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MORPHOLOGICAL STUDY OF FOETAL AUTOPSIES TO EVALUATE CAUSE OF DEATH

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INTRODUCTION:

Autopsy has been important in medicine since 15th century and has contributed greatly to the clinical knowledge.[2]Neonatal autopsy has a particular valuable role in the counselling of the families after the loss of an infant as it can help the grieving process, improve parental understanding, and alleviate concerns over prenatal events. Genetic conditions or obstetric factors of relevance to future pregnancies may also be identified [3].

Foetal death is defined as death prior to the complete extraction or expulsion from its mother of a product of conception irrespective of the duration of pregnancy. Further, it is divided as early (<22 week of gestational age); intermediate (22-27 week gestational age) and late (≥28 week gestational age). Of these early are designated as abortions whereas intermediate and late are known as stillbirths [4].

Intrauterine death (IUD)/ stillbirth forms a major part of perinatal mortality which is a good indicator of pregnancy loss and the quality and quantity of health care provided[5]. The key objectives of autopsy examination are identification of cause(s) of death, elucidation of pathogenic mechanism and quality control of clinical mechanism. The key objective of autopsy examination are to identify the causes of death, understanding of pathogenic mechanism and quality control of health care[4]. The aim of this study was to identify the prevalent causes of IUD on autopsy thereby taking appropriate measures and offer parental counselling.

MATERIAL AND METHODS:

The present study included 20 consecutive cases of foetal autopsy received in the histopathology section of the Department of Pathology over a period of 7 years. Only those cases where both maternal and foetal records were available along with foetus and placenta were included in the study. Macerated and autolysed foetuses were excluded from the study. Autopsy was performed as per standard protocol followed by

the department, after a written consent, which included name of the mother, mode of delivery, sex of the foetus, anthropometry, external examination, internal examination of thoracic and abdomino-pelvic cavities as well as removal of viscera, examination of head & neck, brain and spinal cord, examination of placenta and umbilical cord. Sections obtained were routinely processed and stained with haematoxylin & eosin. Special stains were used wherever required. Approval was obtained from the institutional ethics committee.

The cases were categorized according to the classification proposed by Cunningham & Hollier [5]as follows:

1.Foetal(25-40%)

Chromosomal anomalies, Non-chromosomal birth defects, Non-immune hydrops, Infections-viruses/bacteria/protozoa.

2.Placental(25-35%)

Abruption, Foetal-maternal haemorrhage, cord accident, placental insufficiency, intrapartum asphyxia, placenta previa, twin to twin transfusion, chorioamnionitis.

3.Maternal(5-10%)

Diabetes, hypertensive disorders, trauma, abnormal labour, sepsis, acidosis, hypoxia, uterine rupture, post-term pregnancy, drugs, antiphospholipid antibodies, unexplained.

RESULTS:

In the study 20 cases of foetal autopsy were included over a period of 7 years. The mean maternal age was 23.2 years. Mode of delivery in most cases was vaginal (15 cases). The other 5 were lower segment caesarean section (LSCS).

Most of the foetal deaths in our study were early foetal deaths, 8 cases (40%), 5 cases (25%) were intermediate and 7 cases (35%) were late foetal deaths. The number of cases in various categories and causes of foetal death have been shown in Table 1.

Categories	**Causes**	**Number of cases**	**Percentage (%)**
Foetal (35%)	Congenital Anomalies	7	35
Placental (55%)	Utero-Placental insufficiency	10	50
	Chorioamnionitis	1	05
Maternal (10%)	Sepsis	2	10
Total		20	100

The most prevalent cause of death was placental insufficiency (10 cases, 50%), followed by congenital anomalies (7 cases, 35%) and then sepsis (2 cases, 10%).

Placental causes were observed in highest number of cases (55%).

One case of foetal autopsy with chorioamnionitis gave history of some form of maternal interference in early weeks of pregnancy. The two cases with chorioamnionitis gave history of some form of manual interference during the early weeks of pregnancy. The case with maternal sepsis had a history of high fever with pleural effusion. Other case of maternal sepsis also gave history of high fever.

Various histomorphological features in foetus, placenta and the umbilical cord have been tabulated in Table 2

	Causes of foetal death	**Gross & Microscopic Findings in Foetus on Autopsy**	**Gross & Microscopic features in Placenta and cord**
1.	Congenital abnormalities (7 Cases)	1)Polycystic kidneys, meningocele, polydactyly, congenital talipes equinovarus, pulmonary stenosis with right heart hypertrophy Collapsed lung alveoli and congested lung parenchyma	Placenta showed focal areas of hyalinized villi (Figure 1)
		2) Defect in anterior abdominal wall between rectus abdominis muscles and enlarged and hypertrophic bladder	Placenta showed syncytial knots (Figure 2)
		3.Neural tube defect-meningomyelocele and skeletal deformities-congenital talipes equinovarus and scoliosis	Unremarkable
		4.Non development of limbs-absence of left foot,right leg, right hand and fingers.Gastroschichis-intestinal loops present out of the abdominal wall Microscopy:Congestion and ischemic changes in internal	Congested vessels (Figure 3)

	Causes of foetal death	**Gross & Microscopic Findings in Foetus on Autopsy**	**Gross & Microscopic features in Placenta and cord**
		organs	
		5.Spina bifida involving multiple upper cervical vertebral bodies with associated meningomyelocele Gross- kyphoscoliosis Microscopy-Congestion of internal organs	Unremarkable
		6.Spina bifida involving upper cervical vertebrae	Congestion of vessels (Figure 3)
		7.Neural tube defects-meningomyelocele and scoliosis	Congestion of vessels (Figure 3)
2.	Placental insufficiency 10 cases	Features of IUGR	Placenta showed varying degree of syncytial knots, thrombosed blood vessels,atrophic villi and dystrophic calcification (Figure 4,5)
3	Chorioamnionitis 1 case	Non-specific Gross & M/E findings. Mild non-specific inflammation in lung ,liver, kidney seen	Inflammation of membranes (Figure 6)
4	Sepsis 2 cases	Gross-Unremarkable M/E-mild non-specific inflammation seen in sections of lung, heart ,kidney and liver	Features of inflammation (Figure 6)

DISCUSSION:

Foetal autopsies performed by an experienced pathologist in association with clinical specialists could identify the cause of death in 94% cases [6]. Some type of foetal abnormalities like congenital anomalies, infection, non-immune hydrops, malnutrition etc. account for 25-40% of all stillbirths [7,8].A study conducted by Pasztor et al., showed exact cause of death in 57.9% cases .In the first half of third trimester placental insufficiency predominated as cause of death whereas umbilical cord complications occurred around the term [9].

The reported incidence of major congenital malformations in still born is highly variable. Congenital malformations remain a common cause of perinatal death and account for 25-30% in developed countries like India[10]

In all 3% neonates have a major congenital malformation and 0.7% has multiple congenital defects. Cases with multiple congenital malformations were specific to autosomal recessive single gene disorder that have recurrence risk of 25% [10]. Majority of stillbirths attributed to foetal causes in the Winsconsin Stillbirth Service Program had a major structural malformation identified at autopsy [8]. Faye Petersen and colleagues [5] found that one-third of foetal deaths were caused by structural anomalies of which neural tube defects, hydrops and congenital heart disease were the most common. Neural tube defects have recurrence risk of 5% [10]. Birth defects are currently the leading cause of infant mortality accounting for 20% of all infant deaths [11]. Placenta, membranes and cord abnormalities known to cause foetal deaths constitute about 25-35% of the causes of foetal deaths[12].Table 3

Irregularly matured villi are frequent in placentas associated with a variety of chromosomal abnormalities. The trisomy D (12-15) chromosomal anomaly exhibits variable Placental maturation, reduced villous vasculature and giant cytotrophoblast in 50% or more of villi Table/Figure 4. Tetrasomy 12 is a well-recognised chromosomal error with usually lethal anomalies, severely malformed foetus with normal birth weight and essentially normal placenta [14]. Shepard et al.,[15] undertook 20 analysis of aborted specimen and found that 19% of foetus had a localized defect.

Neural tube defects existed in 15% cases. Other abnormalities like PCKD, polydactyly and hypertrophic bladder were also seen.

Davies and Arroyo [16]were able to ascertain the cause of perinatal death by autopsy alone in 47.6%. For the purpose of ascribing a cause of death, a placental study was necessary in an additional 34%. Salafia and Vintzilcos [17]were equally emphatic about the need to examine all placentas. Abnormal placental findings were also seen in premature and anomalies infants [13]. Bonetti et al., were able to find reasonable cause of death in 79.8% cases of foetal autopsy in their study. They found that the major relevant conditions associated to stillbirth were feto-placental infection in early

gestational age (GA) and placental insufficiency both in early and late GA, mainly associated with intrauterine growth retardation [18].

Placental findings in cases of vascular insufficiency and infection correlated well in those reported by other authors. Placental anomalies were mainly represented by avascular villi with stromal fibrosis associated with thrombosis of major and minor vessels in placental insufficiency cases [18]Table /Figure 5,6. Soma and colleagues [19] found placental infarction in 54.7% cases of toxaemia which was the most common lesion found in pregnancy induced Hypertension (PIH)/ pre-eclamptic toxaemia (PET). Wentworth [20]examined 679 consecutive placentas of which 12 were from severe and 77 from mild PIH patients. Infarction was present in 67% cases with severe PIH and in 11.7% cases with mild PIH. Naeye [21]deduced that placental infarction caused 2.26 of 1000 perinatal deaths.

Increased syncytial knotting is also referred to as Tenny-Parker change [22]who emphasized that increased budding of placental syncytium is characteristic of preeclampsia Table/Figure 6. When > 30% of tertiary villi possess syncytial buds especially in premature placenta it is diagnostic of a perfusional compromise. Increased incidence of syncytial knotting points to abnormal villous shape and are usually found under hypoxic conditions typically as in Hypertensive disorder [23].

Patients with severe toxaemia even had higher values of calcification when they delivered prematurely but not at term [24]. Fox [25]stated that calcification is in no way related to degenerative changes but that foetal distress and neonatal asphyxia were more common with calcified placenta Table/Figure 8.

Infection are not only much more common in premature deliveries, they are indeed probably a main reason for most premature births before 30 weeks of gestation [26]. Bengston et al., [27] ascertained chorioamnionitis in 45.8% of 59 patients with premature rupture of membranes before 26 week of gestation, of which 49.1% had perinatal mortality signifying chorioamnionitis as significant cause of IUD. The most important feature of ascending infection is the type of infectious agent and perhaps the time of onset but not the degree or type of inflammatory response [13]. It is well known that attempted abortion with non-sterile instruments is frequently followed by sepsis and chorioamnionitis [27] as was the history given in both of our cases of chorioamnionitis. The predominant opinion now is that amnionic sac infection is a primary cause of premature rupture of membranes and preterm labour at least in those pregnancies that terminate spontaneously before 30 week of gestation [13]. There is also evidence that these infections have an important role in the causation of stillbirth and neonatal deaths [29]. The histological hallmark of CMV infection is a chronic lymphoplasmacytic infiltrate [13]and this is one of the major causes of chronic villitis .

Although maternal causes appear to make only a small contribution to foetal deaths, maternal factors may be underestimated because pathologies with a strong maternal component often are attributed to foetal or placental causes. Hypertensive disorders

and diabetes are the two most commonly cited maternal diseases associated with 5-8% of stillbirths [8,12]. Causes like trauma, infection, cord accident are preventable causes, which if taken care of, would lead to a favourable outcome in future pregnancies. Even congenital abnormalities due to exposure to a known teratogen or poor glycaemic control are preventable. Though a higher degree of recurrence is associated with maternal medical disorders like hypertension, diabetes but appropriate clinical intervention either preconceptionally or early pregnancy may improve the outcome in subsequent pregnancies.

CONCLUSION:

Thus, determining the cause of foetal death facilitates the psychological adaptation to a significant loss and helps to assuage the guilt that is a part of grieving. It also makes counselling regarding recurrence more accurate and may prompt therapy or intervention to prevent a similar outcome in the subsequent pregnancy.

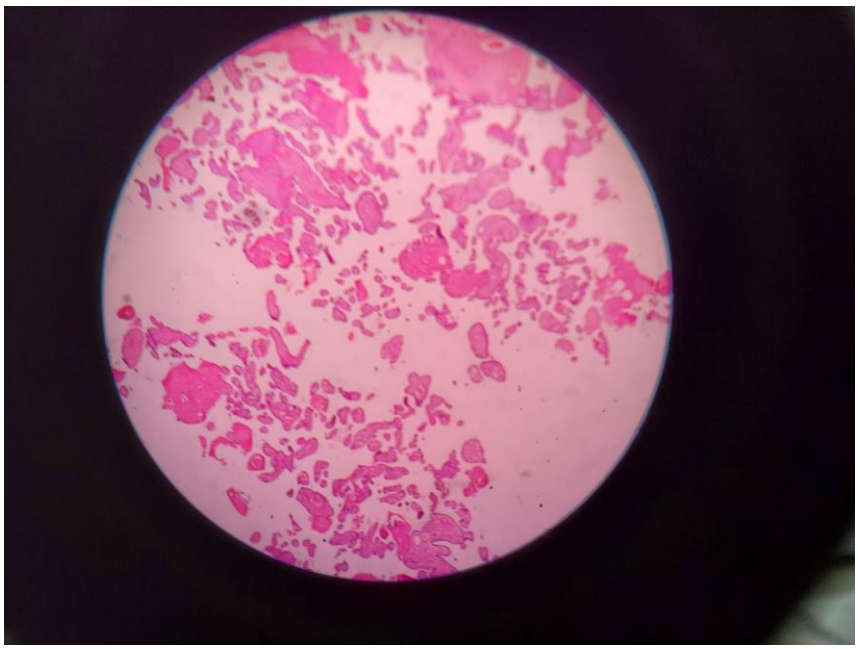

Figure 1

Placenta showed focal areas of hyalinized villi

H&E (100X)

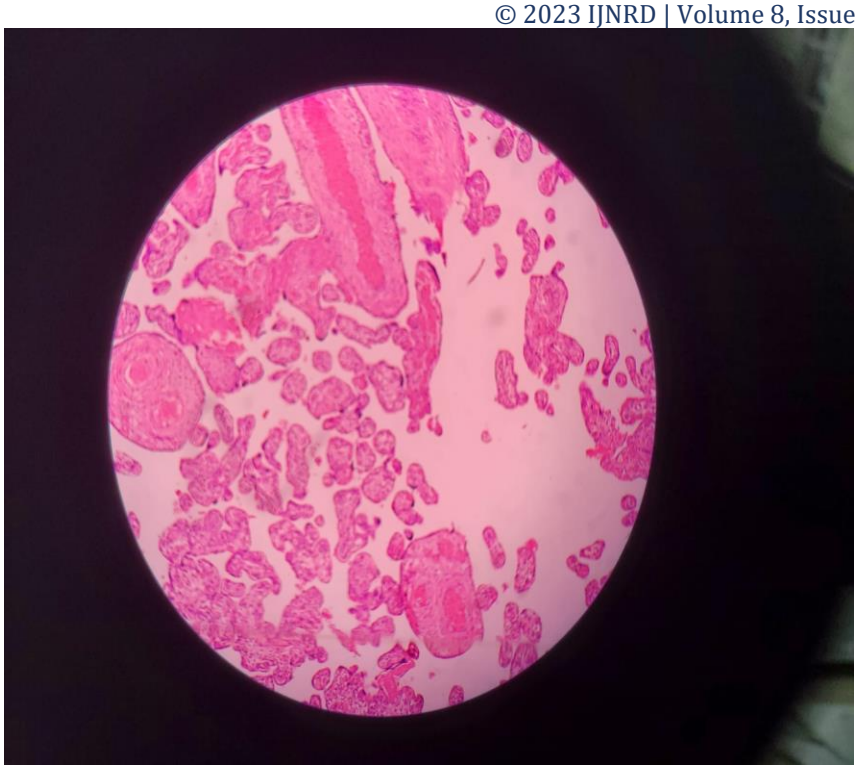

Figure 2

Placenta showing syncytial knots

H&E (100X)

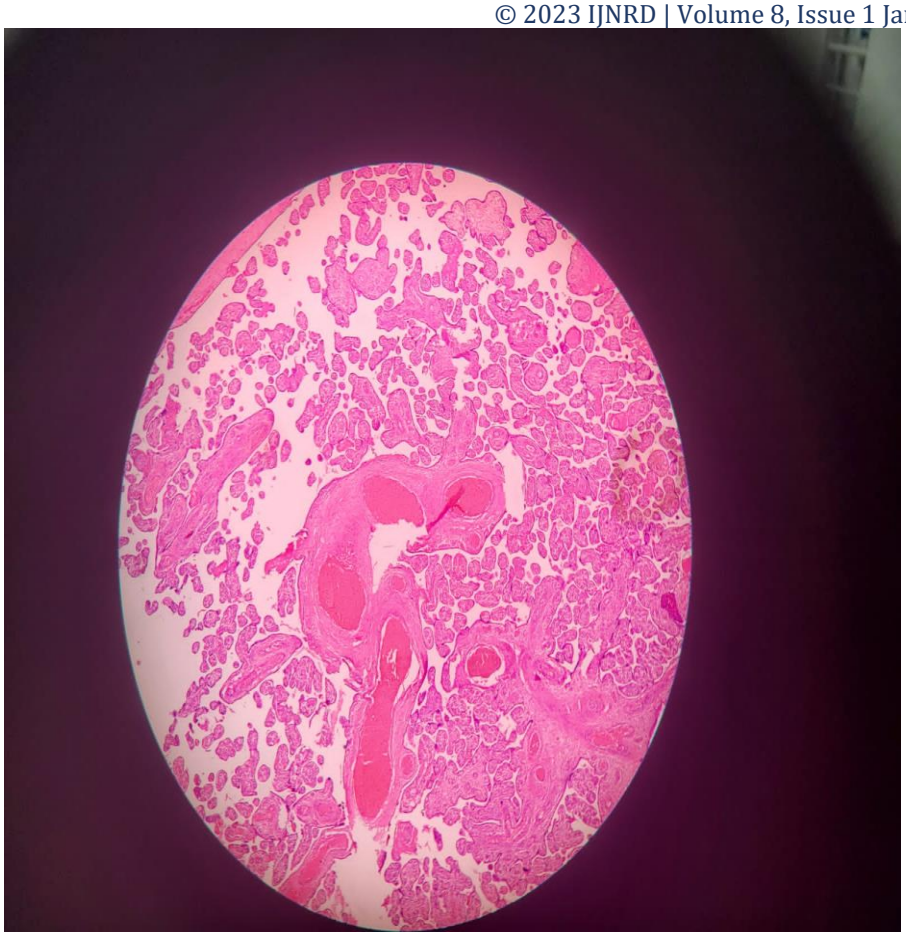

Figure 3

Placenta showing congested vessels

H&E (100X)

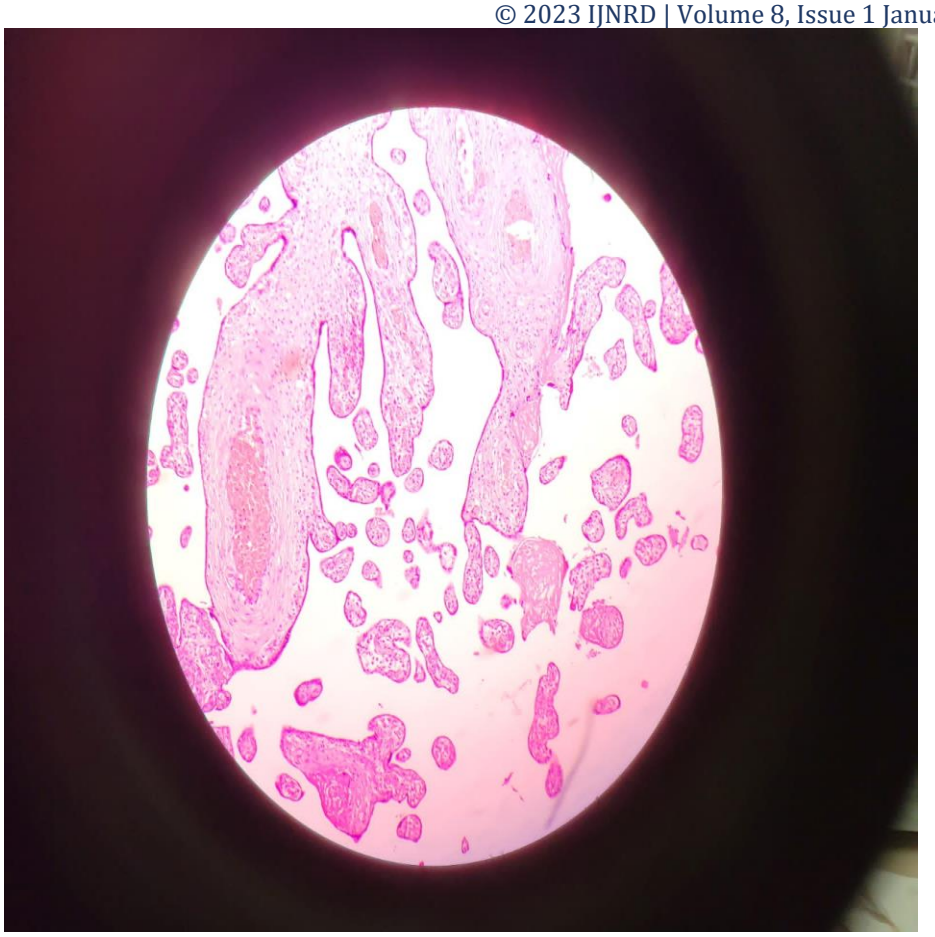

Figure 4

Placenta showing varying degree of syncytial knots, thrombosed blood vessels,atrophic villi and dystrophic calcification

H&E (100X)

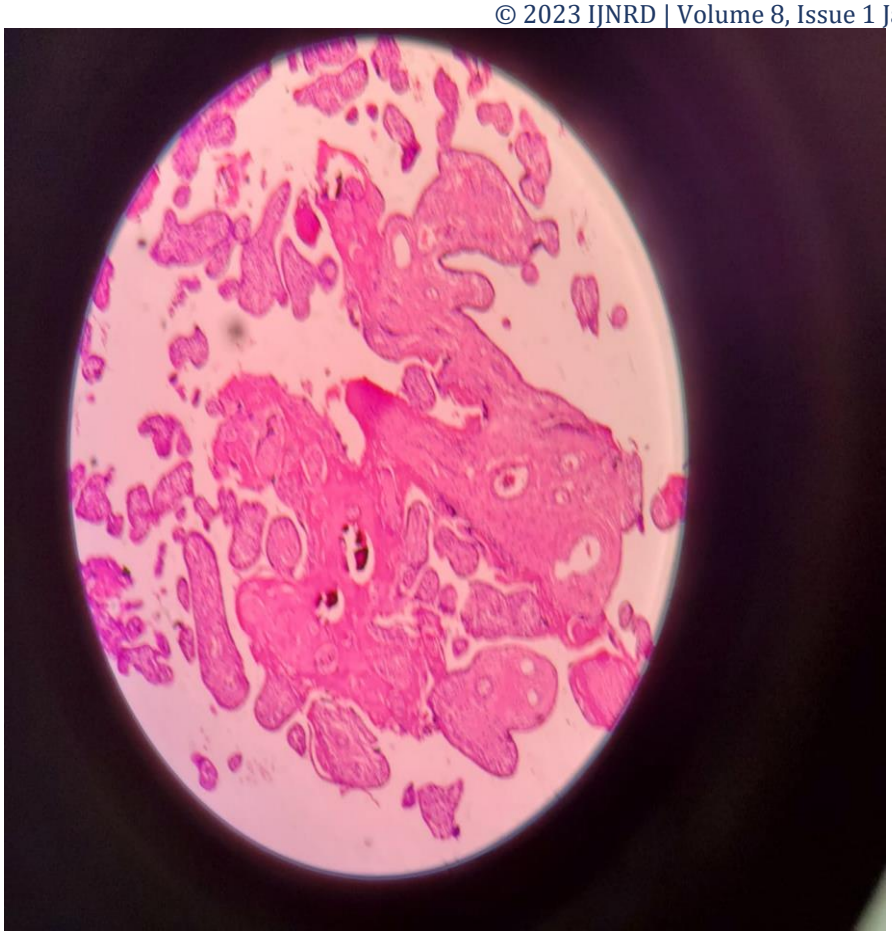

Figure 5

Placenta showed varying degree of syncytial knots, thrombosed blood vessels,atrophic villi and dystrophic calcification

H&E (100X)

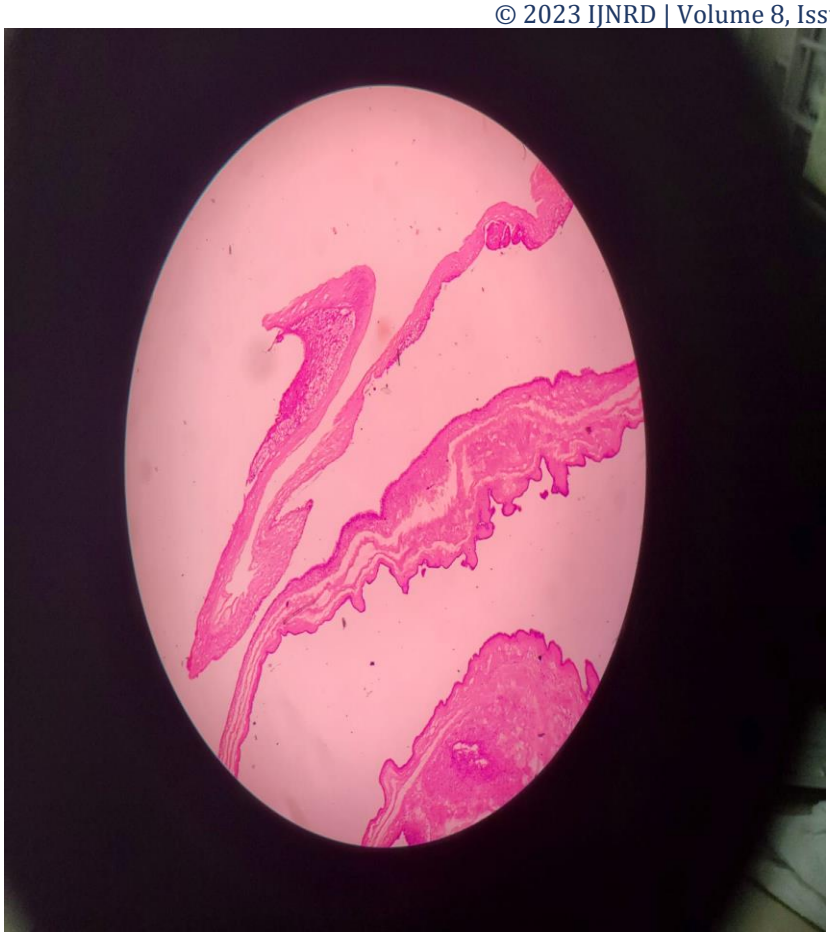

Figure 6

Inflammation of membranes

H&E(100x)

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