

# Unusual Presentation Of A Case Of Liver Rupture Associated With HELLP Syndrome: A Case Report And Rapid Review

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## Abstract

**Introduction:** Liver capsule haematomas and rupture are uncommon serious complications in pregnancy where it is often associated with HELLP syndrome (Haemolysis, Elevated Liver Enzymes and Low Platelets). Hepatic bleeding occurs in 5% of cases with HELLP syndrome with associated high mortality and morbidity to both mother and fetus. This report explores the management of a case of liver rupture in a patient in the 31+4 week of gestation, with maternal and fetal survival.

**Methods:** A retrospective review of an unusual case of Liver rupture with underlying HELLP syndrome managed across two hospital sites. A Database search (PubMed and Embase) was performed for all cases of Liver rupture associated with pregnancy in the literature in English language for the time-period 2009-2020. Extraction and Analysis using the PRISMA tool.

**Results:** 57 published articles were identified with a total of 94 patients identified. 10 cases of liver rupture in pregnancy secondary to underlying liver pathology, including cancer have been excluded. An overview indicates that the mean maternal age at presentation was 33 years with rupture, commoner in primiparous women. Average gestational age was 33 weeks. Right liver lobe was the most common site of rupture. 9 required liver transplantation, with 8 maternal mortalities and 15 fetal losses.

**Conclusions:** An unusual case of Liver capsule rupture in pregnancy with a discussion of different management approaches (interventional radiology inclusive) and outcomes following a rapid review of available case series. The risk of significant maternal mortality and morbidity with fetal loss is recognised, often in cases of delayed diagnosis especially in primiparous women.

As there is a close association between HELLP and liver rupture, a vigilant approach and high index of suspicion is required to recognize cases of atypical presentation of liver rupture in patients with severe PET which are often quiet and insidious.

## INTRODUCTION

HELLP Syndrome is a triad of (haemolysis, elevated liver enzymes and low platelets). It is a serious and can be a fatal complication of severe pre-eclampsia (PET). It is associated with 92.8% of cases of liver capsule haematomas [1]. Spontaneous liver rupture which was first described by Abercrombie in 1844 [2]; is a rare complication of HELLP syndrome and is associated with a high maternal mortality of 60-86% [3] with a significant fetal mortality and morbidity. Spontaneous rupture of a subcapsular liver haematoma in pregnancy is a rare incident occurring in 1/40,000-1/250,000 deliveries and in about 1 to 2% of the cases with HELLP syndrome [1]. The trigger factor for the liver capsule rupture

is not clear however it is believed to be secondary to underlying vascular endothelial damage and intravascular platelets aggregation.

There is a strong association between PET (Pre-eclamptic toxemia of pregnancy) and HELLP syndrome. Patients who develop HELLP syndrome requiring delivery prior to 34 weeks gestation have a 33% risk of developing pre-eclampsia in future pregnancies. In patients with pre-eclampsia, there is a 5 folds increased risk of developing hypertensive diseases later on life with 2 times increased risk of later developing a major cardiovascular disease with resultant mortality [4].

While most liver rupture cases have a common clinical picture of right hypochondrial pain, epigastric pain, vomiting, sudden hypotension, not all do leading to a non-specific presentation such as isolated shoulder pain, as demonstrated in our report. A delay in diagnosis and management until other alarming features manifest, can ensue. Hepatic rupture may also present in postpartum period [5,6 ] leading to a possible delay in diagnosis.

HELLP syndrome and spontaneous liver rupture is a medical emergency. Although, the imaging modalities like ultrasonography, computed tomography scan, peritoneal aspirate and angiography can diagnose Liver capsule haematoma +/- active bleeding, however the diagnosis is usually made based on the clinical picture. Patients usually present as acute cases which require urgent intervention including emergency caesarean section and laparotomies. There are different modalities to treat liver capsule haematomas including packing, resection, hepatic artery ligation or embolisation and liver transplantation. However in patients with coagulopathy, less aggressive management is preferable [7].

This is an unusual case of hepatic rupture in pregnancy as well as a rapid review of the recent case series.

## **MATERIALS AND METHODS**

A retrospective reviewed database in English language literatures were searched for 'hepatic rupture' and 'pregnancy' using PubMed, Medline, Cochrane Library, Cinahl and BJOG in order to identify all cases of Liver rupture in pregnancy over the duration of time (2009-2020).

The PRISMA model was used to identify papers across different databases: screen and eliminate unsuitable papers using Liver rupture, hepatic bleeding and pregnancy as keywords. An overview was obtained which was further streamlined and then analysed depending on available datasets.

The management of our individual case was compared to the optimum modality of management alongside maternal and fetal outcomes in the above dataset analysis using an Excel spreadsheet after the PRISMA model was used. Appropriate ethical approval was obtained.

## **CASE REPORT**

A 36 year old lady, primigravida .31+3/40 weeks pregnant presented to A&E in a district general hospital with sudden

onset of sharp pain in right shoulder that woke her up from sleep. This was followed by abdominal pain and dizziness. The initial diagnosis in A&E was that of a pulmonary embolism given the additional background history of prolonged immobility following recent cross-country travel during her ongoing holiday. Initial blood picture showed thrombocytopenia and elevated liver enzymes [Platelets (98) normal value is  $150 - 400 \times 10^9/L$ : ALT (390) normal value is 7-35 U/L ]. As a result obstetric review was requested in view of a possible HELLP diagnosis.

Her obstetric review revealed a previously low risk pregnancy with no significant past medical history however on examination she had borderline tachycardia with a raised blood pressure though within limits of normal and a trace of proteinuria. There were no neurological nor additional renal concerns. A working diagnosis of evolving PET/HELLP was made. More so as she was not anaemic with a normal coagulation screen [PT: 11.1s, APTT: 29.3s and INR: 0.9]. Other differentials such as gestational thrombocytopenia and Immune thrombocytopenia of pregnancy were thought to be unlikely.

Whilst undergoing further work-up, there was a need for immediate Caesarean Section due to sudden fetal compromise as indicated on the fetal cardiotocograph. The baby was delivered by low transverse incision, intubated and admitted to NICU in fairly good condition [A female baby weighs 1500 gram at delivery with Apgar scores of 8, 9 at 1 and 5 minutes respectively]. This was then converted to laparotomy following the presence of large clots in the pelvis which could be traced back to active bleeding from the liver.

Once the woman was initially resuscitated with the local protocol regarding massive obstetric haemorrhage (a combination of blood, platelets and fresh frozen plasma products with the concomitant use of antifibrinolytics), the surgical and vascular teams packed the liver to ensure some degree of haemostatic control whilst further intraoperative imaging was arranged to identify the extent and size of the underlying liver haematomas.

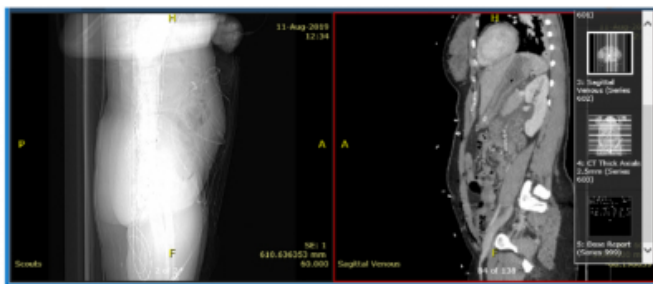
Imaging had identified multiple liver capsule haematomas with a probable active bleeding vessel from the liver capsule adjacent to anterior segment of right hepatic lobe and a moderate amount of peritoneal blood adjacent to the right lobe. Further exploration was performed, securing haemostasis leaving in a drain. The total blood loss was

1700 ml.

She was then transferred for the embolization of the hepatic artery at the second hospital, a tertiary centre (fig.2) following which she was admitted to ITU for conservative management (with daily haematological surveillance and support) under joint obstetric and surgical care. She made good recovery over 14 days and was discharged home with no further intervention: follow-up was in a month whilst the neonate made good progress.

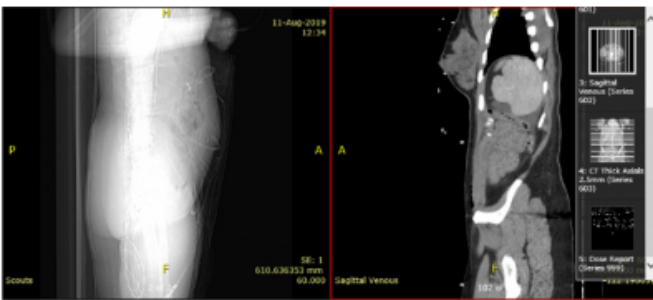
**Figure 1a**

CT scan after laparotomy showing multiple Liver capsule haematomas confined to right haepatic lobe with probable active bleeding.



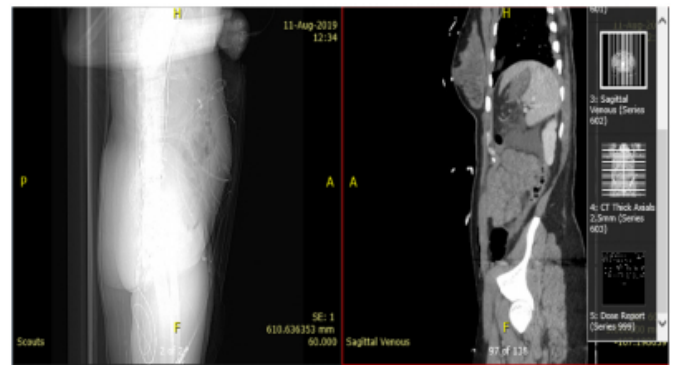
**Figure 1b**

CT scan after laparotomy showing multiple Liver capsule haematomas confined to right haepatic lobe with probable active bleeding.



**Figure 1c**

CT scan after laparotomy showing multiple Liver capsule haematomas confined to right haepatic lobe with probable active bleeding.



**Figure 2ab**

Hepatic artery vessel before and after embolization



## DISCUSSION

The first case of hepatic rupture in pregnancy was described in 1844 by Abercombe [3,8]. A century later, Pritchard et al first described the association of haemolysis, elevated liver enzymes and thrombocytopenia in 1954 [2][3]. The idiom HELLP was first instated by Weinstein in 1982 [3,9].

Despite this, the pathophysiology of HELLP syndrome is not completely understood. It is thought to be secondary to endothelial dysfunction [1,3]. Like pre-eclampsia, defective placental invasion can lead to increased uterine arterial resistance with resultant increased sensitivity to vasoconstriction and thus chronic placental ischemia and oxidative stress [1,3]. This results in the release of a variety of substances and cytokines, particularly products of abnormal metabolism of nitric oxide, prostaglandins, endothelin, free radicals, oxidized lipids, cytokines, and serum soluble vascular endothelial growth factor 1 [1,3].

These events induces endothelial dysfunction responsible for the signs and symptoms of HELLP observed in the mother: haemolysis due to microangiopathic changes then causes

shearing stress and red blood cells fragmentation as they pass through small blood vessels with damaged endothelium compounded with fibrin deposits: elevated liver enzymes secondary to damage to hepatic vascular endothelium: thrombocytopenia due to platelets aggregation and consumption secondary to damaged small vessels intima [1]. Neurological symptoms including eclampsia, is due to impairment of cerebral endothelium [1]. Blockage of the slit diaphragms in renal basement membranes ,as a result of increased endotheliosis , in addition to the decrease in glomerular filtration rate causes proteinuria .The microangiopathic haemolytic anaemia, low albumin level and vascular hypermobility leads to oedema particularly in lower and upper limbs and can be in lungs in severe cases[1]. The microthrombi and fibrin mesh deposits then obstruct the hepatic sinusoids which causes ischemia, hepatic swelling and ultimately liver rupture [3].

Liver rupture in pregnancy presents a challenge to both diagnosis and management. Typically, it has a biphasic presentation [10,11]. The prodromal phase is caused by development of liver haematomas and manifests as abdominal pain, nausea and vomiting. And the acute phase, caused by haematomas rupture, presents as hypotension and dizziness. Bleeding into the abdominal cavity causes diaphragmatic irritation with resultant shoulder pain. Liver rupture can present in the antepartum, intrapartum or postpartum period [3][5]. A high index of suspicion, vigilant approach and identification of deterioration is required to diagnose cases of liver rupture in association with pregnancy especially when present with non-specific symptoms.

**Diagnosis** is based mainly on the clinical picture at presentation with intra-operative findings as a rapid course of deterioration is expected in most cases. There is a limited role of imaging for pre-operative diagnostic work and in most cases the diagnosis is made based on the findings of significant hemoperitoneum at the time of emergency caesarean section.

However, in clinically stable patients with no urgency for fetal delivery, abdominal ultrasonography, CT scan and MRI can be used to diagnose underlying liver pathology following review of haematological and biochemical indices. It is worth noting that the ultrasound identification is operator-dependant with subtle liver capsule haematomas and bleeding easily missed by the non-vigilant operator. CT scan and MRI can also be used for follow up of patients with

confirmed liver capsule haematomas / rupture that have been managed conservatively [3,12].

The general blood picture of low platelets and haemolysis might not present initially at the time of presentation which in itself presents a diagnostic dilemma. Elevated Liver enzymes secondary to liver injury can be the first alarming feature that raises the suspicion of HELLP [3].

**Management** plan should rest on early recognition of the signs and symptoms with appropriate assessment of the clinical situation. It is crucial to deliver the baby and placenta whilst securing haemostasis in all patients before deciding further management plan. This may be by a combination of peri-hepatic packing followed by intraoperative imaging +/- interventional radiology +/- a re-look laparotomy depending on resource availability. Conservative management is the preferred option in cases of liver haematomas without rupture and is possible with appropriate support in cases of confined haematomas [13].

The trajectory of symptoms following conservative management is variable as a few patients required a re-laparotomy for further bleeding highlighted by the sudden onset of hypotension and haemodynamic instability postoperatively. A wide range of surgical techniques can be used including peri-hepatic packing, fibrin gluing, use of Tachosil plates, suturing, drainage, hepatic resection and liver transplantation, if conservative management with tamponade effect from peri-hepatic packing and close monitoring is insufficient.

When the liver bleeding is confined to a particular anatomical lobe then hepatic artery embolization is the preferred intervention [14]. Percutaneous hepatic artery embolization can be used as the first line of management especially in haemodynamically stable patients with postpartum liver capsule rupture [15].

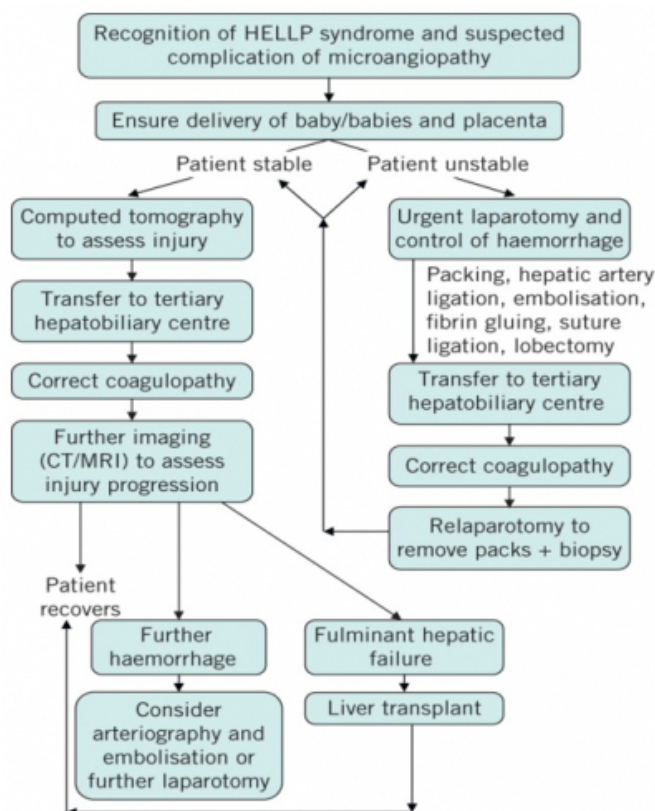
Hepatic lobe resection is done when the liver biopsy suggests tissue necrosis. Diffuse hepatic necrosis with no significant normal liver parenchyma, fulminant liver failure and uncontrolled haemorrhage during laparotomy are indications for liver transplantation. It is difficult to determine the post-operative course.

It is important to remember that the delivery of the fetus does not eliminate the risk of liver rupture in cases with HELLP syndrome [14] and should not obviate a need to identify and treat in the postpartum period.

The best approach is still not established with a unique common strategy yet to be defined [13].

**Figure 3**

Flow chart of management of HELLP syndrome and suspected liver injury .Flow chart adopted from [Wilson et al, 2014] with permission



## RAPID REVIEW

Our review of the available case reports and series revealed 94 cases of liver rupture in 57 publications over an 11-year period related to severe PET complications. 10 cases of liver rupture in pregnancy secondary to underlying liver pathology, including cancer have been excluded

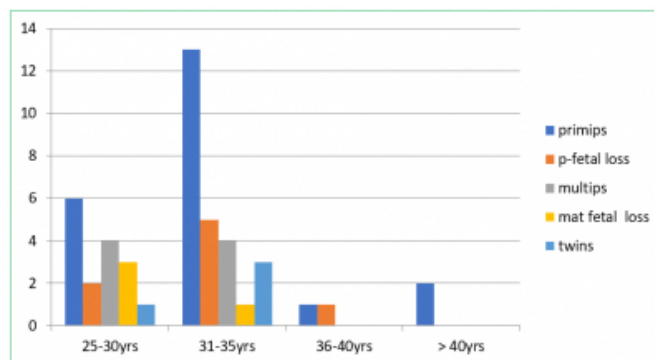
Our review of the 84 cases shows that the prevalence of liver rupture is double in primiparous women. Right liver lobe was the most common site of rupture.

Further breakdown of data whilst using the PRISMA format; excluding those with incomplete datasets (age, parity, maternal or fetal outcomes and management) show a predominance of primiparous women within the antenatal period in the 30 identified cases with a variation of management protocol which was largely focused on suturing, liver surface packing and sometimes hepatic artery embolisation. There was a case identified in the postpartum

period.

**Figure 4**

Bar chart comparing fetal losses in primips/ multips across age ranges



A maternal mortality was recorded in each group, both were in their early 30's. Of the 5 twin sets (4 sets in the primiparous women), there was loss of a twinset at 37 weeks gestation age in one of the primiparous women.

A deviation to a higher incidence in primiparous women could not be fully explained. As the higher prevalence in multiparous women as seen in older previous studies [14,15], was supported by the theory that unlike pre-eclampsia, HELLP syndrome is more common with increasing parity and is more severe in older women [16]

The validity of these findings is affected due to the paucity of available information as patient's demographic information were not reported fully in several publications alongside parity in over half of the cases in studies which were largely case reports or series due to the fairly uncommon incidence of a potentially fatal condition.

Another theory to explain the increased incidence of Liver rupture in primiparous women could be rising numbers of parturients particularly of an advancing maternal age [18-25]; a reflection of the times due to a desire to delay childbearing in favour of socioeconomic stability supported by readily available fertility treatment options.

This is more pertinent as advanced maternal age remains a significant singular risk factor for increased severity and morbidity associated with HELLP syndrome. Surprisingly the older mothers fared much better than their younger counterparts. This could be due to chance or positive bias reporting.

Few patients required re-laparotomy for further bleeding

highlighted by the sudden onset of hypotension and haemodynamic instability postoperatively. [26-28]. Management was seen to be varied and described in no certain order, therefore conferring no superiority to any one approach but seen more as a response to deteriorating maternal condition[29].

An overview of the 84 cases described maternal mortality in 7 patients with a total of 15 fetal losses including late miscarriages and IUD, 12 patients treated by hepatic artery embolization and liver transplantation in 9 patients.

Our case aligned closely to some of the findings of the review. But more research is needed to identify causal links and help formulate a treatment algorithm.

## CONCLUSION

A large series of patients with Liver capsule rupture in pregnancy with different management approaches and outcomes has been presented vis-à-vis our experience. Recent MBRRACE-UK report, a national audit tool, shows that maternal death secondary to PET complications (2%) continues to be low which reflects proper identification and management of patients with PET. However, as there is a close association between HELLP and liver rupture, a vigilant approach and high index of suspicion is required to recognize cases of atypical presentation of PET patients with veiled liver complications in a timely fashion.

As interventional radiology offers a minimally invasive, safe and approachable alternative to conventional surgical techniques in securing haemostasis and reducing the morbidity associated with further laparotomies and mortality; an increased use of this intervention in management of the relatively stable patient should be considered in carefully selected cases whilst an optimum treatment protocol is created pending further research.

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