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# Risk factors related to intra uterine fetal death in Iran, A case-control study.

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**Abstract:**

Intra uterine fetal death (IUFD) is a traumatic event for the family which occurs in for about 1% of all pregnancies. In comparison with other countries this rate is increasing in Iran. Statistical reports from health centers of Firoozabad estimated the rate of 2.2% per year. Although obstetrical management has improved significantly, more than 50% of these cases are still unexplained. This research was a case-control study to determine risk factors for intra uterine fetal death. A standard questionnaire was designed consisting of four major parts: Maternal, fetal, placenta and umbilical cord factors. The questionnaire was filed by using medical records, between 1998-2003. Samples included 450 records, including 150 cases (those who had IUFD) and 300 controls (those who had live newborn). Generally, mother's education (P=0.000), and gestational age (P=0.001) were found as major risk factors. Moreover, season of delivery had a statistically significant association with IUFD (P=0.000). Maternal risk factors included ), receiving prenatal care (P=0.001), and consanguinity (P=0.004), pregnancy complications (P=0.06), the history of IUFD (P=0.000), ruptured amniotic fluid (P=0.007). Structural abnormality (P=0.000) such as impaired neural tube (P=0.000), fetal sex (P=0.000) and fetal weight (P=0.000) were major fetal risk factors. Intra uterine growth retardation (IUGR) (p=0.000) and third trimester bleeding (P=0.000) were the risk factor related to placenta and cord prolapse (P=0.01) was the only umbilical risk factor for IUFD. Logistic regression analysis was further clarified the role of confounding variables. Risk factors related to mother, fetus, placenta and cord were investigated for IUFD. It is difficult to identify preventable factors of IUFD, however consultation, proper prenatal care, early diagnosis of complications and careful evaluation may reduce the incidence of IUFD. This study suggests that certain measures has to be taken by Iran's health Ministry to make the women aware of the risk factors related to IUFD. Also during teaching sessions to medical students and staff, preventive medicine should be taken into consideration with emphasis on the local studies.

Key Words: Intrauterine fetal death, Iran, Risk Factors.

## Introduction:

Fetal death at any point during gestation is a traumatic event not only to the family but also to the caregiver. Certain causes of intra uterine fetal death (IUFD), including syphilis, Rh isoimmunization, toxemia, and diabetes, have shown significant declines over the past several decades (1). However, many fetal losses continue to occur from intrauterine infections, lethal malformations, fetal growth retardation, and abruptio placentae. Fetal death with no identifiable specific cause is another consideration when dealing with these cases. Other risk factors can include maternal, sociodemographic, and medical care factors. Although overall perinatal mortality rates have fallen considerably in the past several decades, fetal deaths have not decreased as rapidly as the neonatal portion (2). Despite efforts to identify the etiologic factors contributing to fetal death, a substantial portion of fetal deaths are still classified as unexplained intrauterine fetal demise. This proportion of unexplained deaths has remained fairly constant over the decades. These deaths are therefore difficult to prevent because the determinants have not been adequately identified. Even in cases in which a cause of death can be determined, the lack of uniformity in data collection and classification of causes of fetal death has made comparisons and accurate reporting difficult. Many previous studies have been limited to fetuses weighing more than 1000 g, whereas other studies included both antepartum and intrapartum fetal deaths, thus clouding the association between risk factors and causes of fetal death (3, 4, 5).

The rate of fetal death in Fars (one of the large provinces in Iran the capital of which is Shiraz) was 1020 cases in year 2000, 49.6% of which were male fetuses. Most of the cases occurred during summer time (37.6%) (6, 7). The cause of fetal death was reported as follows: 75.69% of cases were unknown, 17.65% were as the result of postpartum delivery and intra uterine growth retardation, complicated delivery (1.76%), congenital abnormality (1.57%), complications with placenta and amniotic membrane (1.37%) and trauma at delivery (0.78%). Consensus studies in Firoozabad (a district hospital in Shiraz) has revealed that the incidence of IUFD or early fetal death as defined by World Health Organization in Shiraz has increased from 0.83% in 1997 to 2.2% in 2001. These results were calling for further investigations. The purpose of this retrospective study is to help identify the maternal, sociodemographic, fetal, and medical care factors involved in fetal deaths.

## Materials and Methods:

This was a case-control study approved by the institutional review board at the Iran University of Medical Science.

Study filed was Firoozabad hospital, one of the major district hospitals in Shiraz the capital of Phars, Iran. This field was chosen because of health reports from the ministry of health regarding high IUFD rate and because of easy access.Overall the study population consisted of 450 subjects. All of the cases that were admitted in Firoozabad Hospital from last 5 years (1998-2003) were included in the study (n=150). A simple sampling method was used to select 300 subjects (two times more than that of the case group) for control group. For each subject taken for the case group, two cases that were admitted to the hospital at the same day were chosen for the control group.

Gestational age assignment in these data files was predominantly based on the last menstrual period (LMP). IUFD was defined as the fetal death (where there is no sign of life) at equal or more than 20 weeks of gestation and /or birth weight of equal or more than 500 gram (8).

The data for this case-control study was gathered using a standard questionnaire, which included the following sections: 1. Descriptive data such as occupation, level of education, gestational age (weeks), newborn birth weight (gram), living in rural or city area. 2. Risk factors related to the mother including age, number of pregnancy, receiving prenatal care, family relation with husband, birth season, history of diabetes, gestational diabetes, chronic blood pressure, blood pressure at admission, infectious diseases during pregnancy (TORCH), complicated delivery, history of IUFD, ruptured membrane more than 12 hours, glucosuria and proteinuria at admission. 3. Risk factors related to the fetus including obvious structural abnormality, RH incompatibility, and fetal distress before birth, fetal sex. 4. Risk factors related to placenta such as intra uterine growth retardation (IUGR), postdated delivery, third trimester hemorrhage, and multiple pregnancies. 5. Risk factors related to the cord such as true cord knot, cord prolaps, and cord around the neck.

Questionnaire was validated using content validity method. Reliability of questionnaire was found 90% using the inter-observer method.Statistical analysis: Descriptive analysis for quantitative variables was done using SPSS software. A p value of less than 0.05 was considered significant. T-student test was used to compare mean values for qualitative data. Quantitative variables however were tested using X2 and Fisher test. Non-parametric Colmogrov-spirnov test was used for Season variable. Odd ratio and confidence interval was used to investigate the correlation between IUFD and study variables.

## Results:

Descriptive data: Overall 450 subjects were analyzed in this study. Table 1 shows some of the main characteristics of the subjects.

Table 1: Comparing descriptive characteristics of the subjects in the case (n=150) and control (n=300) groups.

| Variables | Case (n=150) | Control (n=300) | P value |
|---|---|---|---|
| Age (year) | | | |
| >20 | 13(8.7) | 32(10.7) | |
| 20-24 | 45(30) | 109(36.3) | |
| 25-29 | 44(29.3) | 91(30.3) | |
| 30-34 | 27(18) | 41(13.7) | |
| >35 | 21(14) | 27(9) | |
| Mean | 26.87(5.93) | 25.54(5.52) | 0.024 |
| Occupation | | | |
| Working | 4(3.7) | 11(3.2) | |
| Housewife | 146(97.3) | 289(96.3) | 0.577 |
| Education | | | |
| Illiterate | 61(40.7) | 51(17) | |
| Literate | 89(59.3) | 249(83) | 0.000 |
| Gestational Age (days) | 108(72) | 30(10) | |
| >260 | 35(23.3) | 253(84.3) | |
| 260-280 | 7(4.7) | 17(5.7) | 0.000 |
| <280 | | | |
| Birth Weight (gr) | | | |
| <500 | 35(23.3) | 3(1) | |
| 500-1499 | 42(28.1) | 2(7) | |
| 1500-2500 | 35(23.3) | 14(4.7) | |
| >2500 | 38(25.3) | 281(93.6) | |
| Mean | 1659.53(1168.90) | 3306.58(590) | 0.000 |
| Number of Pregnancies | 53(39.6) | 126(44.8) | |
| 1 | 81(60.4) | 155(55.2) | 0.309 |
| 2-5 | | | |
| Received Prenatal Care | 88(58.7) | 273(91) | |
| Yes | 62(41.3) | 27(9) | 0.000 |
| No | | | |
| Place of Living | | | |
| City area | 70(46.7) | 164(59.7) | |
| Rural area | 80(53.3) | 136(45.3) | 0.109 |
| Family Relation | | | |
| Yes | 71(47.3) | 61(20.3) | |
| No | 79(52.7) | 239(79.7) | 0.000 |

The mean value for age was found to be significantly different between the two groups (P=0.024). The age of women in the high-risk groups (less than 20 and more than 35) were separately compared with those within the age range of 20-24. No significant difference was found (P= 0.622, P= 0.122 respectively).

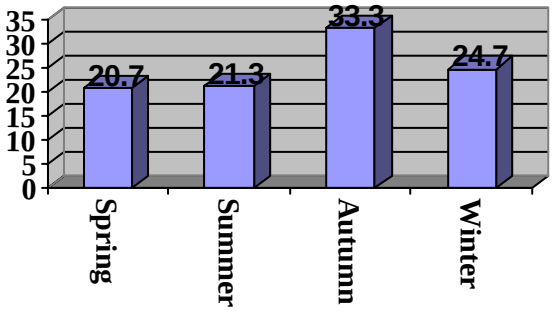
Only 4 subjects from the case group and 11 from the control group were working. The rest were housewives. There was a significant correlation between maternal age and illiteracy (P=0.003). Number of pregnancies was not found to be significantly different between the two groups (P=0.309) however the incidence of IUFD was higher in

those with number of pregnancies more than 2 in comparison with that of the primiparus (16.5% vs. 10.9%). There was a significant correlation between the number of pregnancies and receiving pregnancy care (P=0.000) as 63% of subjects with more than 5 pregnancies did not received any prenatal care.

As it is shown in the table number 1, receiving prenatal care was found to be significantly different between the two groups. Those who did not receive the prenatal care were 7 times more likely to loss their babies. The incidence of IUFD was higher in women living in rural areas (53.3%) however the comparison between the two groups did not reach any significance. Family relation with husband was found to be a risk factor (P=0.000).

Figure 1 shows the number of birth in the case group according to the season. The frequency of IUFD in autumn and winter was found to be higher than any other season (33.3% and 24.7%, respectively).

**Frequency of birth (%) in different seasons among cases (n=150)**




The number of cases who were suffering from high blood pressure, diabetes at the time of pregnancy and/or before pregnancy, was low. Therefore, a sum of all those complications was used for comparison between the two groups. As it is shown in Table 2, no significant difference was found between the two groups (P= 0.061). Also number of subjects with glucosuria and proteinuria were small and there were no screening tests recorded or available in the files. Only those patients with pre-eclampsia had their proteinuria recorded which their difference between the two groups were not found to be significant (P= 0.384). Two subjects within the case group had suffered from eclampsia.

Table 2. A comparison between risk factors relating to mother, fetus, placenta and cord in case (n=150) and control groups (n=300).

| Variables | Case Number (%) | Control Number (%) | P value |
|---|---|---|---|
| Maternal Risk Factors | | | |
| Pregnancy Complication* | 21(14%) | 25(8.3%) | 0.06 |
| High Blood Pressure at admission | 15(10) | 20(6.7) | 0.215 |
| Infectious Diseases & | 5(3.3) | 10(3.3) | 1 |
| Complicated Delivery | 13(8.7) | 29(9.7) | 0.731 |
| History of IUFD | 10(6.7) | 5(1.7) | 0.000 |
| Ruptured Amniotic Fluid | 15(10) | 11(3.7) | 0.007 |
| Proteiuria | 14(9.3) | 21(7) | 0.384 |
| Fetal Risk Factors | | | |
| Structural Abnormality | 26(17.3) | 4(1.3) | 0.000 |
| Impaired Neural Tube | 15(10) | 1(0.3) | 0.000 |
| RH Incompatibility | 7(4.7) | 15(5) | 0.877 |
| Fetal Distress | 17(11.3) | 39(13) | 0.614 |
| Fetal Sex | 100(66.7) | 154(51.3) | 0.002 |
| Postpartum | 5(3.3) | 17(5.7) | 0.532 |
| Placenta Risk Factors | | | |
| Intra Uterine Growth | 20(13.3) | 3(1) | 0.000 |
| Retardation | 25(16.7) | 9(3) | 0.000 |
| 3rd Trimester Hemorrhage | 3(2) | 6(2) | 1 |
| Multiple Pregnancy £ | | | |
| Cord Risk Factors | | | |
| True Cord Knots | 8(5.3) | 10(3.3) | 0.307 |
| Cord Prolaps | 8(5.3) | - | 0.000 |
| Cord Entanglement Around Neck | 9(6) | 34(11.4) | 0.068 |

* Patients suffering from diabetes, gestational diabetes, chronic hypertension.
& Mainly included urinary infections.
£ Fisher Test

Only proven infectious diseases (using urine samples), which were found to be recorded in the files were urinary infections. The rate of urinary infection was found to be similar between the two groups (3.3%).

There was a positive correlation between the history of IUFD and its repeated occurrence (P=0.005). However, there was no correlation between this variable and family marriage (P=0.356).

From the fetal risk factors, structural abnormalities were found to increase the risk of IUFD by 15.5 times. Overall, thirty cases were found, 17.3% of which was in the case group and 1.3% in the control group. The most prevalent

abnormality was neural tube defect including anencephaly (6.8%), spina bifida (0.7%), and hydrocephal (2%) which were all within the case group. There was a significant correlation between the family marriage and structural abnormality. The number of subjects with neural defect was higher in the case group (10% vs. 0.3%) and this difference was found to be significant (P=0.000). A case of female psudohermaferodism was found in the case group, which was categorized as female. The incidence of IUFD was found to be higher in boys than girls (66.7% vs. 33.3%).

Table 3. Logistic regression analysis of the relevant variables.

| Variable | B | P value |
|---|---|---|
| Literacy | -2.19 | 0.199 |
| Gestational age | -1.07 | 0.159 |
| Birth weight | -1.84 | 000 |
| Mother's age | 1.730 | 0.535 |
| Receiving prenatal care | -0.141 | 0.001 |
| Family relation with husband | 9.80 | 0.004 |
| History of IUFD | 0.109 | 0.195 |
| Rupture of membrane | 5.183 | 0.440 |
| Structural abnormality | 0.305 | 0.000 |
| Fetal sex | 0.109 | 0.000 |
| Intra uterine growth retardation | 0.138 | 0.063 |
| Third trimester hemorrhage | 0.180 | 0.002 |
| Cord prolaps | 0.303 | 0.01 |

Third trimester hemorrhage included the hemorrhage from placenta previa and placenta abruption. Sixteen percent of IUFD cases had placenta abruption as compared to 4.7% of controls. Cord prolaps was found to increase the risk of IUFD by three times. All 8 cases of prolaps occurred in the group with IUFD.

Logistic regression analysis was done for all relevant variables (Table 3). Since the birth weight is affected by the gestational age, both variables were entered in the logistic model. It was concluded that birth weight on its own could be considered as a risk factor. Other risk factors included as follows: Not receiving prenatal care (P=0.01, B= -0.141), family relation with husband (P=0.004, B=9.80), fetal structural abnormality (P=0.000, B=0.305), fetal sex (P=0.000, B=0.180), third trimester hemorrhage (P=0.0.002, B=0.180) and cord prolapse (P=0.01, B=0.303). Variables such as literacy, history of IUFD, rupture of amniotic membrane for more than 12 hours and growth retardation which were a risk factor in the simple models, in fact were under the influence of other factors and cannot be considered as a risk factor on their own.

## Discussion:

Early Fetal death has been defined by the World Health Organization as those death that occur at less than 20 completed weeks of gestation or with birth weight > 500 gram (9). Over the past several decades, the pattern of fetal death has changed. Some causes of fetal death, such as syphilis, are no longer a significant problem; others, such as cord accidents, have remained relatively unchanged for decades; some, like antiphospholipid antibodies, have only recently been recognized. Several causes, like chromosomal abnormalities, are not preventable, even with modern medical knowledge, whereas others, like postmaturity, are completely preventable. Intrauterine fetal death secondary to Rh isoimmunization, toxemia, and diabetes has shown significant declines over the past three decades; however, many fetal losses continue to occur from intrauterine infections, lethal malformations, fetal growth retardation, and abruptio placentae. Fetal death with no identifiable specific determinant is still the most common cause of fetal death throughout the past three decades (1).

Risk factors for fetal death can be classified into general and specific categories. General category includes sociodemographic data such as education, occupation and place of living, etc. Specific data includes maternal, fetal, placenta, cord factors. Showghy (10) has stated that pregnancy at the age of 16 years and less can increase the IUFD risk factor by 4 times. In his study he has found that illiteracy increased as the age of mothers decreased. Current study however showed otherwise. As the maternal age decrease the literacy rate increased (P=0.003). This might be due to the fact that Iran's Ministry of education has moved forward in the recent years to eradicate illiteracy. Better education can directly influence the implementation of reproductive health.

Unlike the study of Fretts and colleagues (1) who showed pregnancy at the age of 35 and more can increase the risk of fetal death at the rate of 1.5 times, our study did not show any significant difference between the two groups of case

and controls. Smith (11) suggests that maternal age is not solely the reason for IUFD but the major diseases such as diabetes or high blood pressure accompanied by the higher age can act as a confounding variable. The majority of our samples with more than 35 years of age did not have any major complications before their pregnancy, which in turn can lead to a delivery of a healthy baby. Number of pregnancies in the current study was not found to be a significant risk factor. Abu-Heija (12) has introduced pregnancies more than 10 as the major risk factor as compared with 2-5 ($P<0.025$). His subjects were from a low economical -social status and they did not receive any prenatal care. The incidence of pre-eclampsia was high in his sample. He believed if the subject would have received a proper prenatal care IUFD could be prevented. In our study a significant correlation was found between the number of pregnancies and receiving prenatal care ($P=0.000$). Sixty three percent of subjects who had more than 5 pregnancies did not receive any prenatal care (Table2). This is probably due to the level of confidence a multiparous feel to deal with pregnancy complication or it could be simply because she is too busy looking after her other children that could not attend the prenatal clinic. The lack of follow-up and screening in the management of prenatal clinic cannot be ignored, however. Whatever the reason, this could lead to a major complication in the health of pregnant women and her pregnancy outcome. Hyattsville (13) and Nathnagle (14) both believed that limited access to prenatal care can increase the risk of IUFD dramatically. Low income, limited medical coverage, and considering pregnancy as a complete natural phenomenon with no complication have been considered the major reasons for not enquiring prenatal care.

Geography was not found to be a significant risk factor for IUFD. Firoozabad is a district area with more than 20 health sites and health clinics, which are mostly managed by the midwives. Rural area on the other hand is covered by the community health workers (Behvarz) who are not confident in taking care of pregnant women especially the high-risk group and usually refer them to the health clinics out of the rural area. It is hard for rural pregnant mothers to travel

to the city area. It is therefore suggested that qualified midwives be sent to the rural area on a regular basis to provide proper prenatal care and to prevent pregnancy complications. Kiely (15) in a study of IUFD between hospitals of first and third level (in terms of their facilities) suggests that even for low risk pregnancies, the rate of IUFD is lower when mothers receive proper prenatal care.

Family relation with husband is a part of many cultures. It can be due to immigration of big families as a result of war, bad economical situation or in search of suitable field and it has been considered as one of the major reasons for IUFD, low birth weight, fetal structural abnormalities and the heredity of many genetic diseases (16, 17). Our study also showed the same result. Firoozabad is the mainland for Ghashghai Tribe who migrate from one place to another within the province in search of green field for their sheep. Internal marriages are very common among these tribes.

Deliveries during winter or autumn were found to be more at risk of IUFD in our study. This is compatible with the findings of Froen (16). Rosham (18) also relates the high incidence of very low birth weight and premature birth to the winter climate. He suggests that low-economical status of families and their vulnerability to sickness and urinary infectious disease might be the main reason. The majority of our subjects were living in the rural area. Firoozabad's roads can get frosty in the winter; make it hard for women to travel. On the other hand, the timing of implantation for most of the IUFD cases would be the end of winter or the beginning of spring when the prevalence of viral diseases are high.

**Maternal factors:**

Prenatal complications such as diabetes, hypertension, pre-eclampsia was not prevalent in our data base. However, high blood pressure can increase the risk of fetal death. His sample size was much bigger than ours (19). Gunton (20) emphasizes on diabetes mellitus and suggests that proper pre-pregnancy consultation can decrease the probability of unsafe pregnancy.

Oxygenation of placenta can completely be blocked due to seizures of eclampsia, leading to fetal death. The number of subjects with eclampsia in our data set was too narrow to draw any conclusion from it. However continuous monitoring of blood pressure is suggested by other authors (21). A prospective study with a bigger sample such as that of the Moyo (1995) has shown that infections such as toxoplasmosis, E-coly, gram

negative and gram-positive bacteria can increase the risk of IUFD more than 4 times. Carrena (22) suggests that infections common to human and animals such as Listeria, Leptosperia, Lym disease although rare but can led to IUFD. Twenty four percent of IUFD cases in his sample were suffering from infections diseases.

Shiener (23) did not find any correlation between IUFD and difficult labor. Difficult labor in his study was defined as use of forceps and vacuum only. However, adding to that definition, lengthening of the 2nd stage of labor for more than 2 hours, the same conclusion was drawn from our study.

As it is shown in our study, history of IUFD can also be a risk factor. Thus, performing electronic monitoring as soon as 32 weeks of gestation is recommended. Rabson (24) found that gestational diabetes and abnormal glucose tolerate test in women with the history of IUFD is 4 times more prevalent. However, Seppo (25) did not report the repeated IUFD in his sample group. He only mentioned the birth of immature infant and low birth weight at the time of delivery.

Rupture of amniotic membrane more than 12 hours in our study and that of the Pajantar (26) found to be correlated with IUFD. He found that the incidence of cesarean section, instrumental delivery, fetal distress, and mild to severe hypoxia increased in his study group ($P<0.05$). Also, he found that longer period of ruptured membrane can lead to higher risk of chorioamninitis.

**Fetal factors:**

Structural abnormalities were found to be highly prevalent in the case group. Incerpi (8) findings is also consistence with our findings. One of the major links could be family marriage although the neural tube defect in our study was not correlated with this variable.

RH incompatibility was not found as a significant risk factor. Surkan (27) also came to the same conclusion. Although both our and his study only looked at the death of fetus, it is well known that RH incompatibility can cause severe crenicterus, mental disability and finally death in the new born.

Male fetus seems to be more vulnerable to death (28). Airass (29) showed that true cord knots are more prevalent for male fetuses although he does not mention the mechanism. Divon (30) attributes the male sex of fetus to the postpartum pregnancies. However, our study did not show any significant correlation between the post term pregnancies and the IUFD.

**Placental factors:**

Intra uterine growth retardation (IUGR), postdate delivery (more than 280 days), 3rd trimester hemorrhage and multiple pregnancy were investigated in this category. The IUGR was significantly correlated with IUFD. Cenantigus (31) found that IUFD is associated with very low birth weight (less than 1500 gr). The rate of death in this group was found 16 to 45 per thousand cases, which was significantly different than that of the normal weight babies (more than 2500 gr) (4 to 4.6 per thousands). Divon (30) also found that limited uterine growth rate can increase fetal death by 10 times at the 41 weeks of gestation.

Hemorrhage during 3rd trimester was found to increase the risk of IUFD 6.4 times more. Most of the IUFD cases were accompanied with placenta abruptio (16% in the case group vs. 4.7% in the control group). Surkan (27) also stated the strong correlation between the IUFD and placenta previa ($P<0.001$) and placenta abruptio ($P<0.02$). Incerpi (8) reported 27 cases of placenta abruptio out of 178 IUFD cases.

Dikenson (32) reports an increase in the death rate of twin pregnancies. The rate of fetal and newborn survival has been estimated around 63 percent in his cohort study. Paulli (33) also adds that monozygotic twins have a higher death rate.

**Cord Factors:**

Cord prolaps was the only variable within this category, which had a significant correlation with IUFD. Incerpi's (8) also showed that cord prolaps is a risk factor for IUFD (27 cases out of 158). However, Prabolus (34) study showed no fetal death out of 65 study cases. In his study the duration of management for cord prolaps (the duration between diagnosis of prolaps and delivery) was estimated about 20 minutes on average for complete prolaps and 25 minutes for occurred prolaps. All of these cases were of course happened in the hospital setting. The delivery rate in that city hospital is 5000 per year 21% of which are referred from private clinics meaning that all the clients have received prenatal care during their pregnancies. Sixty general practitioners and 20 Gynecologists provide hospital service. In our study hospital, however, an estimation of 1700 deliveries per year is handled single handedly by one gynecologist and 5 midwives. This hospital covers all the district area of Firoozabad. The authors therefore suggest an urgent need for staff development

Logistic regression analysis on the whole variables showed that some of the factors are confounding variables, which can be omitted and not be considered as the major risk factors.

In conclusion, gestational age (in general) and not receiving prenatal care, family relation with husband, structural abnormalities, fetal sex, 3rd trimester hemorrhage and cord prolaps (in specific) were found to be risk factors for IUFD. Women should be encouraged to come to the hospital for prenatal visits. For remote areas, temporary satellite health centers can be established. Information regarding the hazard of uncontrolled pregnancy and family marriage can be disseminated through the health workers. Midwives can be assigned to visit pregnant mothers at their homes on regular basis. Pre-marital consultation should be mandatory to issue marriage certificates. If couples are still interested in family marriage, genetic consultation before pregnancy should be provided. Prenatal screening for viral infections specially those pregnancies, which occur during spring or winter, should be carried out for this specific region. Ultrasound can be used to diagnose placenta situation. Fetal monitoring for cases with the high risk can lead to prevention of IUFD.

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