - 0.2 to 0.6% of all pregnancies
- Pre eclampsia- 5 to 7% of all pregnancies
- 20% incidence of HELLP in women with pre eclampsia.
- 70% cases diagnosed in antenatal period while 30% after delivery.[3]

Causes and Risk Factors

The cause of HELLP syndrome is unknown, but there are certain factors that may increase your risk of developing it.

Preeclampsia is the greatest risk factor. This condition is marked by high blood pressure and swelling, and it typically occurs during the last trimester of pregnancy. However, not all pregnant women with preeclampsia will develop HELLP syndrome.[3]

Other risk factors

- Being over age 30
- Being caucasion
- Being very overweight
- Having previous pregnancies
- Having a poor diet
- Having diabetes

- History of preeclampsia

Pathophysiology

HELLP is a syndrome characterized by thrombocytopenia, hemolytic anemia, and liver dysfunction believed to result from microvascular endothelial activation and cell injury. growth factor (PGF), causing endothelial cell and placental dysfunction by preventing them from binding endothelial cell receptors. The result is hypertension, proteinuria, and increased platelet activation and aggregation. The pathophysiology of HELLP syndromeis ill defined. Some theorize that, because HELLP is a variant of pre eclampsia, the pathophysiology stems from a common source. In pre eclampsia, defective placental vascular remodeling during weeks 16-22 of pregnancy with the second wave of trophoblastic invasion in to the decidua results in inadequate placental perfusion. The hypoxic placenta then releases various placental factors such as soluble vascular endothelial growth factor receptor-1(Svegfr-1), which then binds vascular endothelial growth factor(VEGF) and placental

Furthermore, activation of the coagulation cascade causes consumption of platelets due to adhesion on to a damaged and actvated endothelium, in addition to microangiopathichemolysis caused by shearing of erythrocytes as they traverse through capillaries laden with platelet-fibrin deposits. Multiorgan microvascular injury and hepatic necrosis causing liver dysfunction contribute to the development of HELLP.

Another hypothesis proposes acute maternal immune rejection due to immunocompetent maternal cells coming in to contact with a genetically distinct fetus , altering the maternal- fetal immune balance and causing endothelial dysfunction, platelet activation and aggregation, and arterial hypertension.

Other theories include inborn in born errors of fatty acid oxidative metabolism secondary to long and medium-chain fatty acid mutations, which cause liver damage secondary to insufficient mitochondrial oxidation of fatty acids required for ketogenesis.

Yet another theory suggests a placental instigated acute inflammatory condition targeting the liver.

In addition, dysfunction in the complement system via excessive activation or defective regulation for a given amount of endothelial injury has been proposed to cause damage to hepatic vessels in HELLP.

Many hypothesis attempt to define the pathogenesis of HELLP syndrome, but the true pathology remains a mystery.[6]

Signs and Symptoms

HELLP syndrome symptoms are very similar to those of the flu. The symptoms may seem to be “normal” symptoms of pregnancy. The symptoms of HELLP syndrome may vary from person to-person, but the most common ones include:

- Nausea/vomiting/indigestion with pain after eating
- Abdominal or chest tenderness and upper right upper side pain(from liver distention)
- Shoulder pain or pain when breathing deeply
- Bleeding
- Changes in vision
- Swelling
- Feeling generally unwell or fatigued
- Headache
- Excessive and sudden weight gain

signs to look for include
high blood pressure
protein in the urine[4]

Diagnostic Evaluation

Certain tests can also help your doctor make a diagnosis. Your doctor may also order a:

- Blood test to evaluate platelet levels and red blood cell count
- Urine test to check for elevated liver enzymes and abnormal proteins
- MRI to determine whether there’s bleeding in the liver

Blood tests

- Complete blood count with platelet count
- Peripheral smear evaluation
- Serum AST, lactate dehydrogenase, bilirubin, and coagulation studies.
- Creatinine

Controversial

Hemolysis

Serum lactate dehydrogenase>600U/L characteristic peripheral smear

Indirect hyberbilirubinemia-usually present, but not necessary for presumptive diagnosis

Elevated liver enzymes

Serum aspartateaminotransferase>70U/L

Lowplatelets(<100 109/L).

Absence of hemolysis; i.e. HELLP syndrome and partial HELLP syndrome are other diagnoses that can be entertained.

Partial HELLP syndrome

- Elivated liver enzymes(serum aspartate
- Aminotransferase>40U/L),
- Low platelets(<150 109/L)
- withor without evidence of hemolysis.

Severe thrombocytopenia

Portends poor prognosis and urgent need for management. Abnormally elevated prothrombin time signifies an underlying DIC Haemolytic uremic syndrome and thrombotic thrombocytopenic purpura

Albeit uncommon in pregnancy, are other mimics of HELLP syndrome.

Liver biopsy

- Changes of sinusoidal congestion with fibrin plug formation
- Hemorrhage and hepatocyte necrosis are similar to patients with pre-eclamptic liverdysfunction[5]

Management of Pregnant Women With Hellp Syndrome

In general, there are three major options for the management of women with severe preeclampsia and HELLP syndrome. these include

1. Immediate delivery which is the primary choice at 34 weeks gestation later.
2. Delivery within-48 hours after evaluation, stabilization of the maternal clinical condition and cs treatment. At 27 to 34 weeks of gestation, this option appears appropriate and rationale for the majority of cases.
3. Expectant (conservative) management for more than 48-72 hours may be considered in pregnant women before 27 weeks gestation. In this situation, cstreatment is often used, but the regimens vary considerably.

Conservative Management (>48 Hours)

Large randomized clinical trials aimed to compare conservative versus aggressive management with immediate delivery of women with the HELLP syndrome are missing. However, expectant management before completed 34 weeks gestation may be an acceptable option in selected cases if it is performed in tertiary care units under close maternal foetal surveillance (e.g. antihypertensive treatment, ultrasound and Doppler examination). Possible advantages due to limited prolongation of pregnancy should be carefully weighed against the increased risks of maternal and foetal complications (abruption placentae, acute renal failure, pulmonary oedema, DIC, perinatal and maternal death) If the maternal condition worsens, immediate caesarean section is inevitable. Conservative treatment is contraindicated in women with DIC.

The benefit of temporizing management of HELLP syndrome is questioned; some authors warn against expectant management to optimize maternal condition before delivery beyond 24-48 hours or conservative management is disregarded. However, expectant management of pregnant women with HELLP syndrome remote from term is common practice in the Netherlands, conditional on the safety of the mother.

Corticosteroid (CS) treatment Promotion of fetal lung maturation in threatening preterm delivery

Irrespective of the underlying condition, preterm delivery (<37 weeks 'gestation) carries the risk of RDS in neonates because of insufficient surfactant production in foetal lungs. The neonates can be treated with corticosteroid and surfactant. Prenatal corticosteroid treatment has been shown to accelerate foetal lung maturation through a complex interaction of hormonal and intercellular signaling that leads to differentiation of the surfactant lipid-protein pathway and through less well-defined increases in lung compliance. The foetal lung must be biologically ready for a corticosteroid to "trigger" maturation in humans this window of biological readiness of the lungs seems to occur most often between 26 and 33 weeks' gestation.

Recently, betamethasone, instead of dexamethasone, has been recommended as a drug of choice for promotion of foetal lung maturation in threatening preterm delivery. In clinical trials as well as observational studies antenatal corticosteroid treatment is associated with a decreased risk of IVH and CP. Betamethasone may be safer and more protective of the immature brain than dexamethasone.

In a retrospective cohort study by Baud et al. comprising 883 infants with gestational age between 24 and 31 weeks it was reported an odds ratio for cystic periventricularleucomalasia of 0.5 for betamethasone compared with no treatment and 1.5 for the dexamethasone treated group. Treatment of severe preeclampsia with betamethasone in the time span between 26 and 34 weeks' gestation has been shown to significantly reduce the rate of RDS, IVH and perinatal death in preterm delivery. A Cochrane update from 2006 advocated a single course of antenatal corticosteroid (12mg betamethasone twice) in gestational ages between the 26^{th} and 35^{th} gestational weeks. Thus a single course of corticosteroid is advocated in threatening preterm delivery, including severe preeclampsia.

Corticosteroid Treatment for the Women With Syndrome Hellp

Whereas delivery is the mainstay of treatment for the HELLP syndrome, corticosteroid treatment is a possible addendum. Present alternatives for corticosteroid treatment are:

1. Standard corticosteroid treatment to promote foetal lung maturity
2. High-dose dexamethasone treatment of the mother or
3. Treatment with repeated doses to reduce maternal morbidity and hastening recovery.

Evaluation of standard corticosteroid treatment on maternal HELLP

It remains uncertain if standard corticosteroid treatment to induce foetal lung maturation has been convincingly shown to benefit the woman with HELLP. A recent review confirmed that corticosteroid increased the PLT count without improving maternal morbidity in the HELLP syndrome. Thus, standard corticosteroid treatment has only minor clinical effects in the HELLP syndrome. Strong evidence for recommending standard corticosteroid treatment in women with the HELLP syndrome has not been presented.

High dose dexamethasone treatment of maternal HELLP

Retrospective and small randomized studies suggested that the use of high dose dexamethasone in the HELLP syndrome reduced maternal morbidity and induced more rapid improvement of the PLT counts. There by the rate of regional anaesthesia could be increased, consequently allowing vaginal delivery. In a publication from 2006 by Martin et al. aggressive use of potent GS was recommended as a cornerstone of management for women with the HELLP syndrome class 1 and 2 or for women with class 3 HELLP syndrome accompanied with epigastric pain, eclampsia, severe hypertension or evidence of major organ morbidity. corticosteroid treatment was recommended only as short-term intervention. Continuation of pregnancy for more than 48 hours after CS administration for very preterm HELLP syndrome can lead to significant maternal and foetal morbidity and mortality.

Other Treatment Options

Treatment with antithrombin has been suggested as a possible therapeutic option for preeclampsia. In a randomized study of severe preeclampsia it was shown that antithrombin supplementation may correct hypercoagulability, stimulate

prostacyclin production, regulate thrombin- induced vasoconstriction, improve fetal status and promote fetal growth. The potential benefit from antithrombin treatment of women with HELLP syndrome might be a reasonable objective to be tested in future well designed multicenter studies.

Management of Post-Partum Hellp Syndrome

In most women with a HELLP syndrome, the maternal PLT counts continue to decrease immediately post-partum with an increasing trend on the third day. About 30% of the HELLP syndromes develop after birth; the majority with in the first 48 hours. However, the time of onset might range from a few hours to 7 days after delivery. In women with post- partum HELLP syndrome, risk of renal failure and pulmonary oedema is significantly increased compared to those with an antenatal onset. Since early post-partum administration of high-dose CS might accelerate recovery, its routine administration is highly advocate.[7,8,9,10]

Possible Complications of Hellp Syndrome

Complications associated with HELLP syndrome include

- Blood clots
- Liver rupture
- Kidney failure
- Acute respiratory failure
- Fluid in the lungs
- Excessive bleeding during delivery
- Placental abruption, which occurs when the placenta detaches from the uterus before the baby is born
- Stroke
- Death

Early treatment is the key to preventing these complications, however, some complications may occur during treatment. Symptoms of HELLP syndrome can also affect you and your baby.[sx]

References

1. Haram K, Svendsen E, Abildgaard U. The HELLP syndrome: clinical issues and management. A Review. BMC pregnancy and childbirth. 2009 Feb 26; 9(1):8.
2. Weinstein L. Syndrome of hemolysis, elevated liver enzymes, and low platelet count: a severe consequence of hypertension in pregnancy. American journal of obstetrics and gynecology. 1982 Jan 15; 142(2):159-67.
3. kristeenmoore. Tylerwalker, MD. Hellpsyndrome (INTERNET). healthline; on April 10, 2017.available from:www.healthline.com/health/hellpsyndrome#overview1
4. Sibai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. *Obstetrics & Gynecology*. 2004 May 1; 103(5, Part 1):981-91.
5. http://emedicine.medscape.com/article/1394126-overview#a3

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6. https://www.ncbi.nlm.nih.gov/pmc/articles/pmc2654858/
   a. Pritchard JA, Weisman R,Jr, Ratnoff OD, Vosburgh GI Intravascular hemolysis, thrombocytopenia and other hematologic abnormalities associated with severe toxemia of pregnancy. *N Engl JMED*.1954;250:
7. Murphy MA, AYAZIFar M. permanent visual deficits secondary to the HELLP syndrome. *J Neuroopthalmol* 2005; 25:
8. Visser W, Wallenburg HC. Temporising management of severe preeclampsia with and without the HELLP syndrome. *Br J obstetgynaecol*. 1995;
9. Van Runnard Heime lPJ, Franx A, schobben AF, Huisjes AJ, Derks JB, Bruinse HW. corticosteroids, pregnancy, and HELLP syndrome: a review, *obstet Gynaecolsur*
10. Wilke G, Rath W, Schutz E, Armstrong VW, Kuhn W. Haptoglobin as a sensitive marker of hemolysis in HELLP-syndrome. *Int J Gynaecol Obstet*. 1992; 39:29-34. doi: 10.1016/0020-7292(92)90776-F. [PubMed] [Cross Ref
11. Rath W, Faridi A, Dudenhausen JW. HELLP syndrome. *J Perinat Med*. 2000; 28:249-260. doi: 10.1515/JPM.2000.033. [PubMed][Cross Ref

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