

# An Insight into Maternal Deaths: A Retrospective Analysis and Pathologists Perspective in Series of 16 Autopsy Cases

VAISHALI A WALKE<sup>1</sup>, SONALI DATAR<sup>2</sup>, ANJALI DHOTE<sup>3</sup>, AMRAPALI GAIKWAD<sup>4</sup>,  
AISHWARYA TOSHNIWAL<sup>5</sup>, BALWANT KOWE<sup>6</sup>



## ABSTRACT

**Introduction:** Maternal mortality continues to be of great concern with most maternal deaths occurring in developing countries which accounts for about one in 180 deaths during childbirth as compared to 1 in 4,900 in developed nations.

**Aim:** To determine the common causes of maternal deaths and to study their clinicopathological profile.

**Materials and Methods:** The present observational, retrospective study included series of 16 cases of maternal deaths from January 2018 to June 2020. The study was conducted at Indira Gandhi Medical College, Nagpur, Maharashtra, India. The postmortem examination in all these deaths was conducted as per institutional policy. The external, in-situ examination along with histological findings are studied in each case.

**Results:** The study group comprised of 16 cases, in the range of 21-37 years with a mean age of 27 years. Seven deaths antepartum, 2 intrapartum while seven postpartum period and all the deliveries took place in hospital. Amongst these 16 deaths, 11 were brought dead while in rest five, deaths were hospital based.

**Conclusion:** The autopsy provides an invaluable information and insights about pathophysiological changes and sequence of events leading to death. Usefulness of relevant clinical data in complementing the diagnosis cannot be overemphasised. Their in-depth analysis can certainly help to prevent future maternal deaths and also in early picking up of complications; which further can avoid this preventable and inevitable loss and reduces the national burden on maternal mortality.

**Keywords:** Maternal mortality, Obstetric complications, Postpartum haemorrhage

## INTRODUCTION

Maternal mortality as per the International Statistical Classification of Diseases and Health-related problems (ICD-10) is defined as a death occurring during pregnancy or within 42 days of childbirth or an abortion related or aggravated by pregnancy or its management but is not from accidental or incidental causes [1]. The deaths that occur during 43<sup>rd</sup> day to 1 year of childbirth are termed as late deaths. Maternal deaths are further classified into direct, indirect and fortuitous deaths [1]. The autopsy provides valuable information and insights about pathophysiological changes in various organs which are important in delineation of the sequence of events leading to death. However, without accompanying relevant clinical data, its utility cannot be overemphasised [2]. If no macroscopic cause of death can be identified, then the histopathological examination can add on to arrive at a definitive diagnosis. The current study is carried out to determine the possible causes of maternal deaths and to study their clinicopathological profile.

## MATERIALS AND METHODS

This observational, retrospective study was conducted on a series of total 16 maternal deaths, at Indira Gandhi Medical College, Nagpur, Maharashtra, India, during the period from January 2018 to June 2020 were included in the study.

**Inclusion and Exclusion criteria:** The inclusion criteria consist of willingness to give consent for performing autopsy and brought dead cases or referrals or hospital admissions as per definition of maternal deaths were included. While deaths not fulfilling the criteria of maternal deaths or cases in which consent was not possible were excluded from the study.

## Data Collection

In each case, the detailed clinical information such as age, parity, history of any systemic illness, previous obstetric history, antenatal

check-up visits, nature and method of delivery, postpartum period of hospital stay, treatment received were procured from the deceased's records and from relatives at the time of autopsy. The autopsy protocol followed was that for routine clinico-pathological autopsies, however, specific findings meticulously examined were frothy bubbles in right atrium, acute fatty liver of pregnancy or evidence of pulmonary or amniotic fluid embolism.

## Study Procedure

In each case, external as well as in-situ examination with dissection and preservation of the visceral organs was done in 10% neutral buffered formalin. Blood culture and culture of other tissue specimens was performed as per indication. A detailed gross examination of all the organs and histopathology of atleast one representative section from each organ such as brain with meninges, heart, liver, spleen, kidney, pituitary and adrenal glands was carried out. Additional sections were also examined from lungs in an attempt to identify pulmonary emboli and also from grossly abnormal areas when required. Tissues from placenta and uterus were also studied whenever indicated. Paraffin sections then stained with routine Haematoxylin and Eosin (H&E); along with special stains like Ziehl Nielsen, Periodic Acid Schiff whenever applicable.

The autopsy findings were related with detailed clinical information and investigation in each case to establish the accurate cause of death. No statistical tests were applied as the study includes a small series maternal death.

## RESULTS

The study group comprised of 16 cases, in the range of 21-37 years with a mean age of 27 years. Seven deaths were in antepartum, seven in postpartum while 2 in intrapartum period and all the deliveries took place in hospital. Amongst these 16 deaths, 11 were brought dead while, in rest five deaths were hospital based. Out

of 11, death occurred during transfer to the hospital in 10, while in one it occurred at home. Eleven mothers were primigravida, four gravida 2 and one was gravida 6. All 16 cases data are presented in [Table/Fig-1]. The mode of delivery was normal in five while it was by caesarean section in two cases, amongst total seven deaths that took place in postpartum period. Out of seven postpartum deaths, two occurred within 48 hours, three within first six days, and one each on day 13<sup>th</sup> and 15<sup>th</sup> of delivery. Nine mothers died due to direct causes, Postpartum Haemorrhage (PPH) (25%) being major cause of deaths followed by puerperal sepsis [Table/Fig-2].

preeclampsia/eclampsia. One patient amongst two cases of puerperal sepsis died on day 6<sup>th</sup> of child birth while other during 8<sup>th</sup> month of gestation. In both cases, all organs were found to be congested on gross examination. The significant finding on histology was chronic passive venous congestion of liver and multiple foci of haemorrhage in lung in case one, while all visceral organs were congested, and lung showed features of interstitial pneumonia in other case. Out of two eclampsia cases, one died during 28 weeks of gestation, who revealed subdural and subarachnoid haemorrhages, multiple petechial haemorrhage in liver, while rest all visceral organs were congested.

Case	Age (years)	Clinical diagnosis	Cause of death	Period and time of death	Parity	Mode of child delivery	Place of death	Histopathology diagnosis
1	21	PPH	D	PP (2 <sup>nd</sup> day)	Primigravida	VD	On the way to hospital	Consistent with PPH and CCF with CPVC
2	25	PPH	D	PP (4 <sup>th</sup> day)	Primigravida	VD	On the way to hospital	Consistent with PPH and CCF with CPVC
3	23	PPH	D	PP (2 <sup>nd</sup> day)	Primigravida	VD	On the way to hospital	Consistent with PPH and ATN
4	27	PPH	D	PP (5 <sup>th</sup> day)	Primigravida	VD	On the way to hospital	Consistent with PPH and ATN
5	23	Puerperal sepsis	D	PP (6 <sup>th</sup> day)	Primigravida	VD	In hospital	Puerperal sepsis with? DIC
6	21	Puerperal sepsis	D	AP (32 weeks)	Primigravida	-	On the way to hospital	Puerperal sepsis with interstitial pneumonia
7	28	Preeclampsia/eclampsia	D	AP (28 weeks)	Multigravida	-	On the way to hospital	Consistent eclampsia with DIC
8	24	Preeclampsia/eclampsia	D	AP (30 weeks)	Primigravida	-	On the way to hospital	Consistent with eclampsia with DIC
9	29	DIC	D	Intrapartum	Multipara	LSCS	In hospital	DIC with intracerebral and subarachnoid haemorrhage
10	30	Hepatitis E infection	I	AP (26 weeks)	Primigravida	-	In hospital	Massive hepatic necrosis post HEV infection
11	37	Pneumonia	I	AP (28 weeks)	Multigravida	-	On the way to hospital	Lobar pneumonia
12	24	Sickle cell anaemia	I	AP (24 weeks)	Primigravida	-	On the way to hospital	Sickle cell anaemia with vaso-occlusive crisis with septicemia
13	33	Tuberculosis	I	AP (24 weeks)	Primigravida	-	On the way to hospital	Disseminated tuberculosis
14	30	Status epilepticus	I	Intra partum	Multigravida	LSCS	In hospital	Marked pulmonary oedema
15	22	Viral meningoencephalitis	I	PP (13 <sup>th</sup> day)	Primigravida	LSCS	In hospital	Pyogenic meningoencephalitis with septicemia
16	24	Head injury	I	PP (15 <sup>th</sup> day)	Multigravida (second gravida)	LSCS	At home	Intracerebral haemorrhage

[Table/Fig-1]: Clinicopathological summary of all maternal deaths (N=16).

I: Indirect cause of death; D: Direct cause of death; PPH: Post partum haemorrhage; DIC: Disseminated intravascular coagulation; P: Ante partum period of deaths with weeks of gestation; PP: Postpartum period with time after delivery of baby; Primigravida: 1<sup>st</sup> pregnancy; Multigravida: 2<sup>nd</sup> or subsequent pregnancy; LSCS: Delivery by Caserian section; Intrapartum: Death during delivery or less than one hour; VD: Normal vaginal delivery; CPVC: Chronic passive venous congestion; ATN: Acute tubular necrosis

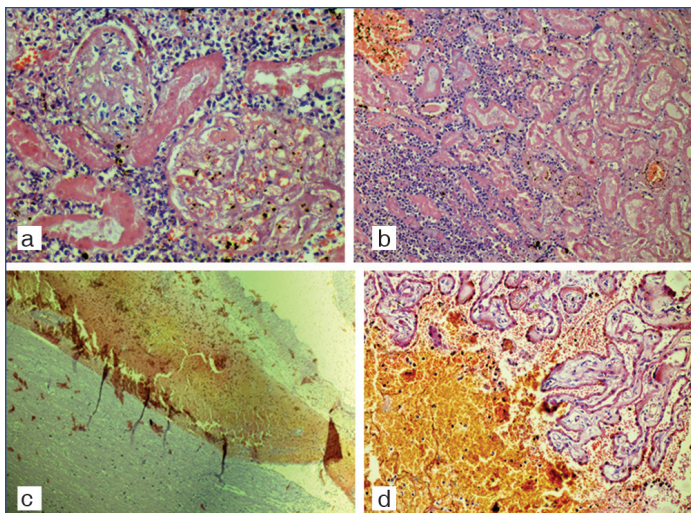
Cause of death	Percentage
<b>Direct</b>	
Postpartum haemorrhage	25%
Puerperal sepsis	12.5%
Preeclampsia	12.5%
Eclampsia	12.5%
DIC	6.25%
<b>Indirect</b>	
Hepatitis E virus	14.28%
Pneumonia	14.28%
Sickle cell anaemia	14.28%
Tuberculosis	14.28%
Status epilepticus	14.28%
Viral Meningoencephalitis	14.28%
Head injury	14.28%

[Table/Fig-2]: Cause of maternal death.

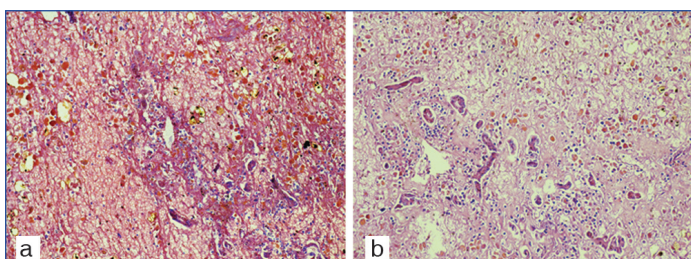
The maternal deaths that occurred due to PPH, were primigravida and had history of normal vaginal delivery. On examination, they revealed conjunctival pallor and all visceral organs were grossly pale. There was no evidence of cervical/vaginal tear. The lungs on histology, in first 2 cases of PPH displayed features of Chronic Passive Venous Congestion (CPVC). In another two cases, the significant finding was acute tubular necrosis of kidney. There were two cases each of puerperal sepsis and of

On histology, significant findings were, chronic passive venous congestion in lungs, fatty change in liver, multiple foci of haemorrhages in spleen and acute tubular necrosis of kidney. Other patient was brought dead, she had bilateral pedal oedema with minimal labial oedema and bilateral pleural effusion; the histology showed marked pulmonary oedema. One case of disseminated intravascular coagulation, was P2L2 post Lower Segment Caesarean Section (LSCS) death, had haemorrhagic pleural and peritoneal effusion, multiple petechiae spots all over visceral organs. The uterine cavity also contained around 50 cc blood and blood clot. The renal parenchyma revealed foci ischaemic necrosis and presence of fibrin thrombi in blood vessels [Table/Fig-3a,b]. Lungs showed pulmonary oedema and fibrin thrombi in its microvasculature. The cerebrum and cerebellum displayed marked congestion and presence of subarachnoid haemorrhage that was extending into the ventricles [Table/Fig-3c,d]. In the group of indirect causes, a young 26 weeks primigravida admitted with jaundice. Her serological markers for HEV infection were positive. Physical examination revealed yellowish discoloration of scalp and conjunctiva. Microscopy displayed extensive, pan-acinar necrosis with collapse of architectural framework [Table/Fig-4a]. There was also evidence of intrahepatic cholestasis and periportal mononuclear inflammation in surrounding viable areas [Table/Fig-4b]. These features were consistent with diagnosis of fulminant hepatitis.

Another case was of a 37-year G2P1L1 with 28 weeks of gestation. The significant findings on in-situ examination revealed heavy and



**[Table/Fig-3]:** A case of Disseminated Intravascular Coagulation (DIC)- a) Kidney shows fibrin thrombi in small blood vessels (H&E;10X); b) Foci of infarction seen as coagulative necrosis of renal parenchyma and surrounding neutrophilic infiltrate (H&E;10X); c) Cerebrum shows area of subarachnoid haemorrhage (SAH) (H&E;10X); d) The extension of SAH into ventricles seen as choroid plexus with surrounding haemorrhage (H&E; 10X).



**[Table/Fig-4]:** A case of Hepatitis E virus infection- a) Massive areas of necrosis in liver parenchyma with loss of architecture (H&E; 20X); b) Liver displays features of intrahepatic cholestasis and periportal mononuclear inflammation (H&E; 20X).

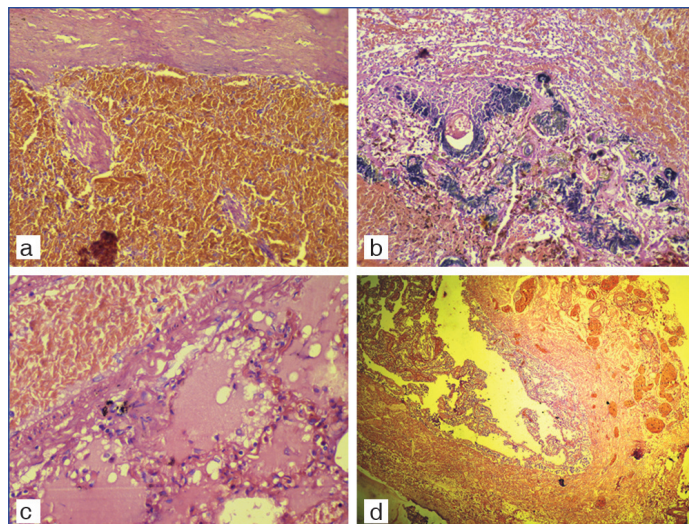
firm lungs while liver was pale and grossly enlarged. Histology of lung revealed features of lobar pneumonia.

A 24-year-old primigravida-24 weeks gestation was a known case of sickle cell anaemia. Her in-situ and gross examination showed marked congestion of visceral organs such as liver, brain, lung and spleen. On histology, spleen revealed marked congestion, the sinuses are dilated and engorged with plenty of sickled Red Blood Cells (RBC) [Table/Fig-5a]. The splenic parenchyma also shows yellowish brown to black, refractile sidero-fibrocalcific nodules called Gandy-Gamna Bodies [Table/Fig-5b] There was also evidence of marked pulmonary oedema and the blood vessels were packed with sickled RBCs[Table/Fig-5c]. The uterus and fallopian tube also displayed marked congestion [Table/Fig-5d]. The placenta showed marked congestion and the intervillous maternal spaces show numerous sickled RBCs.

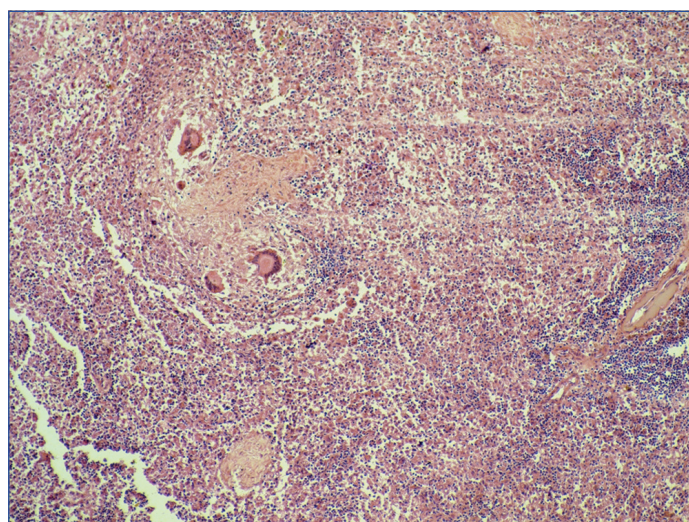
Another primigravida, of 24 weeks of gestation brought dead to hospital for postmortem examination. Her in-situ examination revealed bilateral, multiple, greyish white, firm patches of consolidation. Microscopic examination from lung, spleen and liver showed numerous caseating granulomas, diagnostic of tuberculosis [Table/Fig-6]. The Zeil Neilson Stain was positive for acid fast bacilli.

Another maternal death was a gravida six, patient died within few hours of delivery by caesarean section. She was a referral case, brought dead with a diagnosis of status epilepticus with anaemia. Significant findings on in-situ examination were bilateral pleural adhesions and effusion while the cranial cavity and brain was unremarkable. The lung revealed features of chronic passive venous congestion.

A primigravida, was admitted on day 13<sup>th</sup> of postpartum period, with diagnosis as viral meningoencephalitis. In-situ examination revealed purulent exudate on cerebral convexities, while rest of the organs were unremarkable. Microscopy of cerebrum, lung, kidney



**[Table/Fig-5]:** A case of sickle cell anaemia, specimen of spleen: marked congestion of sinusoids in red pulp which are packed with sickled RBCs (H&E;40X); b) (inset for 3a): Spleen shows siderofibrocalcific nodules called Gandy Gamma Bodies (H&E;10X); c) Lung shows marked pulmonary oedema and the blood vessels were packed with sickled RBCs (H&E 40X); d) Marked congestion of wall of fallopian tube (H&E;10X).



**[Table/Fig-6]:** Spleen shows numerous caseating epithelioid cell granulomas consistent with the diagnosis of tuberculosis (H&E;10X).

and spleen showed multiple abscesses with numerous foci of bacterial colonies admixed with acute inflammatory exudates. The bacterial colonies were also visualised inside the microvasculature; thus, favouring diagnosis of septicaemia with multiple pyemic abscess. The microbiological culture later on confirmed the growth of bacteria.

A 24-year-old, second gravida, 15 days postdelivery; brought dead to the hospital with history of head injury after sudden fall and death. Examination of cranial cavity and brain did not reveal any evidence of subdural, subarachnoid or intraparenchymal haemorrhage. The lungs showed features of pulmonary oedema and foci of intra-alveolar haemorrhage. Subscapular and intraparenchymal haemorrhage was noted in spleen. There was also evidence of cerebral oedema.

## DISCUSSION

Maternal mortality continues to be of great concern with almost (99%) all maternal deaths occurring in developing countries. One in 180 pregnant women die during childbirth as compared to 1 in 4,900 in developed countries [3]. Globally it has been estimated that about half a million women die each year due to pregnancy related causes with 99% of them in developing countries [4]. Mean age of the maternal deaths in the present study was 27 years with oldest patient of 37 years of age [1]. The causes of maternal deaths have been classified as direct (resulting from obstetric complications of pregnancy, labour or puerperium) or indirect (resulting from pre-existing

disease or disease aggravated by the physiological effects of pregnancy) depending upon their relationship with pregnancy.

The direct causes of maternal mortality include the haemorrhagic disorders of pregnancy, preeclampsia or eclampsia, hepatic disorders due to pregnancy, amniotic fluid embolism, pulmonary embolism, abortion-related causes, puerperal sepsis and Intrauterine Foetal Death (IUD)- induced maternal deaths. The indirect causes of death were classified further into hepatic, pulmonary, neurological, cardiovascular, renal, haematological, gastrointestinal, malignancy and infectious disease [5]. The direct cause of maternal death in present study were postpartum haemorrhage, eclampsia and preeclampsia, puerperal sepsis. The indirect causes included were one case each of pneumonia, hepatitis E virus infection, sickle cell anaemia, tuberculosis, status epilepticus, viral meningoencephalitis and head injury. Majority (42.85%) of maternal deaths occurred within first 24 hours, where the direct causes of death predominate while indirect cause were more common when deaths occurred after 24 hours of hospital admission.

In a retrospective study of 95 maternal autopsies by Kavatkar AN et al., there were 47 (49.5%) direct obstetric deaths and 33 (34.7%) indirect obstetric deaths [6]. Hypertensive disorders were associated with pregnancy in 24.2% and anaemia 14.7% cases. In the hypertensive group, important findings were disseminated intravascular coagulation, haemorrhages in different organs and thromboembolism.

In autopsy group of 277 cases, studied by Panchabhai TS et al., the most common cause of maternal mortality was preeclampsia/eclampsia in 14.44% and haemorrhage in 11.55%; while amongst indirect causes, infectious origin in 9.75% and cardiac disease in 9.75% contributed to the cause of maternal death [2] [Table/Fig-7].

Cause of death	Jashnani KD et al., 2009 [1]	Panchabhai TS et al., 2009 [2]	Kavatkar AN et al., 2003 [6]	Present study, 2022
<b>Total autopsy cases</b>	89	277	95	16
<b>Direct causes</b>	<b>38.2%</b>	<b>49%</b>	<b>49.4%</b>	<b>56%</b>
Postpartum haemorrhage	5.6%	11.5%	8.4%	25%
Puerperal sepsis	11.2%	5.78%	12.6%	12.5%
Preeclampsia/Eclampsia	13.4 %	14.44%	24.2%	12.5%
DIC	-	-	-	6.25%
<b>Indirect causes</b>	<b>61.8%</b>	<b>51%</b>	<b>34.7%</b>	<b>44%</b>
Hepatitis E	41.5%	5.42%	-	6.25%
Pneumonia	-	-	-	6.25%
Anaemia/Sickle cell anaemia	5.6%	4.69%	-	6.25%
Tuberculosis	2.2%	6.5%	4.2%	6.25%
Others	-	-	-	19.75%
Total	-	-	-	100%

[Table/Fig-7]: Category wise distribution of cause of maternal death.

In developing countries, postpartum haemorrhage still remains the primary cause of maternal mortality [2,7]. In the present study, maximum deaths amongst direct causes occurred due to postpartum haemorrhage followed by two deaths each due to preeclampsia/ eclampsia and puerperal sepsis and one case due to DIC. Almost 100% of the obstetric haemorrhage related death occurred in primipara.

The diagnosis of preeclampsia was made in presence of arterial hypertension with systolic pressure of 140 mmHg and/or diastolic pressure 90 mmHg, proteinuria and hyperuricaemia, oedema related or not. Eclampsia has been diagnosed as the occurrence of tonic-clonic generalised convulsion in patients with preeclampsia [8]. Acute pulmonary oedema was the principal cause of maternal death in patients with preeclampsia/eclampsia in our study. Puerperal sepsis is an infection of the genital tract, which occurs due to rupture of amniotic sacs and within 42<sup>nd</sup> day of delivery. It happens mainly

within first 24 hour of parturition. It is the third leading cause of direct maternal mortality in developing nations; and preventable conditions [9]. The DIC is a systemic thrombo-haemorrhagic disorder seen in association with well-defined clinical situations and laboratory evidence of procoagulant activation, fibrinolytic activation, inhibitor consumption and biochemical evidence of end-organ damage or failure. It is always a secondary phenomenon and the inciting clinical events are in plenty, ranging from obstetrical complications to malignancy. Obstetrical conditions include amniotic fluid embolism, placental abruption, placenta previa, severe preeclampsia/eclampsia, HELLP syndrome (haemolysis, elevated liver enzymes, low platelet count), retained dead foetus, miscarriage, hypovolemia, septicemia, and acute fatty liver of pregnancy [10,11].

Hepatitis E virus infection has a bad prognosis in pregnancy, often leading to fulminant hepatic failure and death in upto 60% of cases. In our case, the clinical revealed history of jaundice and altered sensorium with signs of hepatic failure and deranged parameters of liver function test. Her serological markers for Hepatitis E were positive and she died within 4 days of admission. Liver on microscopy revealed extensive areas of pan acinar haemorrhagic necrosis, with few viable areas of liver parenchyma, features were consistent with fulminant hepatitis. It can here be reinforced that serology for viral markers should be carried out in each and every pregnant woman who presents with jaundice [1]. Out of total 89 autopsies examined by Jashnani KD et al., acute fulminant viral hepatitis was the commonest cause of indirect maternal deaths (37 cases, 41.5%). This was followed by direct causes like pregnancy-induced hypertension (12 cases, 13.4%) and puerperal sepsis (10 cases, 11.2%) [1].

Pneumonia is the most common cause of fatal non obstetric infections in pregnant women. The risk of pneumonia during pregnancy appears to be lowest during the first trimester however advanced gestational age has proven to be an independent risk factor for pneumonia. The other risk factors include anaemia, asthma, smoking, and use of antepartum corticosteroids and tocolytic agents [12]. Sickle Cell Disease (SCD) is the most common inherited haemoglobinopathy and is associated with increased risk of complications and early mortality. Pregnancy is frequently complicated in sickle cell anaemics with mortality upto 4%. The physiological changes of pregnancy like increased metabolic demand, increased blood viscosity and hypercoagulability gets aggravates the precipitating factors thereby leading to increased incidence of complications like a vaso-occlusive crisis, osteonecrosis, hepatic necrosis, leg ulcers, and thromboembolic events.

Vaso-occlusion seen in placenta leads to villous fibrosis, necrosis, and infarction, thereby causing impaired uteroplacental circulation, which leads to chronic foetal hypoxia and adverse outcomes [13]. Maternal mortality is high among women co-infected with Human Immunodeficiency Virus (HIV) and Tuberculosis (TB). Tuberculosis as such is associated with increased mortality both during pregnancy and postpartum. In high-burden countries like India, it's in the range of 0.07-0.5% among HIV-negative and 0.7-11% among HIV- positive mothers. Both pregnancy and tuberculosis can have adverse effects on each other and linked with poor outcomes [14]. The overall mortality is increased in young people with epilepsy as compared with those without disease; however, for the women of child bearing age, the mortality is 15 times higher. The most important risk factor for sudden unexplained death in epilepsy is generalised tonic-clonic seizures, but it is not always possible to retrieve the information about seizure type and frequency [15]. During pregnancy, women may prone for increased risk for certain infections and severity of its manifestations. The complain of seizures, headache, or altered behaviour in pregnant females, in addition to viral encephalitis can be attributed to number of other structural and metabolic causes which must also be excluded.

Viral encephalitis usually presents as febrile illness with headache, impaired cognition, reduced consciousness, changes in personality/behaviour and seizures [16].

### Limitation(s)

This is a single institution-based study comprising of small sample size and was carried out over a period of two and half year. The reasons attributed to small size could be the reduced number of maternal deaths that might reflect a better patient care or it might be due to a smaller number of maternal deaths reported to this government medical college for autopsy. Another reason might be the issue of obtaining consent from next to kin for performing the autopsy.

### CONCLUSION(S)

Maternal mortality contributes to significant proportion of deaths in women. The deep analysis of its cause, proper and complete antenatal check-up visits as per the national programme to monitor pregnancy along with postpartum care can assist in early pick-up these complications. Thus, can help to avoid this preventable and inevitable loss. The knowledge gained from such studies can provide crucial and valuable insight for formulating strategies or policies to handle this crucial issue of national importance.

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#### PARTICULARS OF CONTRIBUTORS:

1. Professor, Department of Pathology and Lab Medicine, All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, India.
2. Assistant Professor, Department of Pathology, Indira Gandhi Government Medical College and Hospital, Nagpur, Maharashtra, India.
3. Assistant Professor, Department of Pathology, Indira Gandhi Government Medical College and Hospital, Nagpur, Maharashtra, India.
4. Assistant Professor, Department of Pathology, Indira Gandhi Government Medical College and Hospital, Nagpur, Maharashtra, India.
5. Postgraduate Student, Department of Pathology, Indira Gandhi Government Medical College and Hospital, Nagpur, Maharashtra, India.
6. Professor and Head, Department of Pathology, Indira Gandhi Government Medical College and Hospital, Nagpur, Maharashtra, India.

#### NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Vaishali A Walke,  
65C, Shree Gajanan Apartment, Gajanan Nagar, Nagpur, Maharashtra, India.  
E-mail: drvaishaliw@yahoo.com

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- Manual Googling: Apr 02, 2022
- iThenticate Software: Apr 11, 2022 (12%)

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