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Original Research Article

Histopathological study of direct causes of maternal deaths

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Abstract

Background: Maternal mortality is an index of reproductive health of the society. The leading cause of maternal deaths are direct, which include sepsis, haemorrhage, hypertensive disorders, obstructed labour, abortions and others.
Aim: To study the histopathology of various organs in direct causes of maternal deaths.
Materials and Methods: This is an observational descriptive type of study carried out in the department of Pathology, in a tertiary care hospital for a total period of 4 and half years from 1st January 2016 to 30th June 2020. Histopathological examination was performed on organs from maternal autopsies which were performed in our institute.
Results: A total of 65 cases were studied. Maximum number of cases were seen in the age group of 21-25 years and in multigravida. The commonest mode of delivery was vaginal delivery. Puerperal sepsis was the most frequent cause of death which constituted 26.15% followed by postpartum haemorrhage (21.54%) and Toxaemia of pregnancy (20%).
Conclusion: Puerperal sepsis was the most common, but preventable cause of death. Histopathological findings of organs from maternal autopsies with clinical correlation always helps to finalise a cause of death in maternal deaths and is therefore always recommended.

Keywords: Histopathological, Maternal death, Sepsis, Haemorrhage.

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1. Introduction

Motherhood is an event of joy and celebrations for every family. Pregnancy is a natural phenomenon and is considered a physiological state, while also carries risk of serious maternal morbidity and at times death, various complications that may occur during pregnancy, labour or thereafter. The United Nations (UN) launched the Sustainable Development Goals (SDG) in 2015, and came into force from 1st January 2016, with goal 3: “Ensure healthy lives and promote well-being for all at all ages” and target 3.1 to reduce the global maternal mortality ratio to less than 70/100,000 live births by 2030.[1]

Maternal death is defined as death of a women occurring while pregnant or within 42 days of termination of pregnancy irrespective of the duration and site of pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes.[2] A high incidence of maternal deaths reflects low socioeconomic status of the community, poor quality of maternal services, and late referral.[3] The causes of maternal death have been classified as direct (resulting from obstetric complications of pregnancy, labour or puerperium) and indirect (resulting from pre-existing disease or disease aggravated by physiological effects of pregnancy). [4,5]

The exact cause of death is usually evident from the histopathological study in correlation with clinical information in maternal deaths, which will help to achieve the goal. The present study is initiated to analyse histopathological findings of various lesions in organs in direct causes of maternal death.

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2. Materials and Methods

The present study is an observational descriptive type of study carried out in the department of Pathology, in a tertiary care hospital for a total period of 4 years and 6 months from 1st January 2016 to 30th June 2020. The sample size was 65 cases which included maternal deaths from direct cause of death. The study includes organs from maternal autopsies which were performed in our institute. In all the cases, the gross and microscopic features of various lesions from different organs were studied to arrive at histopathologic diagnosis. The cause of death was declared from the clinical details along with available investigations, histopathologic diagnosis and from the discussion on these cases during maternal mortality meetings.

3. Results

All the cases were medicolegal autopsies and representative tissues whole or part of organs were received for histopathological examination. The total number of medicolegal autopsy specimens received during this period was 722; out of these, there were total 65 maternal autopsy specimens with direct cause of death.

Among total 65 cases, age of the patients ranged from 18- 42 years. The maximum number of cases were seen in the age group of 21-25 years, constituting 34(52.3%) cases. Thirty seven (57%) cases were multigravida.

In our study majority of the cases were delivered vaginally (n-31, 47.7%), followed by Lower segment caesarean section 19(29%). Abortion and antenatal deaths (undelivered cases) constituted 5(7.7%) and 10(15.4%) cases respectively.

Postpartum deaths (77%) were more common than antepartum deaths (23%). Among postpartum deaths, 21(42%) occurred in 1-6 days, 15(30%) occurred within 24 hours and 14(28%) deaths occurred after 7 days of delivery.

In our study out of antenatal deaths, most of the patients died in third trimester 58(89.2%), followed by 4(6.2%) cases in 2nd trimester and 3(4.6%) patients in first trimester. Minimum gestational age in maternal death was 10 weeks and maximum gestational age was 40 weeks.

Cause of death in all the cases was finalised after correlating clinical information and diagnosis from the requisition forms with postmortem findings and histopathology findings. The cases were also discussed in maternal mortality meetings. **Table 1** shows distribution of cause of maternal deaths.

Table 1: Distribution of cause of maternal deaths

S. No.	Cause of Death	No.	%
1.	Puerperal sepsis	17	26.15
2.	Postpartum haemorrhage	14	21.54
3.	Toxaemia of pregnancy	13	20
4.	Disseminated intravascular coagulation	7	10.76
5.	Pulmonary thromboembolism	6	9.23
6.	Spontaneous abortion	2	3.08
7.	Ruptured ectopic pregnancy	2	3.08
8.	Antepartum haemorrhage	1	1.54
9.	Peripartum dilated cardiomyopathy	1	1.54
10.	Acute fatty liver of pregnancy (AFLP)	1	1.54
11.	ARDS	1	1.54
	Total	65	100

Among the direct causes, puerperal sepsis was the most frequently seen cause which constituted 26.15% of the cases followed by postpartum haemorrhage (21.54%) and Toxaemia of pregnancy (20%).

3.1. Puerperal sepsis

In our study puerperal sepsis was the most common direct cause of maternal death. Various histopathological findings were seen in the uterus (**Table 2**). The histopathology in death due to sepsis showed varied findings in different organs. A case of disseminated candidiasis was observed.

Table 2: Histopathological findings in uterus in puerperal sepsis

Histopathological finding	No of cases (%)
Acute deciduitis	10 (58.8%)
Acute myometritis	8 (47%)
Endometritis	2 (11.7%)
Chronic myometritis	1 (5.9%)
Micro abscesses in myometrium	3 (11.6%)
LSCS suture site inflammation	1 (5.9%)
Thrombi in myometrial vessels	2 (11.7%)
Retained products	1 (5.9%)
Focal haemorrhages in myometrium	1 (5.9%)

Commonest finding observed in uterus was acute deciduitis showing infiltration of polymorphs in decidualised endometrium. Other findings included acute myometritis, micro abscesses (**Figure 1** A,B) etc.

Along with findings in uterus, various findings were observed in other organs.

Pneumonia was seen in 5 cases, which constituted bronchopneumonia (3), lobar (1) (**Figure 1** C) and organizing pneumonia (1). Among these ones were confluent bronchopneumonia with abscess formation and acute fibrinous pleuritis. Micro abscesses in lung were seen in 2 cases, out of which one case had yeast forms of candida within the abscess.

In liver the findings were periportal inflammation in 5 cases, micro abscesses (**Figure 1** D) in 2 cases out of which one had bacterial colonies.

In kidney, focal chronic nonspecific interstitial nephritis was seen in 7 cases and acute on chronic tubulointerstitial nephritis in one. Multiple micro abscesses were seen in 3 cases out of which 2 cases had bacterial colonies and one case had yeast forms of candida. Acute pyelonephritis and acute tubular necrosis were seen in one case each.

Findings observed in heart included multiple micro abscesses in 3 cases, out of which one case had bacterial colonies and one case had yeast forms of candida. Focal myocardial neutrophilic infiltration and focal nonspecific myocarditis was seen in one case each.

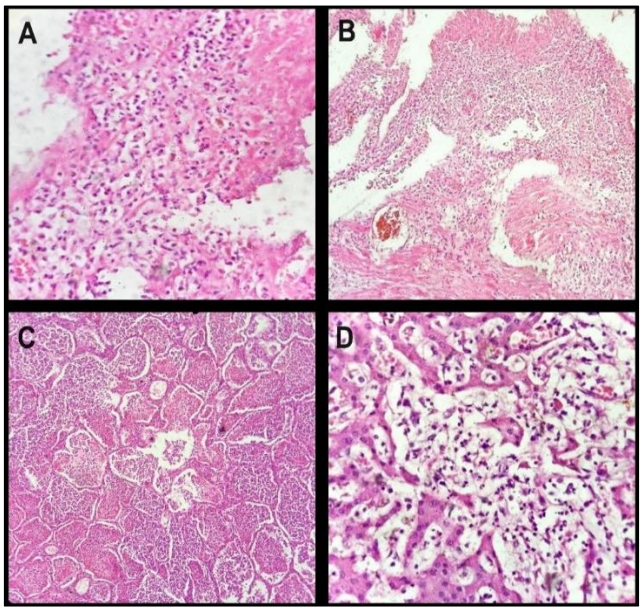

Figure 1: A): Photomicrograph of myometrium showing micro abscesses (H&E, X100); **B):** Photomicrograph of myometrium showing micro abscesses (H&E, X40); **C):** Photomicrograph of lung showing Lobar pneumonia (H&E, X40); **D):** Photomicrograph of liver showing micro abscesses (H&E, X400)

3.2. Postpartum hemorrhage

In our study PPH was the second most commonest cause. Causes of PPH are shown in **Table 3**.

Table 3: Distribution of causes of postpartum haemorrhage

Postpartum Hemorrhage	No of cases	%
Atonic Postpartum haemorrhage	7	50
Cervical tear	1	7.14
Retained placenta	3	21.42
Placenta previa with placenta increta	1	7.14
Uterine rupture	2	14.28

Among PPH, Atonic PPH constituted 50% of the cases, followed by cervical tear and uterine rupture.

In cases of postpartum haemorrhage, maximum findings were observed in uterus and cervix. Stromal haemorrhages in cervix were seen in 3 cases (**Figure 2** B), out of which one had retained placenta in cervix. (**Figure 2** C, D) One case had cervical tear with cervical haemorrhage extending into outer myometrium and into left sided fallopian tube and mesosalpinx. Another case showed extensive myometrial haemorrhage with focal pericardial and myocardial haemorrhage in left ventricle and right ventricle of heart.

There was a case of placenta previa with placenta increta, in which we found adherent urinary bladder to uterus. Grossly myometrium appeared thinned out and the placenta was implanted in lower uterine segment. The microscopic examination showed chorionic villi directly resting on myometrium extending into the myometrium without the intervening myometrium.

In 3 cases Obstetric hysterectomy was done, out of which we received two specimens. One case had history of delivery at home and presented with excessive pervaginal bleeding with retained placenta. While in second case, obstetric hysterectomy was done during emergency LSCS. On autopsy, findings were hemoperitoneum with clots in peritoneal cavity. On histopathological examination liver showed centrivenular and midzonal necrosis suggestive of hypoxic hepatitis.

We had two cases of uterine rupture. One was 35 yr old 2nd gravida who presented at 15 weeks of gestation with history of previous lower segment caesarean section. She underwent hysterectomy. After hysterectomy patient succumbed to death within 8 hours. Uterus showed rupture at the site of previous LSCS (**Figure 2** A). At the site of rupture, the sections showed myometrium along with placenta. Myometrium showed focal areas of necrosis, haemorrhage and infiltration by polymorphs. Other case was 30 yr old 4th gravida who had undergone full term normal vaginal delivery presented with excessive pervaginal bleeding. On examination her uterus showed evidence of rupture at lower uterine segment.

Histological findings seen in other organs include chronic venous congestion in lungs in two cases, centrilobular necrosis in liver in two cases, portal triaditis in

liver in one case, bilateral patchy cortical necrosis in kidney in a case, focal interstitial pneumonitis, focal intra-alveolar haemorrhages and pulmonary edema in lungs in one case each. Focal pericardial haemorrhage and myocarditis in heart was seen in one case each.

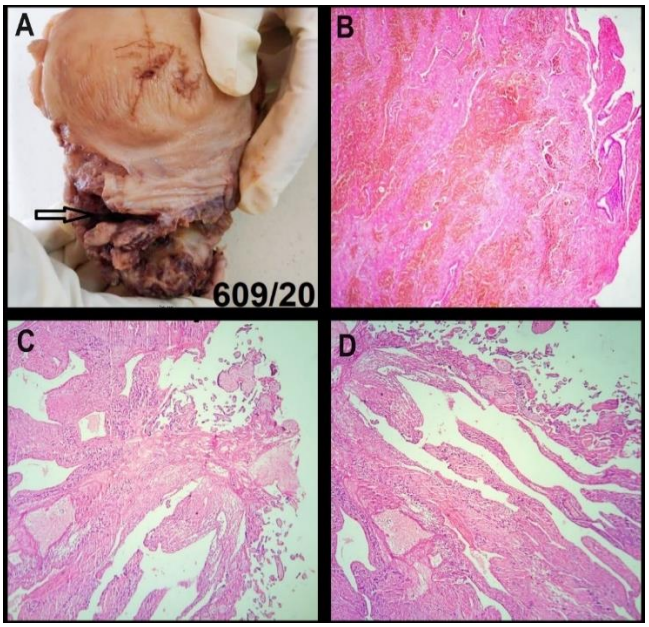

Figure 2: A): Gross photograph showing evident uterine rupture (arrow); **B):** Photomicrograph of Uterus showing stromal haemorrhages in cervix (H&E, X40); **C,D):** Photomicrograph of endometrium of uterus showing retained placenta (H&E, X40)

3.3. Toxaemia of pregnancy

There were 13 cases of toxaemia of pregnancy. Two cases presented with cortical venous thrombosis in known case of eclampsia. One case had cerebral micro haemorrhages. Six cases showed changes in liver consistent with eclampsia which included periportal and subcapsular fibrin deposits, foci of parenchymal necrosis, foci of dropout necrosis, focal subcapsular haemorrhages and lake haemorrhages in parenchyma of liver (**Figure 3**). Acute nonspecific periportal inflammation was seen in one case. In one case we received placenta in which increased intervillous and peri villous fibrin deposition, subchorionic fibrin deposition and increased syncytial knots were seen. Thrombi in meningeal vessels was seen in one case. Two cases showed evidence of bone marrow embolism in lungs. Other one case had bilateral cortical necrosis in kidney.

3.4. Disseminated intravascular coagulation

Disseminated intravascular coagulation was given as a cause of death in 7 cases. In three cases intrauterine death of foetus was seen, out of which one case had history of gestational hypertension and massive concealed abruptio placentae following which she developed DIC. She had haemorrhages in heart, liver and myometrium of uterus. Congestion was seen in lungs, spleen and kidney.

Second case had low platelet count, prolonged prothrombin time and elevated liver enzymes. She had centrilobular haemorrhagic necrosis in liver. Placenta showed intervillous haemorrhage with sickled red blood cells.

In the third case she had ascites and pleural effusion following emergency lower segment caesarean section.

One case had septicaemia along with disseminated intravascular coagulation, in which she had acute on chronic pyelonephritis with multiple abscess formation with occasional thrombi in blood vessels. Lungs had massive intraalveolar haemorrhage. Occasional fibrin thrombi in small pulmonary blood vessels and glomeruli of kidney were also noted (**Figure 4**). There were focal pericardial haemorrhages in heart.

Another case had disseminated intravascular coagulation due to consumptive coagulopathy in a case of haemorrhagic shock. She had thrombocytopenia and her D-dimer was high. She had hematoma on surface of liver and haemorrhages in cervix, and adnexa.

One case had disseminated intravascular coagulation with submassive hepatic necrosis with cholestasis. She also had cervical stromal haemorrhages.

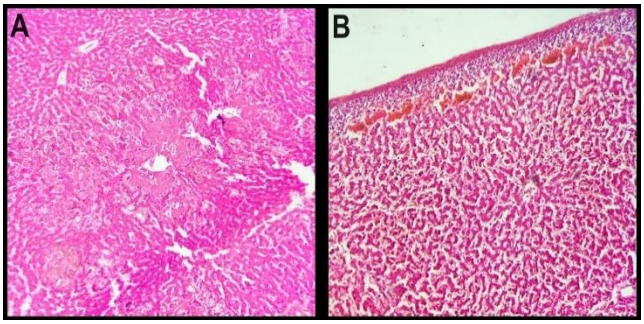

Figure 3: A): Photomicrograph of liver showing periportal fibrin deposit (H&E, X40); **B):** Photomicrograph of liver showing subcapsular haemorrhage (H&E, X40)

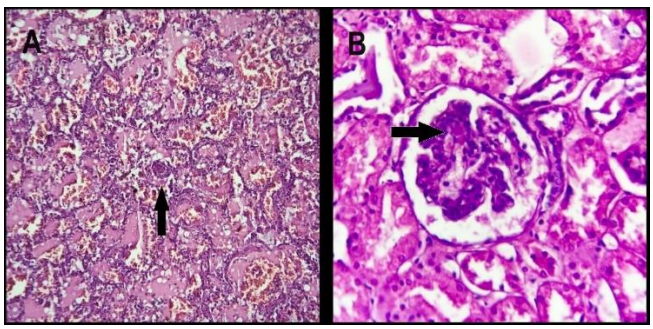

Figure 4: A): Photomicrograph of lung showing fibrin thrombi in small pulmonary blood vessel (H&E, X100); **B):** Photomicrograph of kidney showing fibrin thrombi in glomerular capillaries (H&E, X400)

3.5. Pulmonary thromboembolism

We found pulmonary thromboembolism in six cases which have led to death. All of the cases had thromboemboli in pulmonary vessels, out of which one case had bronchopneumonia as well. One case had thromboemboli in multiple large and medium sized vessels (**Figure 5** A,B), fibrin thrombi and syncytiotrophoblastic emboli in small pulmonary vessels (**Figure 5** D). She also had diffuse alveolar damage with hyaline membrane formation (**Figure 5** C). Occurrence of pulmonary thromboembolism was attributed to diffuse myometrial haemangioma in her uterus. Myometrium also showed multiple thrombi with deciduitis and myometritis. Heart showed focal myocardial necrosis with neutrophilic infiltrate and focal myocardial haemorrhage. Kidney had fibrin thrombi in glomerular capillaries.

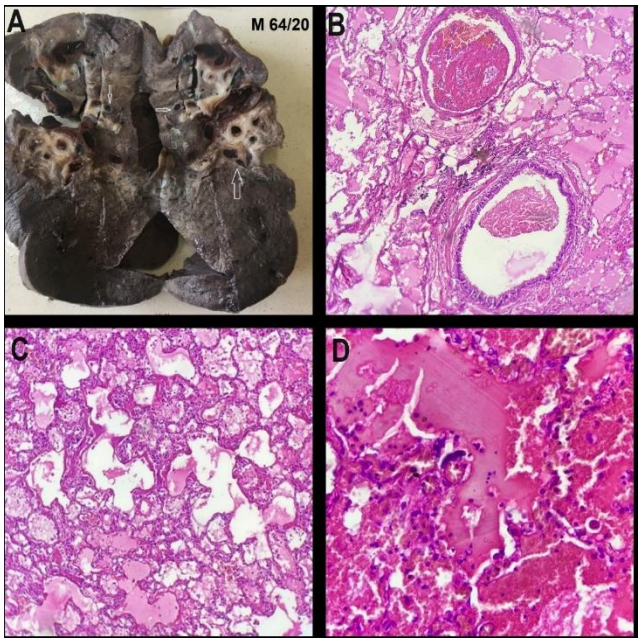

Figure 5: A): Gross photograph of lung showing thromboemboli in pulmonary blood vessel; **B):** Microphotograph of lung showing thromboemboli in large pulmonary blood vessel (H&E, X100); **C):** Photomicrograph of lung showing hyaline membranes with focal pulmonary oedema (H&E, X100); **D):** Photomicrograph of lung showing syncytiotrophoblastic emboli in small pulmonary blood vessel (H&E, X400)

3.6. Ruptured ectopic pregnancy

There were two cases of ruptured tubal ectopic pregnancy. Both were primigravida presented at 10 weeks and 12 weeks of gestation respectively. On examination both cases showed evidence of ruptured ectopic pregnancy (**Figure 6**). One case showed foci of necrosis and focal microvesicular change in liver.

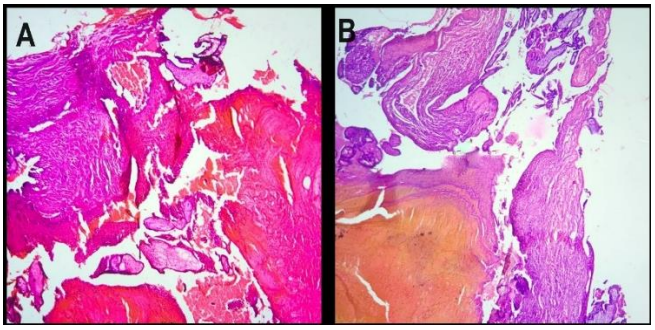

Figure 6: A,B): Photomicrograph of fallopian tube showing ruptured ectopic pregnancy (H&E, X40)

3.7. Spontaneous abortion

There were two cases of spontaneous abortion in our study. Both the cases presented with excessive pervaginal bleeding. One case was primigravida presented at 11 weeks of gestation. On examination Uterus showed products of conception. She also had focal intraalveolar haemorrhages and focal pulmonary edema. The other case was a 3rd gravida who presented at 13 weeks of gestation. Uterus showed placental attachment at upper pole of uterus. In lungs we found aspiration of vegetable matter.

3.8. Antepartum hemorrhage

In our study antepartum haemorrhage was seen in second gravida with 29 weeks of gestation who presented with excessive pervaginal bleeding secondary to arteriovenous malformation. Arteriovenous malformation was seen in cervix (**Figure 7** A) involving body of uterus with multiple thrombi in blood vessels associated with haemorrhages (**Figure 7** B). Bilateral ovaries and right fallopian tube showed congestion with haemorrhages. This case had extensive centrivenular necrosis in liver, findings suggestive of shock liver. Spleen also showed marked congestion and focal haemorrhages.

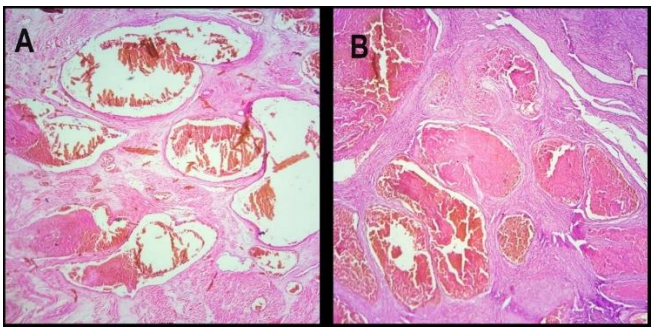

Figure 7: A): Photomicrograph of uterus showing arteriovenous malformation in cervix (H&E, X40); **B):** Photomicrograph of myometrium of uterus showing thrombi in vessels (H&E, X40)

3.9. Acute fatty liver of pregnancy

There was a case of AFLP. A 23yr old primigravida had presented at 39 weeks of gestation with vomiting, abdominal pain, and yellowish discoloration of skin and sclera. Liver

enzymes (SGOT, SGPT) were raised and PT INR was increased. She succumbed to death. We received autopsied organs. On gross examination, external and cut surface of the liver showed yellowish discoloration. There was a haemorrhagic area in interventricular septum of heart. On microscopy liver showed microvesicular fatty change which was seen mostly in pericentral areas (**Figure 8** B). Intrahepatic cholestasis with bile canalicular plugging was noted (**Figure 8** A). Extramedullary haematopoiesis was seen. Heart had focal myocardial haemorrhages. Lungs had focal intraalveolar haemorrhage and focal pulmonary oedema. Uterus showed postpartum changes with extensive myometrial haemorrhages.

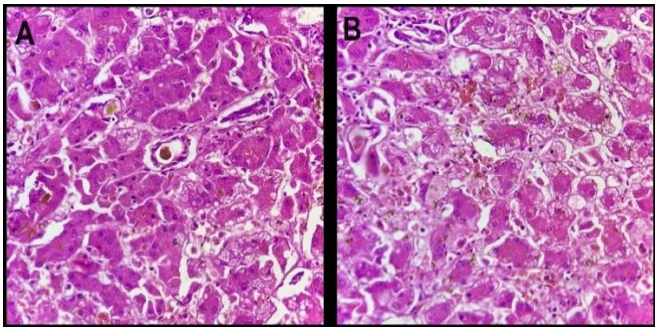

Figure 8: A): Photomicrograph of liver showing acute fatty liver of pregnancy showing bile plugs (H&E, X400); **B):** Photomicrograph of liver showing acute fatty liver of pregnancy showing microvesicular fatty change (H&E, X400)

3.10. Peripartum dilated cardiomyopathy

There was a case of peripartum dilated cardiomyopathy. She was a 30 year old primigravida who had presented with breathlessness after 15 days of full term normal vaginal delivery. On echocardiography she had mild pulmonary arterial hypertension and peripartum cardiomyopathy. On examination, all the four chambers of heart were dilated. She also had bronchopneumonia, intra alveolar haemorrhage and pulmonary oedema in lungs.

4. Discussion

Maternal mortality has severe impact on family, community and eventually the nation. Also maternal mortality is a measure of quality of health care in a community. India being a developing country continues to have a higher rate of maternal mortality as compared to the developed countries.

In our study maximum number of maternal deaths were due to puerperal sepsis (21.54%) followed by postpartum haemorrhage. Despite global progress towards reducing maternal mortality, sepsis remains a leading cause of preventable maternal death. In study done by Poflee et al[6] puerperal sepsis constituted 25% of the deaths by direct cause, while studies done by Padmanabhan A et al[7] and Panchabhai et al[8] showed a less number of cases. Puerperal sepsis is one of the five leading causes of maternal mortality worldwide, and accounts for 15% of all maternal deaths. The physiological changes of pregnancy and the puerperium can obscure the signs and symptoms of sepsis in the obstetric population. A high level of suspicion is therefore needed for the pregnant patients.[9,10]

As for low-income countries, the root causes of puerperal sepsis are mostly related to health system failures and non compliance with long-established infection prevention and management procedures, rather than lack of appropriate technologies.[11]

Postpartum haemorrhage constituted 21.54% of the direct cause of death in our study, which was comparable with Poflee et al[6], Padmanabhan et al[7] and Panchabhai et al[8] where postpartum haemorrhage constituted 28.85%, 25% and 24.43% respectively.

Obstetric haemorrhage remains a major cause of maternal morbidity and mortality. The highest percentages of maternal deaths occur in the immediate postpartum period. A better understanding of the factors associated with PPH maternal mortality is critical for preventing risk of hospital-based maternal death. [12]

There was a case of uterine rupture, she was 2nd gravida with history of previous LSCS presented at 15 weeks of pregnancy. The study by Kanao S et al,[13] also reported a case of 4th gravida with previous LSCS at 15 weeks of gestation presented with uterine rupture.

Histopathological findings we observed in various organs in our study were comparable with study done by Kulkarni AM et al,[4] where findings in lung were CVC, pulmonary oedema, interstitial pneumonia, pulmonary haemorrhage. Heart showed myocarditis. Liver had portal triaditis and midzone necrosis.

Toxaemia of pregnancy was seen in 20% of direct cause of death. Study done by Panchabhai et al. and Padmanabhan et al[7] also found a significant percentage of cases (37.5% and 30.53% respectively).[8]

Histopathological findings in our case were comparable with study by Kulkarni et al[4] and Hecht J et al.[14]

Disseminated intravascular coagulation was seen in 10.76% of the cases in our study. Similarly study done by Padmanabhan A et al[7] found DIC in 8.33% of the cases. In our study 3 cases of intrauterine death were reported where we found DIC, while in study done by Panchabhai et al[8] found 6 cases with IUD in DIC.

In our study, 9.23% of the cases constituted pulmonary thromboembolism. While only 3.85% cases were present in study done by Poflee et al[6] and no cases were seen in studies by Padmanabhan A et al[7] and Panchabhai et al.[8] Pulmonary thromboembolism is common in pregnancy and is associated with significant maternal morbidity and mortality.[15] In our study one of the cases showed syncytiotrophoblastic emboli.

Table 4: Comparison of direct causes of maternal death with other studies

Direct - Cause of Death	Poflee et al[6]	Padmanabhan et al[7]	Panchabhai et al[8]	Present study (%)
1. Postpartum haemorrhage	28.85%	25%	24.43%	21.54%
2. Antepartum haemorrhage	-	-	-	1.54%
3. Ruptured ectopic pregnancy	1.93%	8.33%	-	3.08%
4. Spontaneous abortion	11.53%	-	12.98%	3.08%
5. Toxaemia of pregnancy	11.53%	37.5%	30.53%	20%
6. Pulmonary thromboembolism	3.85%	-	-	9.23%
7. Puerperal sepsis	25%	4.17%	12.21%	26.15%
8. Peripartum dilated cardiomyopathy	-	-	-	1.54%
9. Disseminated intravascular coagulation	-	8.33%	4.58%	10.76%
10. AFLP	9.62%	12.5%	6.11%	1.54%
11. ARDS	-	-	-	1.54%
12. IUD	7.69%	-	-	-
13. Amniotic fluid embolism	-	-	2.29%	-
14. Vesicular mole	-	4.17	-	-
Total	100	100	100	100

Wang Q et al discussed a case of trophoblastic emboli in pulmonary vessels in a case of placenta accreta.[16] Ceausu M et al discussed a case with syncytiotrophoblastic emboli in pulmonary vessels, fibrin thrombi in glomerular capillaries and acute endometritis in uterus. In our case, lungs had thromboemboli in multiple large and medium sized pulmonary blood vessel which led to death and syncytiotrophoblastic emboli in small pulmonary vessels contributed as an adjuvant finding.[17]

In our study we had 1 (1.54%) case of AFLP. While in studies done by Poflee et al, Padmanabhan A et al. and Panchabhai et al[8] found AFLP in 9.62%, 12.5% and 6.11% of the cases.[6-8] AFLP is a rare potentially life threatening pregnancy related disease. It almost always manifests late in pregnancy as in our case, some don't become clinically evident until delivery. Swansea criteria is used for the diagnosis of AFLP.

5. Conclusion

Maternal deaths are commonly observed in younger females in third trimester. Puerperal sepsis and postpartum haemorrhage contributed to the major burden of cases. A wide variety of histopathologic findings were observed in study which helped in achieving a cause in maternal deaths. Histopathological examination of autopsied organs and clinical correlation aids in finalising the cause of death in maternal deaths. Therefore, histopathological examination is always recommended in cases of all maternal deaths.

6. Source of Funding

None.

7. Conflict of Interest

None.

8. Ethical Approval

Ethical No.: GMCM/E-C/12/2018.

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