

# **Pathology of Chorionic Villi in Spontaneous Abortions**

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Spontaneous abortions are quite common. While in a normal multiparous woman, one or two spontaneous abortions are not unusual, recurrent spontaneous abortions may pose serious problems for some couples. Many such abortions may have a background of genetic anomaly that is reflected in abnormalities of chorionic villi. It is therefore, important to study placenta for various pathological lesions in order to understand the etiology & pathogenesis of the abortion. The chorionic villi are the main fetal part and functional unit of placenta. In this study we examined various pathological changes in chorionic villi in 64 cases of spontaneous abortion specimens. These included hydropic change, numbers of vessels, patency of vessels, stromal fibrosis, fibrinoid degeneration and Hofbauer macrophages. We observed that the villi were reduced in 97% of cases, 83% of villi had stromal fibrosis, 75% displayed fibrinoid degeneration, 75% contained reduced numbers of blood vessels while the patency of vessels was seriously affected in 66% of cases, and 67% cases had prominent Hofbauer macrophages. We conclude that vast majority of spontaneous abortions have abnormal chorionic villi and the most common abnormalities are marked fibrosis and severely compromised vasculature incompatible with fetal development and viability.

**Keywords:** Chorionic villi; Products of conception; Spontaneous abortions.

## **Introduction**

Abortion is the commonest complication of pregnancy. Fifteen percent of recognized pregnancies terminate in spontaneous abortion. There may be many more abortions in early and unrecognized pregnancies.<sup>1</sup> The pathology of spontaneous abortions is therefore an important aspect of understanding the etiology and pathogenesis of the abortions. It is well known that a high number of spontaneous abortions have genetic aberrations. Fetal-placental development occurs hand in hand.<sup>2</sup> The fetal developmental abnormality is understandably associated with fetal part of placenta.<sup>3</sup> Uterus recognizes this aberrant growth of the placenta and expels the products of conception i.e. spontaneous abortion. There may be local, systemic and combined means of recognition of abnormal placental development and induction of abortion.<sup>4</sup>

This study focuses on determining the frequencies of various abnormalities of the chorionic villi, which are the main fetal part of the placenta and serve as functional transport unit for oxygen as well as nutrition to the fetus. These abnormalities of chorionic villi abnormalities

were graded under light microscope and their significance is explored.

## **Patients and Methods**

All specimens of products of conception after spontaneous abortion submitted to pathology department PIMS Islamabad from both gynecology units PIMS Islamabad over a 15 months period (from Jan, 2003 to March, 2004) were reviewed. Sixty four satisfactory specimens from a total of eighty specimens were examined during study period. Sixteen unsatisfactory specimens were excluded from the study.

All specimens received in formalin were routinely fixed & stained with hematoxylin & eosin. These slides we examined by a qualified histopathologist for different histological lesions in chorionic villi. These lesions included hydropic change, number of vessels, patency of vessels, fibrosis, fibrinoid degeneration and Hofbauer macrophages. Each lesion was graded into normal, mild, moderate and severe according to the severity of the abnormality. For example, in reviewing number of vessels in chorionic villi, 8-10 vessels per villous was considered normal, mild abnormality was assigned to

5-8 vessels, moderate to 3-4 and severe to less than three vessels per chorionic villi. Data collected on proformas and frequencies of different lesions were interpreted in the form of tables.

### Results

Three percent of specimens showed no histological lesions in chorionic villi (Fig 1), while 97% showed some form of abnormality in histology (Table 1). 83% of chorionic villi had stromal fibrosis and 17% showed no fibrosis. Out of 83%, 20% had mild, 17% had moderate and 46% had severe fibrosis (Fig 1). 74% specimens showed fibrinoid degeneration while 26% were normal in this group. 36% cases had mild, 26% had moderate and 12% severe fibrinoid degeneration (Fig 2).

<b>Table 1</b>		
<b>Status of Histological Lesions</b>	<b>No. of Specimens</b>	<b>Percentage</b>
Normal	02	3%
Abnormal	62	97%
Total	64	100%

The number of vessels in 25% of chorionic villi was normal while 75% of chorionic villi had reduced number of vessels. 6% showed mild reduction, 16% had moderate reduction while 53% showed severe reduction of the number of blood vessels.

The patency of vessels was affected in 66% of cases. It should be noted that normal or slightly reduced patency in significantly reduced number of blood vessels may still cause severe ischemia. 8% of specimens had moderate and 48% had severe obliteration of vessels (Fig 3).

Sixty seven percent cases had Hofbauer

macrophages; amongst them 22% cases had mildly increased, 23% had moderately increased while 22% had markedly increased number of macrophages (Fig 4).

Fifty two percent cases showed various grades of hydropic degeneration. 16% had mild, 26% had moderate and 10% had severe hydropic change. (Fig 5). (Tables 2 & 3)

### Discussion

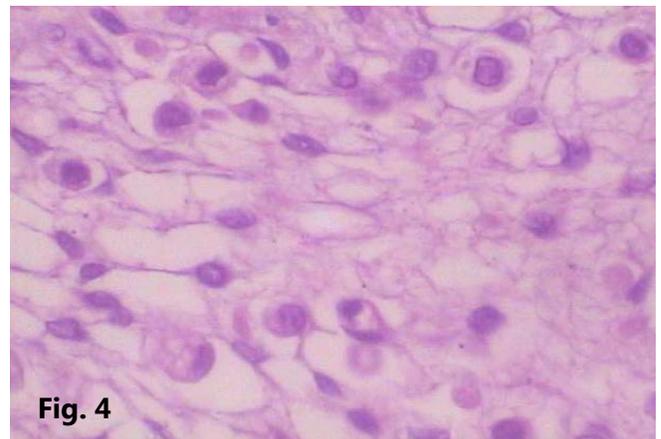
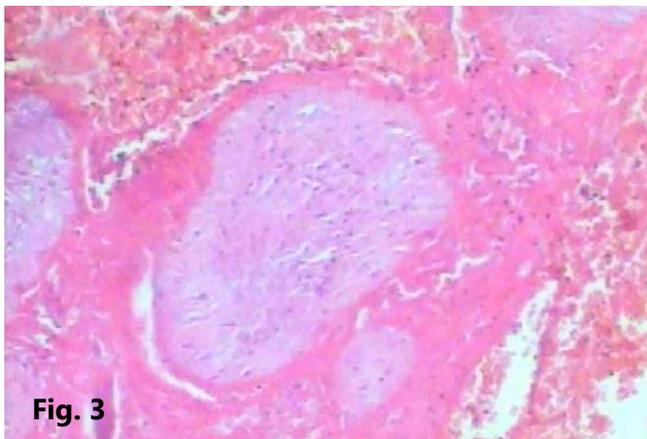
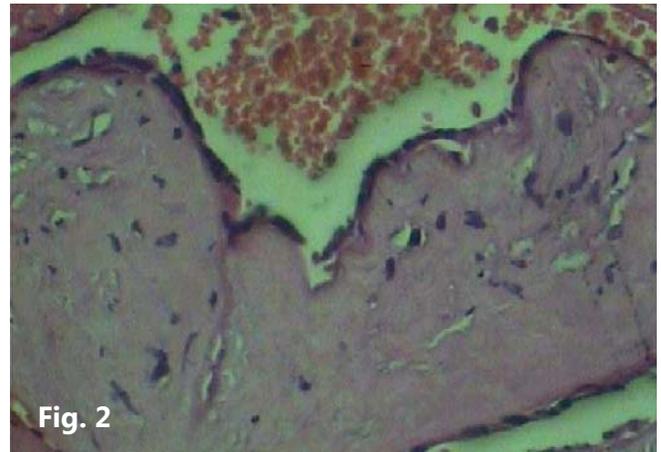
The chorionic villi are the functional unit of placenta and provide oxygen & nourishment to fetus & also serve as excretory unit.<sup>5</sup> Thus it can be regarded equivalent to lung acinus as well as renal glomerulus. The histological appearance of chorionic villi varies with the gestational age and with the stage of development & maturations of villous tree. There is a basic villous structure that is independent of these variables. A trophoblastic mantle that consists of 2 layers, an outer layer of syncytiotrophoblast and an inner layer of cytotrophoblastic cells covers the outer surface of the villi.<sup>6</sup>

Many of the ills that can beset a pregnancy have their roots during early stages of gestation when there is limited blood supply to fetoplacental unit. In this study we had tried to evaluate frequent pathological lesions in chorionic villi of spontaneous abortions under light microscope.<sup>7</sup>

Fibrosis is the final common pathway for nearly all forms of disease that progress towards end stage organ failure. Concomitantly with inflammation and injury, a number of factors are released by infiltrating cells and resident cells and these can stimulate other cells in the inflamed tissue to produce basement membrane and extra cellular matrix molecules such as type 1,111,1V collagens fibronectin and proteoglycans.<sup>8</sup>

<b>Table 2</b>			
<b>Histological Lesions in Chorionic Villi</b>	<b>Normal</b>	<b>Abnormal (mild + moderate + severe)</b>	<b>Total</b>
Fibrosis	11 (17%)	53 (83%)	64 (100%)
Number of vessels	16 (25%)	48 (75%)	64 (100%)

Fibrinoid Degeneration	17 (26%)	47 (74%)	64 (100%)
Hofbauer Macrophage	21 (33%)	43 (67%)	64 (100%)
Patency of vessels	28 (44%)	36 (66%)	64 (100%)
Hydropic Change	31 (48%)	33 (52%)	64 (100%)



**Fig. 1: Normal well vascularized chorionic villi (H&E X 100)**

**Fig. 2: Marked fibrosis of chorionic villi (H&E X 100)**

**Fig. 3: Fibrinoid degeneration of chorionic villi (H&E X 100)**

**Fig. 4: Prominent Hofbauer macrophages (H&E X 400)**

**Fig. 5: Marked hydropic degeneration of chorionic villi (H&E X 100)**

Histologically, stromal fibrosis consists of variable density of collagen in the villous stroma. Initially the collagen is soft which later it gets condensed and hyalinized. The finding is well described in preeclampsia and diabetic pregnancies.<sup>6</sup> However in our cases the villous stromal fibrosis was the most common finding as it involved 83% cases. The scarring of the villi may be regarded equivalent to the

glomerular crescent formation and or severe interstitial pulmonary fibrosis. Stromal fibrosis of terminal villi is a consequence of regression after intra-uterine fetal death or may possibly result from impairment of placental circulation of different causative background. Certain forms of fibrosis may

**Table 3**

Histological Lesions of Chorionic Villi.	Abnormal			Normal	Total
	Severe	Moderate	Mild		
Fibrosis	29 (46%)	11 (17%)	13 (20%)	11 (17%)	64 (100%)
No of vessels	34 (53%)	10 (16%)	04 (6%)	16 (25%)	64 (100%)
Patency of vessels	31 (48%)	05 (8%)	Zero	28 (44%)	64 (100%)
Fibrinoid Degeneration	7 (12%)	17 (26%)	23 (36%)	17 (26%)	64 (100%)
Hofbauer Macrophages	14 (22%)	15 (23%)	14 (22%)	21 (33%)	64 (100%)
Hydropic change	06(10%)	17 (26%)	10(16%)	31(48%)	64 (100%)

possibly develop via stromal edema (e.g. diabetes mellitus, blood group incompatibility, immunological disorders) together with edema-activated mesenchymal proliferation. Edema of villous stroma may be of diffuse or focal manifestation in the terminal villi and in advanced cases may affect all parts of the placenta. It is usually linked to disturbed haemodynamics related to chorionic villi vasculature. Severe stromal edema leads to formation of cisterns and is gradually replaced by fibrosis. There are no known lymphatic vessels to drain the edema fluid from placenta.<sup>9</sup>

Fibrinoid “degeneration” is the deposition of fibrinoid material, initially external to basement membrane of syncytiotrophoblast. Later it appears in the villous stroma.<sup>6</sup> We have observed that fibrinoid material is derived from hemorrhages. The hemorrhage seeps through adjacent decidua and forms a membrane like sheet around chorionic villous. Later the material breaks into the villous stroma at a few places. If carefully searched red blood cells can be demonstrated in this fibrinoid material. It seems that prematurity, preeclampsia, diabetes and Rh- incompatibility etc.favor such small

hemorrhages and lead to increase fibrinoid degeneration. Sariu et al showed that intravillous fibrin deposition was observed in 46.1% in spontaneous abortions vs. 14.4% in medical abortions. Hyaline change was observed in 67% of spontaneous abortions vs. 7.8%; hydropic change observed in medical abortions.<sup>10</sup>

Normal villi contain many thin walled patent vascular channels. Various cross sections of chorionic villi on average reveal between 8-10 blood vessels. Avascular or hypo vascular villi mean poor blood supply to the fetus and will result into fetal retardation. The reduced number of vessels may be due to their de-novo poor formation or secondary to fibrosis.<sup>6</sup> As almost all our cases did not show thickened vessels, the possibility of de-novo poor formation remains high. 75% of our cases had markedly reduced blood vessels in the chorionic villi.

Similarly in another study there was marked difference between vasuclarization of spontaneous versus induced abortions. This study revealed that, in cases of embryonic death and blighted ova, there was markedly deficient chorionic villous

vascularization.<sup>11</sup>

Fibrosis can be an important cause of reduced patency of the vessels. Reduced patency of the villous vessels is seen in a variety of immunological disorders, metabolic derangements as well as hypertension.<sup>7</sup> This was observed in 66% of our cases.

Hofbauer cells are tissue macrophages derived from both the mesenchyme of the villi and the circulating blood monocytes.<sup>6</sup> They are equivalent to the alveolar macrophages and the mesangial cells of renal glomerulus. They may be increased in variety of immune mediated disorders. For instance they are increased in Rh incompatibility. In this series they were increased in 67% cases.

Hydropic degeneration is a nonspecific tissue reaction to a variety of pathological insults. Initially there is mild edema in the stroma of the villi. Later the edema fluid may occur in the form of lakes or cisterns. Extreme hydropic degeneration is a characteristic feature of hydatidiform mole.<sup>3</sup> This is also associated with markedly reduced number of blood vessels. If blood vessels are present they show marked reduction in the patency of the blood vessels.

Ladefoged et al studied placental tissue from 160 abortions of 6th-12th weeks, and 109 spontaneous abortions between weeks 5 and 16, for a comparison and quantitation of hydropic degeneration. There was significantly severer hydropic degeneration among the spontaneous abortions ( $p < 0.001$ ).<sup>12</sup>

Thorough Surgical Pathological examination of products of conception is critical in evaluating etiology of recurrent & sporadic abortions. Clinicians must provide relevant data regarding history, physical findings and radiological appearances and the histopathologist must perform meticulous examination of the placenta.<sup>13</sup> The Surgical Pathologist has the responsibility to recognize the histological lesions that contribute to the adverse pregnancy outcome. Appropriate genetic studies in collaboration with histopathological lesions are needed.

## Conclusion

In summary we evaluated 64 cases of spontaneous abortions. We found severe pathological lesions in 97% of cases. It is difficult to postulate whether these histopathological lesions were responsible for spontaneous abortions or these changes were reflective of some primary disorder. It is well known fact that fibrosis could be cause and effect of ischemia. As most early abortions are associated with genetic anomalies, some of these findings may be associated with specific genetic aberration. Further work up is definitely needed in this vast field, which may enhance our understanding of feto-placental as well as other important aspects of pathology.

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