HISTOLOGICAL STUDY OF ABRUPTIO PLACENTAE IN TERM DELIVERY AND ITS IMPACT ON FETAL OUTCOME

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ABSTRACT

Objective: To identify the histological morphology of abruptio placentae and comparing it with that of normal placenta of normal pregnancy at term and to compare its impact on fetal outcome.

Study Design: A case control study.

Place and Duration of Study: The study was conducted at Anatomy Department of Federal Medical and Dental College in collaboration with Department of Obstetrics and Gynecology, Pakistan Institute of Medical Sciences (PIMS)/Shaheed Zulfiqar Ali Bhutto Medical University Islamabad over a period of eight months, from Jul 2015 to Feb 2016.

Material and Methods: Forty mothers with abruptio placentae and forty mothers with normal placentae of normal pregnancy were selected from emergency and outpatient department of Gynecology and Obstetrics Department of PIMS affiliated with Shaheed Zulfiqar Ali Bhutto Medical University (SZABMU) Islamabad. Histological morphology was carried out on these placentae. A case control study with purposive sampling technique was done for comparison between two groups. A structured data collection check list was used to collect the required data. SPSS version 20 and MS Excel were used for statistical analysis. Students T test and Chi-Square tests were applied accordingly to compare the results of two groups, with p-value<0.05 being considered to be statistically significant.

Results: We included eight placentae with forty abruption cases and forty normal placentae. Among these frequent age was 26 to 30 years (50%). The mean fibrinoid necrosis was 11.4 ± 2.2 as compared to controlled group 6.1 ± 1.2. The mean syncytial knots of abruption placentae were 49.6 ± 10.2 as compared to normal placentae 30.7 ± 5.6. While the mean area of calcification was 6.3 ± 3.7 in patients compared to 1.1 ± 1.6 in the controls. Abruption placentae had great impact on fetal weight reduction from 3.1 ± 0.6 to 2.2 ± 0.7 and Apgar Score as well.

Conclusion: The histomorphological changes in abruptio placentae were statistically significant as compared to control group and lead to poor fetal outcome.

Keywords: Abruptio placenta, APH (antepartum hemorrhage), Calcification, Cotyledon, Diameter in centimeters, Fibrinoid necrosis, Syncytial knots, Weight in grams.

INTRODUCTION

One of the most common placental abnormalities is abruptio placenta; this Latin term is explained as 'rending asunder of the placenta', implying and denoting a sudden accident[1]. It is defined as early separation of a normally located placenta after fetal viability. Its incidence is 1/200 (0.5%) pregnancies but sometimes increased to 4.5%[2]. It may be revealed or concealed, while 65-80% cases are usually revealed. A total of 20-35% cases are concealed which is more dangerous and can lead to severe complications even maternal and fetal death[3,4].

Abruptio placenta has high recurrence rate of 20-30 folds in subsequent pregnancies, regardless of its cause; it is associated with an increased incidence of preterm birth and perinatal death with mortality rate of 119 per 1000 births[5]. Histological examination of placental abruption shows changes in decidua basalis, chorionic plate and intervillous architecture. Placental bed shows vascular abnormalities. In abruptio placenta various types of hemorrhages can be recognized grossly and histologically, including marginal or

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retroplacental hemorrhages[6]. There may be intervillous thrombi with pale laminated lesions with acute parenchymal hemorrhages which are usually dark red and laminated with lots of red blood cells. Due to hemorrhages and blood clots the underlying placental parenchymal tissue become compressed and focally necrotic. Acute inflammation leads to villi infarction. The RBCs breakdown and hemosiderin accumulates in 4-5 days with increased perivillous fibrin deposition[7]. In chronic abruption, hemosiderinladen macrophages are visible in membranes and chorionic plate. Thrombi can be red in acute but in chronic cases these are pale tan to white with well demarcated parenchymal lesions. Occasionally there is expansion of the intervillous space by layers of fibrin and red blood cells[5]. Distal villous hypoplasia and increased syncytial knots (aggregation of syncytiotrophoblastic nuclei on the periphery of tertiary placental villi, forming a huge multinucleated protrusion from the villous surface) can also be visualized[8]. Such knots are rarely visible before term pregnancy[9]. Infarction of placenta shows localized area of ischemic necrosis of villi[10]. They have well defined borders and lack the lamination seen in intervillous space with villous crowding and increased perivillous fibrosis. As time passes the nuclear chromatin within the cells of villi becomes clumped and eventually fades away leaving pink acellular villi (ghost villi) and increased surrounding fibrin leading to increased calcification, with some evidence of hypermaturation (distal villous hypoplasia and increased syncytial knots)[11]. In some cases of abruptio placenta fibrinoid necrosis occurs, which are small collection of structureless, eosinophilic, homogeneous material within the villi, usually 3% at term normally but increase in abruptio placenta.

A recent study in Pakistan reported that antepartum hemorrhage is the commonest cause of stillbirths accounting for 33% of cases[12]. Studies done in western countries show perinatal mortality rate of 9.2% and 119/1000 with still birth rate of 83/1000. While in Pakistan, studies show abruptio placenta with still birth 4.4%, with abruption 58.5% from Abbottabad while still birth 4.7%[13]. While a study conducted in Lahore reported fetal loss rate of 56.6%[14].

In year 2005 maternal mortality rate (MMR) was 402/100,000 live births[15]. MMR in developed countries is 10/100,000 while in developing countries it is 2000/100,000[16]. Out of which 30% maternal deaths are due to peripartum hemorrhage including placenta previa and abruptio placenta[17].

It is impotant to identify the etiological/ pathological conditions that require timely clinical intervention by histomorphological examination of abruptio placentae of births (placenta) occurring in public sector hospitals in Pakistan because of its high recurrence rate and associated maternal and fetal mortalities. The main aim of this study is to compare the fetal outcome and histological changes between placental abruption patients (n=40) and normal controls (placenta of normal pregnancy).

MATERIAL AND METHODS

After approval from the ethical committee, a case control study was carried out in Anatomy Department of Federal Medical and Dental College in collaboration with Pakistan Intitute of Medical Sciences (PIMS)/Shaheed Zulfiqar Ali Bhutto (SZAB) Medical University Islamabad over a period of eight months from July 2015 to February 2016. Eighty placentae were collected from labor room and Gynecology Department of PIMS hospital, who delivered either vaginally or by caesarian section with the permission of ethical committee of SZAB Medical University Islamabad. The study was based on purposive sampling technique. The sample size is calculated according to the WHO formula (prevalence ratio) as under[18]:

$n=z2x\alpha/2\ p\ (1-p)\ /\ e2$

n= The preferred sample size

p= The estimated prevalence (1/250=0.004)

e= Margin of error set at 0.02

z= The standard normal deviation who usually set at 1.96 which corresponds to 95% confidence interval.

While at 95% confidence interval α=0.05. Forty placentae from confirmed cases of abruptio placentae (case group) with complete medical and obstetric history were collected and recorded to identify the confounders. Forty control groups were taken from normal placenta and uncomplicated pregnancies. Ages of mothers were below 40 years. After delivery, the specimen samples of placentae were taken in a jar. They were then washed in a running tap water, tagged with numbers and preserved in 10% formalin solution for 48 hours.

Tissue processing and embedding and staining: four sections of each placenta about 2x2cm were taken at 3,6,9 & 12 O'clock position from chorionic plate to basal plate and from central to periphery. Then placental tissues were placed in a tissue processer (leicaTp 1020) for 4 hours fixed in a 70%-100% alcohol. They were then processed to prepare paraffin blocks. Sections of 5um ribbons were taken with the help of rotary microtome (leica rm255) and stained with Hematoxylin & Eosin. The slides were studied under light microscope for identification of syncytial knots, fibrinoid necrosis, stromal fibrosis, congestion and calcification per low power field 10x objective for general architecture and 40x objective for further (conformed fibrosis, calcification and congestions in the slide of abruption placenta). Both qualitative and quantitative findings were noted. Motic images and microscope model (BX-32) were used. Students"t" test was used. A *p*-value less than 0.05 was considered to be statistically significant. Moreover we also noted the weight of fetus at the time of birth on weight machine in kilogram both in control group and abruptio placentae pregnant women. The Apgar score were noted according to WHO criteria in 3 minute and 5 minute[19].

A categorical variable like age was calculated. Chi-square tests were used for categorical vaiables. Whereas mean and standard deviation were calculated for numerical (continuous) variables which included fibrinoid necrosis, calcification, and syncytial knots, and weight and apgar score of fetus were calculated by Student t-test. Statistically the data were analyzed using MS Excel and SPSS version 20.

RESULTS

The slides of abruptio placenta and control group were focused at 10x objective and the number of areas of fibrinoid necrosis were counted per 10 fields and then the mean of each slide was found which was the average number of the area of fibrinoid necrosis across the slide. The procedure was then repeated with each slide[20,21]. In the end the mean of all abruptio and control group slides were calculated. In the abruption patients the mean area of fibrinoid necrosis was 11.4 ± 2.2 compared to 6.1 ± 1.2 in the controls. This difference in the means was statistically found significant (*p*-value<0.001) (table-I).

Mean area of syncytial knots were measured at 12 O'clock in each slide[21]. In the abruptio patients the mean syncytial knot was 49.6 ± 10.2 compared to 30.7 ± 5.6 in the controls and this difference in the two means was also statistically found significant (*p*-value<0.001) (table-I).

The mean area of calcification per low power field was then compared among patients and controls in the study. The mean area of calcification was 6.3 ± 3.7 in patients compared to 1.1 ± 1.6 in the controls. The difference in the two means was statistically found significant (*p*-value<0.001) (table-I)

The birth weight of newborns was compared among patients and controls in the study. The mean birth weight was low 2.2 ± 0.7 kilogram in cases and 3.1 ± 0.6 kilograms in the controls, it was found out that low birth weight was significantly associated with abruptio placenta (*p*-value<0.001) (table-II).

The fetal outcomes at 3 and 5 minutes after birth were compared among patients and controls. There was 1 (2.5%) case of stillbirth in

the abruptio placentae patients whereas none in the control group and no statistical difference were observed in stillbirths among both groups. At three minutes Apgar score of 3 to 6 was significantly associated with patients 27 (67.5%) compared to 6 (15.0%) whereas Apgar score of >6 was found in only 10 (25.0%) patients and 34 (85.0%) controls and this difference was statistically highly significant (*p*-value<0.001) (table-III).

Table-I: Comparison of area of fibrinoid necrosis, syncytial knots and calcification per low power field (10x/10) betweenabruption patients and control group.

	Control (n=40)	Abruptio (n=40)	*p*-value
Area of Fibrinoid Necrosis			
Mean ± SD	6.1 ± 1.2	11.4 ± 2.2	<0.001
Syncytial Knots			
Mean ± SD	30.7 ± 5.6	49.6 ± 10.2	<0.001
Calcification			
Mean ± SD	1.1 ± 1.6	6.3 ± 3.7	<0.001

Table-II: Birth weight (kg) of newborns in the two study groups.

	Abruptio (n=40)	Control (n=40)	*p*-value
Mean ± SD	2.2 ± 0.7	3.1 ± 0.6	<0.001

Table-III: Fetal outcome at three and five minutes after birth.

At 3 minute	Abruptio (n=40)	Control (n=40)	*p*-value
Still birth	1 (2.5%)	0 (0.0%)	1.0
Apgar score 3 to 6	27 (67.5%)	6 (15.0%)	<0.001
Apgar score >6	10 (25.0%)	34 (85.0%)	<0.001
At 5 minute			
Apgar score <3	7 (17.5%)	0 (0.0%)	<0.01
Apgar sore 3 to 6	10 (25.0%)	1 (2.5%)	<0.001
Apgar score >6	23 (57.5%)	39 (97.5%)	<0.001

At 5 minutes after birth low Apgar score of <3 and 3 to 6 was significantly associated with abruptio placenta in 17 (42.5%) compared to only 1 (2.5%) controls and this difference was statistically highly significant (*p*-value<0.001). Similarly, Apgar score of 6 or above was found in 23 (57.5%) patients compared to 39 (97.5%) controls and this difference was found highly significant (*p*-value<0.001) (table-III).

DISCUSSION

Abruptio placenta is the premature detachment of normally placed placenta. It is a process by which placental attachment to the uterus is disrupted by hemorrhage. The incidence of abruption placenta varies from 0.3% to 2.2% in the developed world, however, in Pakistan its incidence is quite high reaching up to 7%. Depending on whether the bleeding is internal or external, different types of abruptio placentae like concealed hemorrhage, external hemorrhage and relatively hemorrhage can occur.

In this study the birth weight of newborns was significantly low in the abruption group compared to controls. A previous study by Jabeen and colleagues reported that around (30.0%) of their cases had low birth weight (<2.5 kg), which is comparable to our study findings[22]. They also noted that (6.3%) of their cases had birth weight of >4 kg. This could be due to diabetes and grand multiparity as a significant number of their study cases were older than 40 years of age. Apgar score was found between 3 and 6 at 3 minutes in most of the study cases (67.5%) and still at 5 minutes Apgar score was low (up to 6) in a significant cases of abruption (42.5%) compared to controls (2.5%) as compared to study of Naseer *et al* 8% has <4,27.5 are

between 4-7% and 15% is >7 in 5 minute[23]. A study by Shukur-ud-din and colleagues reported that (60.0%) of their cases had low Apgar score (<5). Seventy seven many other investigators have also noted a similar trend of low Apgar score in newborn after abruption placenta[14,24,25]. This is comparable to our study findings.

The negative fetal outcome was noted in placental abruption cases compared to controls in this study. There was one still birth which occurred in the abruption patients. Compared to previous literature where high rate of still birth have been found in pregnancies with abruption and other complications (Jabeen, Sarwar), the rate of still birth was quite low in the current study[13,22].

In the present study the mean fibroid necrosis was significantly lower in abruption patients (6.1 ± 1.2) compared to (11.4 ± 2.2) in the controls. Similarly, the mean syncytial knots were significantly higher in abruption patients (49.6 ± 10.2) compared to (30.7 ± 5.6) in the controls. In contrast the study by Dhabhai and colleagues reported that mean syncytial knots were significantly high in pregnancy induced hypertention (PIH) patients compared to normal cases[24]. In this study the mean area of calcification was high (6.3 ± 3.7) in abruption patients when compared with (1.1 ± 1.6) in the healthy controls. According the micrometry the mean area of calcification was high (47.5 ± 16.5) in abruption patients compared to controls (39.3 ± 23.6). This correlates with a study done in sindh Goswami were formed mean calcification rate of 13 ± 4.8.25.

Despite technological advancement in ante-natal surveillance involving scrupulous examination, one of the major issues of disappointment is that the majority of low birth weight infants are not diagnosed until delivery, which is a good indicator of fetal hypoxia at term pregnancy. An abnormal outcome pregnancy was defined as a birth weight below 10th percentile of Kloosterman's birth weight chart, or 2500 grams birth weight.

The normal placental findings are difficult to define and differentiate from the abnormal due to the structural complexity. It is known that excess syncytial knot formation occurs in generalized from whenever the fetal circulation through the villi appears to be reduced. Irrespective of the mechanism which is reducing fetal blood flow through the villi the inevitable result in stromal fibrosis and excessive syncytial knot formation[8].

Moreover, the fibrinoid necrosis of placental villi is a highly characteristic lesion. Many investigators believe that this lesion is due to replacement of the villus by fibrin, this being formed either from the maternal blood in the intervillous space or from the fetal blood in the villous capillaries[25].

The current study has shown significant changes in the morphology of placenta in abruption patients compared to the normal healthy pregnancy. This difference has been found in terms of placental weight, diameter and number of cotyledons and surface area.

There were many advantages of the current study as detailed data on the morphology of placental abruption has been collected. Moreover, this was one of the very few studies on the national level as we found very few studies comparing abruption placental patients with normal controls. Also we found limited literature on the association between morphological studies of placental abruption, pregnancy complications and perinatal outcome.

There were some limitations of the current study as well which were mainly related to lack of long term monitoring of the patients and absence of follow-ups. The maternal outcome parameters were also not targeted, which could have given more in depth sight of women with placental abruption.

CONCLUSION

The histomorphological changes in abruptio placentae were statistically significant as compared to control group and leads to poor fetal outcome.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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