



Spectrum of Direct Maternal Deaths: An Autopsy Study in a Tertiary Care Hospital

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ABSTRACT

BACKGROUND: - Maternal deaths have always been a challenge worldwide. Autopsy based study in cases of maternal mortality serves as an indispensable tool to analyse causes of maternal mortality. **AIMS:** - To study incidence of varying direct causes of maternal deaths. To study the precedent risk factors and analysis of direct causes of maternal deaths with variables like age, trimester of pregnancy, gravidity, duration of hospital stays, etc. To compare clinical diagnosis with autopsy diagnosis. **DESIGN:** This study is retrospective observational study over 6 years and 1 year of prospective observational study in the department of Pathology at a tertiary care centre. **MATERIALS AND METHODS:** - Autopsy records of 75 maternal mortality cases where pathology autopsy was performed in this period were studied. The available gross specimens and histopathology slides were retrieved and studied. **RESULTS:** - Most common direct cause of maternal death in this study was found to be peripartum dilated cardiomyopathy (26.65%), followed by DIC (14.6%). Maternal deaths were found to be more prevalent in age group 21-25 years (32.42%), multigravida & multiparous. Most of the maternal deaths were in postpartum period (57.76%) and in third trimester (6.46%) if antepartum, with vaginal mode of delivery. Hospital stay was between 24 hours to 1 week. **CONCLUSION:** -Peripartum dilated cardiomyopathy was most common frequent maternal death in this study. Since the most frequent etiologies that lead to maternal death are preventable, more autopsy studies can be of great help in eliminating these.

Key Words: *Maternal Mortality, autopsy, direct causes*



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INTRODUCTION

Maternal Mortality remains an essential parameter while evaluating the development of any country in terms of quality of obstetric care. As per International Statistical Classification of Disease and health related problems (ICD-11), maternal death is defined as 'death of a woman during pregnancy and childbirth or within 42 days of termination of pregnancy from any cause related to pregnancy or its management, irrespective of duration and site of pregnancy'. Late maternal death is 'death of a female from direct or indirect obstetric causes in a time period more than 42 days but less than 1 year after termination of pregnancy'. Maternal deaths and late maternal deaths are combined as per 11th revision of ICD under a new group "comprehensive maternal death"[1]. Maternal death can be sub classified as: -

1. Direct maternal death - Direct causes of maternal death are those related to obstetric complications of pregnancy, labour, or delivery.
2. Indirect maternal death -Indirect causes are those relating to pre-existing medical conditions or diseases that developed during pregnancy which got aggravated by physiologic effects of pregnancy.
3. Coincidental or fortuitous maternal death- Coincidental causes include deaths due to homicide, accident, illicit drug toxicity and suicide[2].

Though, there has been a significant decline in the Maternal Mortality Ratio of India from 130 in 2014-16 to 97 per lakh live births in 2018-20 [3], there is yet scope for improvement by eliminating the major preventable and treatable direct causes of maternal mortality. Autopsy is an invaluable tool in accurately determining the cause of maternal death by studying detailed gross and histopathological examination of almost all the organs and clinicopathological correlation. In our institute, a complete autopsy is performed on every case of maternal death. Indirect maternal deaths have been more common with hepatitis E infection related deaths [sub massive to massive hepatic necrosis and encephalopathy] being the predominant cause. These findings [of increased indirect maternal deaths] have been published by us[4].

However, the direct maternal deaths, their incidence, their variability in clinical presentation, and the various causes of death have not yet been studied in detail. So, this autopsy study has been carried out to emphasise that aspect of maternal mortality.

METHODS AND MATERIALS

This was a retrospective observational study over a period of 6 years and 1 year of prospective study in the Department of Pathology at a Tertiary Care Hospital. A total of 3857 pathology autopsies were performed during this study period and 302 cases out of the total were maternal deaths. These maternal deaths cases were classified into direct, indirect, and coincidental causes as per ICD – 11. Total 75 cases of direct maternal deaths that underwent a pathology autopsy during this period were included in the present study as per inclusion and exclusion criteria.

INCLUSION CRITERIA

Direct maternal deaths in medical autopsies

Following are the direct causes of maternal death: -

- 1) Antepartum haemorrhage (APH) due to placenta previa, abruptio placenta, ruptured uterus, disseminated intravascular coagulation (DIC).
- 2) Postpartum haemorrhage (PPH) due to disseminated intravascular coagulation, atonic uterus etc.
- 3) Puerperal sepsis.
- 4) Amniotic fluid embolism (AFE).
- 5) Pulmonary and systemic thromboembolism.
- 6) Acute fatty liver of pregnancy
- 7) Hemolysis, elevated liver enzymes, low platelet count syndrome (HELLP)
- 8) Pregnancy induced hypertension (PIH) including preeclampsia / eclampsia
- 9) Cerebral haemorrhage due to pregnancy induced hypertension
- 10) Peripartum cardiomyopathy, etc

EXCLUSION CRITERIA

- 1) Medicolegal autopsies
- 2) All indirect maternal deaths

A thorough study of all the autopsy records available of these 75 cases of direct maternal deaths was done. Variables like age, trimester of pregnancy, duration of hospital stay, gravidity, mode of delivery, clinical diagnosis and final cause of death were collected from the autopsy records and analysed. Autopsy records were written by the prosector during autopsy which includes relevant clinical details, gross and microscopic examination of various organs and final cause of maternal death. Gross specimens (where available) and histopathology slides were retrieved and studied in retrospective cases. For the prospective arm of the study, sections were taken from the organs as per the guidelines on autopsy practice in case of maternal deaths as suggested by Royal College of Pathologist. Final cause of maternal deaths was given after histopathological examination and clinicopathological correlation. Final diagnosis was compared with the clinical diagnosis.

STATISTICAL ANALYSIS PLAN:

This study was an observation-based study and data was saved in excel sheets. The data was expressed in terms of percentage and numbers. Simple descriptive statistics such as mean and median were used for continuous variables.

RESULTS

As mentioned above, a total of 302 cases of maternal death were encountered during this period that underwent pathology autopsy. Out of which 75 cases were related to direct maternal deaths contributing 25% of all maternal deaths while the rest were indirect maternal deaths.

Maximum number of patients were in the age group of 21 to 25 years (N=32,42%) followed by the age group of 26 to 30 years (N=23,31%) while minimum number of patients were found in the age > 35 (N=3,4%). The mean age was 26 years. Highest direct maternal deaths constituting 76% were noted in the postpartum period (N=57) followed by 17% in the antepartum period (N= 13) and 7% in the postabortal period (N=5).

Out of 57 postpartum deaths, the mode of delivery was vaginal for 39 deaths. (69%), while LSCS (Lower Uterine Segment Cesarean Section) was done in 16 cases (28%), Exploratory Laparotomy following uterine rupture was done in 2 cases of direct maternal death (3%).

Among 13 antepartum deaths, 3 were in the first trimester of pregnancy (23%), 4 in the second trimester (31%) and third trimester pregnancy cases were 6 (46%).

Maternal deaths were more common in multigravida females i.e., gravida 2nd to 5th (N=8, 61.53%) as compared to primigravida (N=5, 38.47%). More patients who succumbed to death were multipara (N=34, 59.65%) than primipara (N=23, 40.35%). The maximum number of maternal deaths occurred between 24 hours to 1 week (N=43,57%) of hospital admission whereas only 1 maternal death occurred after a hospital stay of more than a month (N=1).

The causes of direct maternal deaths shown in table 1.

| Cause of death | Number of cases | Percentage (%) |
|-----------------------------------|-----------------|----------------|
| Peripartum dilated cardiomyopathy | 20 | 26.65 |
| DIC | 11 | 14.6 |
| PIH | 9 | 12 |
| Puerperal sepsis | 8 | 10.6 |
| HELLP Syndrome | 6 | 8 |
| Uterine rupture | 5 | 6.7 |
| Acute fatty liver of pregnancy | 4 | 5.34 |
| Abruptio placenta | 3 | 4 |
| Pulmonary thromboembolism | 3 | 4 |
| Systemic thromboembolism | 3 | 4 |
| Septicemia with DIC | 1 | 1.4 |
| Amniotic fluid embolism with DIC | 1 | 1.4 |
| Pituitary apoplexy | 1 | 1.4 |

Peripartum dilated cardiomyopathy (PPCM) (N= 20, 26.65%) was found to be the most common cause of maternal death in this study, followed by disseminated intravascular haemorrhage (N=12, 14.6%). Of the 12 cases of DIC in total, 4 cases presented as antepartum haemorrhage while 7 as postpartum haemorrhage, one of these cases was found to have amniotic fluid embolism along with APH. Among the 5 cases of uterine rupture, 2 and 3 cases had APH and PPH respectively as their presentation. 3 cases of abruptio placenta were found, 2 presented with APH. Other causes of direct maternal death included pregnancy induced hypertension (N=9,12%), puerperal sepsis (N=8, 10.6%), HELLP syndrome (N=6,8.01%), acute fatty liver of pregnancy(AFLD) (N=4, 5.34%), pulmonary thromboembolism (N=3, 4%), systemic thromboembolism (N=3, 4%) and pituitary apoplexy (N=1, 1.3%).

Out of 75 maternal deaths, we had agreement between clinical diagnosis and autopsy diagnosis of maternal deaths in 57 cases (76%) and dissent in 18 cases (24%). Table no. 2 lists those 18 cases where there was a lack of concordance between clinical and autopsy diagnosis of maternal death.

| Autopsy diagnosis | Clinical diagnosis |
|-------------------|---|
| 1. Myocarditis | PPH with septic shock with? DIC and? HELLP syndrome |

| | |
|--|--|
| 2. HELLP Syndrome | IUFD with hepatic failure with? Hepatic encephalopathy with sepsis, metabolic acidosis with? acute renal failure |
| 3. HELLP syndrome | AFI? Puerperal sepsis |
| 4. Central venous thrombosis | Breakthrough seizures in e/o PRES syndrome |
| 5. Acute fatty liver of pregnancy | IUFD with hepatic encephalopathy |
| 6. Disseminated intravascular coagulation | Abruptio placentae with AKI with LRTI |
| 7. Disseminated intravascular coagulation | LRTI with acute kidney injury with CCF with PIH |
| 8. Disseminated intravascular coagulation | Severe anaemia |
| 9. Abruptio Placenta | PIH with cerebrovascular accident and aspiration pneumonia |
| 10. Peripartum cardiomyopathy | Lower respiratory tract infection with acute kidney injury |
| 11. Pulmonary Thromboembolism | Sepsis with infective endocarditis |
| 12. Myocarditis | Septic shock |
| 13. Puerperal sepsis | Sudden cardiac arrest with IUFD |
| 14. Acute fatty liver of pregnancy | Sudden cardiac death |
| 15. Disseminated intravascular coagulation | Severe pre-eclampsia with IUFD with abruption of placenta |
| 16. Puerperal sepsis | AKI with hepatitis? Gestational cholestatic with DIC, hepatic encephalopathy |
| 17. Peripartum dilated cardiomyopathy | Disseminated intravascular coagulation |
| 18. Myocarditis | DIC with? HELLP syndrome |

DISCUSSION

Maternal mortality is a critical health issue for various developing countries globally. It is argued that most women who die during childbirth, live in developing countries. Moreover, they die from preventable causes which should further alarm the world to mobilise the resources and take actions to combat maternal mortality (WHO, 2019).

The target 3.1 of the Sustainable Development Goal set by the United nation is to reduce the global maternal mortality ratio to less than 70 maternal deaths per 100,000 live births by the year 2030[5]. Government has updated health policies to reduce maternal deaths, however they need reliable and valid information. There are many clinical studies on maternal deaths in India. There are very few autopsy studies of maternal death in India. Hence, we decided to conduct this autopsy study to analyse the causes and pathological basis of maternal deaths in a tertiary care centre.

According to WHO analysis, direct maternal deaths are more common than indirect worldwide[6]. However, in our previous study, indirect causes were found to be more common which is in agreement with the study conducted by Panchabhai et al.⁷ We will focus on direct causes of maternal death in this study. Worldwide most common causes contributing to maternal deaths were haemorrhage, hypertension, sepsis and abortion[6]. In our study, the most frequent cause of direct maternal deaths turned out to be peripartum dilated cardiomyopathy contributing to 26.63 % (N=20). Such high number have not been reported in literature from India[7,8,9,10,11]. A wide range of maternal mortality due to peripartum cardiomyopathy ranging from 0% to 28% were reported by some other studies[12]. As a physiological part of pregnancy, the cardiovascular system changes are associated with increased blood volume, increased metabolic demands, mild anaemia, changes in vascular resistance associated with ventricular dilatation and increased cardiac output[13]. Also, non-specific presentation such as dyspnoea, dizziness, orthopnea, and decreased exercise capacity can further lead to a diagnostic dilemma. Therefore, the onset of PPCM can easily be masked and missed. It is a diagnosis of exclusion in the late part of the pregnancy and early postpartum period. To conclude, due to the rarity of the disease, specific geographical and socioeconomic differences, and a complex heterogeneous presentation, the disease continues to be underdiagnosed[12]. Classic diagnostic criteria for PPCM, as established by Demakis et al[14], limits the diagnosis to the last gestational month or within first 5 months of delivery. Here, among 20 cases, 15 cases had a clinical diagnosis of peripartum dilated cardiomyopathy. The remaining 5 cases had a clinical diagnosis of DIC in 2, septic shock in 2 and lower respiratory tract infection in 1 case. On gross examination, all the cases had an enlarged, globular heart with dilatation of all 4 chambers. (Figure 1a &1b) Tissue sections taken from the heart revealed hypertrophy of myocardial muscles. Myocarditis was present in 6 cases, of which, we had a single case of giant cell myocarditis with histopathological examination showing myocyte necrosis with infiltration of mixed inflammatory infiltrate and multinucleated giant cells. In the present study, complications associated with cases of cardiomyopathy were congestive cardiac failure, ventricular fibrillation, bronchopneumonia, acute respiratory distress syndrome and disseminated intravascular coagulation. Risk factors associated with peripartum cardiomyopathy seen in present study were multigravida, advanced maternal age and PIH.

Discussing DIC further, among 4 cases of DIC. Who presented as APH, one case had amniotic fluid embolism as an additional risk factor for DIC. Incidence of AFE is estimated to be between 1 in 8000 and 1 in 80,000 deliveries[15]. The true incidence is unknown because of inaccurate diagnosis and inconsistent reporting of nonfatal cases. This was a case of a 31 years old lady with post term pregnancy who underwent LSCS following which she developed sudden onset breathlessness and hence amniotic fluid embolism was suspected clinically. Autopsy showed squamous cells in small blood vessels of lungs on histopathology and thus confirmed the clinical diagnosis. There were fibrin thrombi seen in other small vessels of the lung. Previous studies revealed mortality rates due to AFE was as high as 61-86%, but recent estimates suggest a decrease in case fatality to 13-26%[15]. This reduction may be the result of early diagnosis and better resuscitative care. Another case associated with PIH that came with complaints of fever, cough and breathlessness which was suspected as LRTI clinically, demonstrated fibrin thrombi in multiple organs on histology (Figure 2a & 2b). Thus, additional risk factors linked to DIC seen in the present study were intrauterine foetal death (IUFD), PIH and placenta previa. A review article by Jecko Thachil also identified these risk factors[16].

The risk factors associated with uterine rupture, included previous history of LSCS, multiparity, and delivery by LSCS comparable to the study by Kaczmarczyk M[17]. In 3 instances of abruptio placentae, clinical diagnosis of abruptio placentae was suspected in 2 cases (the age group was more than 30 years) while it was not suspected in the 3rd case. Autopsy in these 2 cases which presented as vaginal bleeding showed large blood clots between placenta and uterine wall thus confirming diagnosis of abruptio placentae. 3rd case was a concealed abruptio placenta where the patient presented with cold clammy extremities and altered sensorium, death occurred within 1 hour of hospital stay. Grossly, there was complete separation of placenta with presence of blood clots & blood in the uterus. All 3 cases were causes of hypovolemic shock leading to death. Risk elements associated with abruptio placentae were advanced maternal age, previous LSCS, PIH, grand multipara similar to those found in study by Macheke GS[18].

Expounding other causes of direct maternal deaths, there were 9 cases of pregnancy induced hypertension, 7 with eclampsia and 2 with pre-eclampsia. Intracerebral haemorrhage (ICH) was noted in 6 eclamptic patients while cerebral infarct in the remaining case. Subarachnoid haemorrhage was also seen in one of the cases. Elderly gravida,

hypertension, and obesity were independent risk factors for ICH which were also noted in our study. The 2 pre-eclamptic cases had postpartum collapse with acute renal failure and severe cerebral edema with acute respiratory distress syndrome as final cause of deaths on autopsy.

There were 8 cases of puerperal sepsis, of which 3 women had a home-based delivery which itself is quite self-explanatory cause of sepsis while 1 had history of rupture of membranes. Clinical diagnosis as puerperal sepsis was made in 6 cases. The remaining 2 cases were clinically suspected to be deaths due to sudden cardiac arrest and anaemia with jaundice. Risk factors observed in cases of puerperal sepsis were history of home delivery and prolonged rupture of membranes.

Pulmonary thromboembolism was also a cause of death in 3 cases (4%). In one case thromboemboli was detected on both gross and histopathology. (Figure 3a &3b) while the other 2 causes were confirmed in histology. Pre-eclampsia and multiparity are seen as risk factors in pulmonary thromboembolism.

Other causes of direct maternal deaths were HELLP syndrome (N=6, 8.01%), where one case was diagnosed to have acute kidney injury with raised creatinine which served as a risk element, acute fatty liver of pregnancy (N=4, 5.34%) (Figure 4a) occurs more commonly in primigravida, twin pregnancy, male fetus, thin mother. The presentation of acute fatty liver of pregnancy may range from subclinical disease to hepatic failure, coma and death, usually present late in pregnancy. Deficiency of fetal long-chain-3-hydroxylacyl coenzyme A dehydrogenase can cause hepatic dysfunction in the mother as a result of hepatotoxicity of long-chain 3-hydroxylacyl metabolites produced by fetus. Early diagnosis and termination of pregnancy may benefit the mother.

Systemic thromboembolism (N=3, 4%), and pituitary apoplexy (N=1, 1.3%). The true incidence and prevalence of pituitary apoplexy is difficult to establish because the majority of the studies are retrospective, and the diagnosis of pituitary apoplexy is usually misdiagnosed. It seems to occur in 0.65 -- 10.5%; this proportion increases up to 25% of surgical series[19]. In present study, patients presented with giddiness, loss of vision, diplopia, vomiting, fever, convulsion, deviation of angle of mouth, weakness of left side of body. A clinical diagnosis of tuberculous meningitis with hydrocephalus with pituitary apoplexy was suspected. During autopsy, the pituitary gland was enlarged and weighed 1.2 gms (normal weight being around 0.5 gms). Cut surface showed a tiny well circumscribed nodule measuring 0.5x0.4x0.4 cm. Histopathological examination revealed a normal compressed ring of lobular architecture surrounding adenoma with areas of haemorrhage and necrosis (Figure 4b). Therefore in this case pituitary adenoma served as a risk factor for pituitary apoplexy.

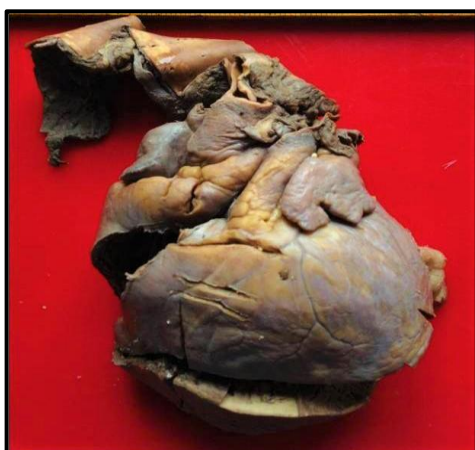


Fig 1A: Gross specimen of peripartum cardiomyopathy showing enlarged and globular heart.



Fig 1B: Dilatation of left ventricle seen on opening the heart

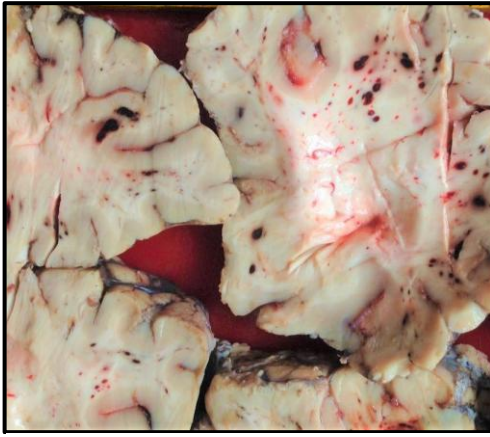


Fig 2A: Gross specimen of cerebrum showing intracerebral petechial haemorrhages in eclampsia.

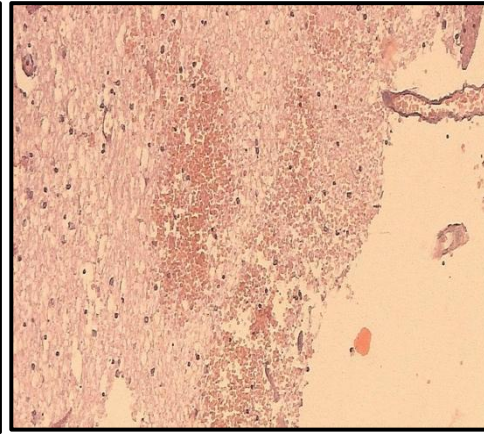


Fig 2B; H&E 400x: Multiple areas of haemorrhage in cerebral parenchyma

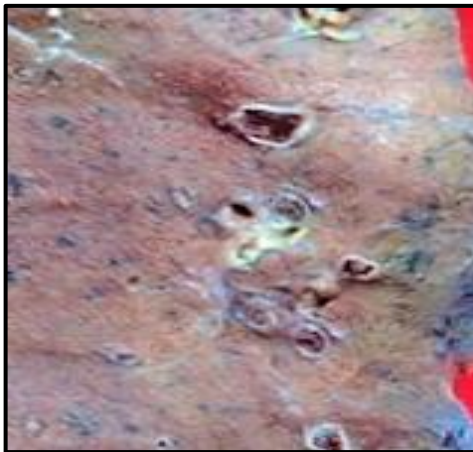


Fig 3A: Gross specimen of pulmonary thromboembolism showing thromboemboli in blood vessels

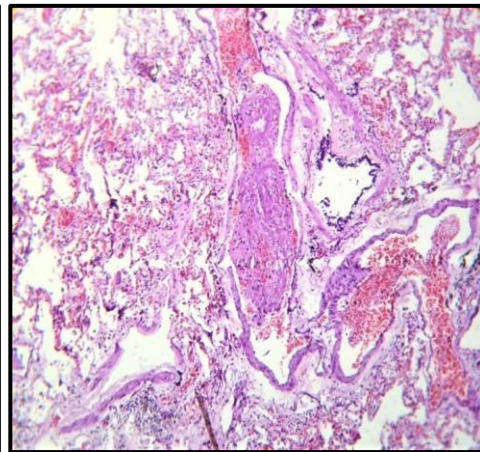


Fig 3B; H&E 400x: Pulmonary thromboembolism showing fibrin thromboemboli in medium sized blood vessels

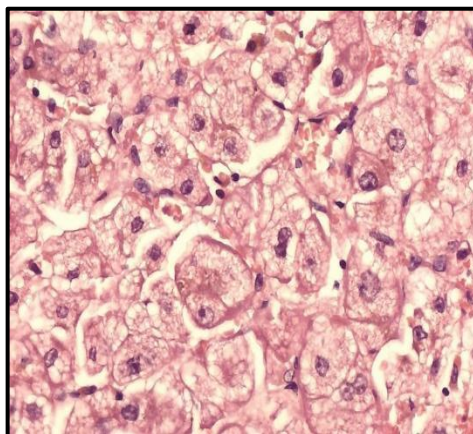


Fig 4A; H&E 400x: Hepatocytes in acute fatty liver of pregnancy showing microsteatosis.

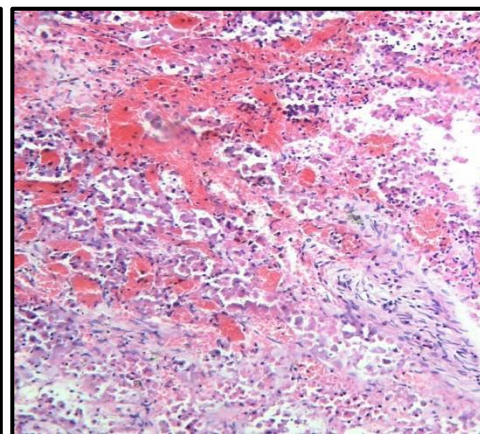


Fig 4B; H&E 400x: Haemorrhage, necrosis and neutrophilic infiltrate was seen in the areas of normal pituitary gland surrounding the adenoma

CONCLUSION

The most common direct cause of maternal death was Peripartum dilated cardiomyopathy in this study. Multicentre registries with long-term follow-up, like the international PPCM registry, will aid in achieving the best medical outcomes in this rare disease. The present autopsy-based study provided detailed pathological analysis of maternal mortality in a tertiary care hospital. By carrying out detailed post-mortem examination (gross and histopathologic) of every maternal death, we identified different causes of direct maternal deaths, their associated risk factors and analysed with different parameters like age, gravidity/parity, trimester of pregnancy and duration of hospital stay. We believe that more autopsy studies can help to elucidate the area of weakness in maternal deaths thus providing directions for community-based interventions.

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