International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Repeated Miscarrigedue to Undiagnosis Down Syndrome Risk

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ABSTRACT

BACKGROUND: One of the main cause of misscarriage is chromosomal abnormalities, because they are more likely to create gametes with unbalanced chromosome rearrangement , carries with balanced chromosome rearrangement are frequently at risk for recurrent pregnancy loss .

OBJECTIVE: Chromosomal abnormalities seen in a couple with a history of primary recurrent pregnancy loss were assessed in this study .

OUTCOME: Genetic testing result of spontaneously produced pregnancy in one patient with a balanced chromosomal rearrangement and chromosomal abnormalities in patient diagnosed with primary recurrent pregnancy loss (3^{rd})

BACKGROUND: Down syndrome (trisomy 21) is the most common chromosomal abnormality. Trisomy 21 occurs in 0.45% of clinically observed pregnancies. However, with the widespread use of prenatal diagnosis, recent reports have shown that trisomy 21 is found in one in 691 live births (0.14%) in the United States and in 22 out of 10,000 live births (0.22%) in Japan. Prenatal genetic testing is gradually becoming more widespread in Japan, with 20% of trisomy 21 cases diagnosed prenatally in 2016. In 2016, approximately 70% of children with trisomy 21 were born to women of advanced maternal age. The incidence of trisomy 21 usually increases with increasing maternal age .

In addition, the risk of trisomy 21 recurring in families with affected children is 1%-2%. There are only a limited number of case reports of trisomy 21 being repeated three or more times, and it is extremely rare. Possible causes for young women repeatedly becoming pregnant with children with trisomy 21 include the possibility of the mother having a slight mosaic trisomy 21 or gonadal mosaicism

We report a rare case of a mother under 35 years who had at least five pregnancies with full trisomy 21.

Frequent miscarriages as a result of unidentified trisomy 21,or down syndrome, is frequent caused by biological predisposition or underlying genetic factor that raise the risk of creating embryos with chromosomal abnormalities. Trisomy 21, also know as down syndrome ,is a multi system genetic disorder that increase the risk of birth abnormalities , intellectual disability, & other health issue. A whole or partial extra copy of the no. 21 chromosome causes down syndrome .

A kid with down syndrome has an extra copy of chromosome 21. normally, a baby is born with 46 chromosome. The development of the baby ‘s body & brain is altered by this extra copy. Physical , intellectual , & linguistic difficulties will be specific to each child born with this illness. The degree of the persons intellectual handicap might range from low to moderate.

Physical characteristics are typically observed at birth , & chromosomal analysis (the baby genetics karyotype) is used to confirm the diagnosis. Widely spaced eyes with a slight upward slant , a small nose with flattened bridge, microcephaly (small head size), poor muscle tone, a large tone, a large tongue , a short neck,small hand & short finger are some of these physical characteristics.

The majority of kids with down syndrome are likewise little in stature. Miscarriages are frequently caused by chromosomal abnormalities, because they are likely to create gametes with unbalanced chromosome rearrangements, carriers with balanced chromosome rearrangement are frequently at risk for recurrent pregnancy loss (RPL).

Describe an unusual instance of a woman under 35 who had at least five babies with complete trisomy 21. Three times on amniotic fluid , three times on misscarriage samples , and once a newborn , chromosome testing was carried out. Five individuals had trisomy 21 , one had trisomy 16, and one had a normal karyotype . The patient and one of her partners underwent chromosome testing in an attempt to determine the cause , but the result showed that their karyotypes were normal.

Blood samples from the patient and her parents were obtained and subjected to whole-exome sequencing (trio analysis); however , the etiology of the recurring trisomy remained unknown. The patient's gonadal mosaicism was most likely the source of recurrent trisomy 21.

GENETIC COUNSELLING:

Due to the recurring trisomy 21 , genetic counselling was carried out multiple times since the initial visit. We informed the patient that neither she nor her partner had any chromosal abnormalitites, that despite her partner changing , she had many pregnancies that resulted in a child with trisomy 21 , and that we were unable to identify any causative genetic variations in WES .

Gonadal mosaicism was therefore a possibility. We informed her , however , that gathering ovarian tissue for the sole purpose of examining gonadal mosaicism was not feasible .

ABORTIONS; karyotype ; recurrent misscarriage; pregnancy loss

Karyotype as a component of the main study . In accordance with our previously outlined criteria (9) ,

Additional presumed causes of abortion were also examined using

1. Glucose tolerance test.
2. Taxoplasmosis serology .
3. Hysterosalpingogram or hysteroscopy to diagnose anatomic abnormalities , intrauterine adhesions , and cervical incompetence;
4. Thyroid function assessment
5. Serum PRL measurement ;
6. Luteal phase assessment based on the length of luteal phase and midluteal plasma P;
7. Anti-nuclear factor assessment using rat liver as a substrate and fluoresceinated rabbit anti human immunofluorescence
8. Evaluation of anticardiolipin antibody using an enzyme-linked immunosorbent test and lupus anticoagulant , based on Russell's viper venom time or kaolin clotting time .

Objective proof of prior pregnancies , such as a possitive hCG test , fetal or placental tissue histology , or ultrasound-based claims of a pregnant sac, was necessary before participation in the study.

Karyotyping of peripheral blood, Peripheral blood cells that were regularly cultivated were used for chromosome analyses. Using Trypsin-Giemsa, slides prepared for G- banding using conventional methods .

Four hours before to the cytologic preparation , colchicine was added .

The selection failure hypothesis, which states that" recurrent miscarriage is the result of failure of the prevention of "poor quality"embryos implanting, allowing embryos that are destined to fail to implant and present clinically as recurrent miscarriage" is used to analyze recent data on RM.

Therefore repeated miscarriages are a result of natures quality control failing .
Evidence relating the role of aberrant embryos and endometrial receptivity is examined , challenging the notion the RM is caused by the mother rejecting healthy fetuses .
To better manage recurrent pregnancy loss, more research is required to comprehend the mechanics of maternal tract-embryo interaction.

EPIDERMIOLOGY

A miscarriage occur when a pregnancy ends spontaneously without the use of medical or mechnical method before the fetus is mature enough to survive.
To put it another way, miscarriage is define as an early pregnancy loss that occur before the 20th week of gestation ,counting from the first day of the last regular menstrual cycle .
Spontaneous pregnancy loss occurs in around 15 percentage of all clinically diagnosis pregnancies end before a women become aware that she is pregnant. Three or more clinically documented pregnancy losses before 20th week of gestation from the last menstrual cycle are referred to as a recurrent spontaneous miscarriage.
Genetics uterine anatomical abnormalities , infection ,endocrine ,& immunological variable have all been identified as potential causes of (RSM). Recurrent miscarriage are also linked to maternal age & the no. of perious spontaneous losses. After the 1st,2nd & 3rd pregnancy losses, women without a history of live birth have a 30 % & 33% chance of experiencing another miscarriage respectively .

PREVALENCE

Spontaneous pregnancy loss occurs in about 15% of all clinically diagnosed pregnancies, and many pregnancies end before a woman becomes aware that she is pregnant. Three or more clinically documented pregnancy losses before 20 weeks of gestation from the last menstrual cycle are referred to as recurrent spontaneous miscarriages (RSM). One to two percent of women are affected.
Genetics, uterine anatomical defects, infection, endocrine, and immunological factors have all been identified as potential causes of RSM. Recurrent miscarriages are also linked to maternal age and the number of previous spontaneous miscarriages**.** After the first two and third pregnancy losses, women without a history of live birth have a 30% and 33% chance of experiencing another miscarriage [2]. There is currently little information available regarding the frequency of repeated miscarriages among Indian women. In order to ascertain the prevalence of RSM of less than 20 weeks of gestation among Indian females, this study was conducted.
The prevalence of female patient with RSM among the included patient was the main study outcome. The campersion of age -specific losses in patient with <3 & >=3spontaneous miscarriage of <=20 weeks of gestation, Uterine anomalies (septate uterus , uni/biocarnuate uterus, leiomyoma, cervical insufficiency) , clotting disorders (factor V leiden, plasminogen activator inhibitor -1, prothrombin gene mutation , antiphospholipid syndrome(APS) , von willebrand disease , idiopathic thrombocytopenic purpura), endocrine disorder (cushings syndrome (PCOD), diabetes ,thyroid); & infections TORCH [toxoplasmosis,other{ syphillis, varicella- zoster, parvovirus B19} rubella , cytomegalovirus ,& herpes infection], listeria monocytogenes); & other general risk factors (smoking drugs,alcohol consumption ,uterine injury).

DISEASE DISCRIPATION

Genetic ,uterine anatomical abnormalities, infection ,endocrine, & immunologyical variables have all been identified as portential causes of RSM. Recurrent miscarriage are also linked to maternal age & the no. of perious spontaneous miscarriage .

CASE PRESENTATION:-

When the patient first came to our hospital early in her pregnancy, she was 31 years old. Consanguineous marriages did not occur. The causes of recurrent pregnancy loss ,A known cause of spontaneous abortion and poor fetal outcomes is rubella infection in the early stages of pregnancy.

Rubella greatly raises the risk of miscarriage even though it is less frequently linked to chromosomal abnormalities like Down syndrome. A potential infectious etiology contributing to recurrent pregnancy loss is suggested by the patient's positive Rubella serology on TORCH screening.

The recurrent pregnancy loss that occurred in spite of standard routine investigations makes this case unique. Only TORCH screening was able to identify rubella infection in the absence of known exposure or typical clinical symptoms. The patient's lack of animal contact or bites raises the possibility of a subclinical infection. Rubella can cause spontaneous abortion, but it is less frequently linked to chromosomal abnormalities like Down syndrome. The case highlights how crucial TORCH screening is for unexplained recurrent miscarriages.

UNIQUNESS OF THE STUDY:-

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RESULT

Laboratory testing for Rubella virus, Rubella IgG serology testing performed gives positive result whereas detection of rubella RNA in a clinical sample provide laboratory confirmation of infection.

DISCUSSION

Patki A(2016), The study revealed a higher prevelence of RSM among the indian women as compared to western data. Age, clotting disorder, immunological factor, infection ,& genetic disorders were the significant risk factors associated with RSM.

Yan J et al. (2012) done a retrospective, observational study including 1589 miscarriages among 543 women with recurrent miscarriage. It was found that in women who had two miscarriages only, 49.17% of both miscarriages occurred in the same gestational period, which was significantly higher than the expected probability of 34.54%. The proportions of all miscarriages occurring in the same gestational period in women with three, four or five or more miscarriages were 28.72%, 19.44% and 18.60%, compared with the expected probabilities of 14.36%, 6.57% and <3.15%. They draw the conclusion that the proportions of the miscarriages occurring consistently in the same gestational period are higher than the theoretical probabilities calculated for the whole population.

Whereas; our study specifically shows Rubella virus infection is the main cause of miscarriage.

LIMITATIONS & FUTURE PROCETIVE

The study describe detail of single patient which does'nt explain overall prevalence and confirmation of recurrent miscarriage. Large scale prospective study required to determine the true prevalence of chromosomal aneuploidy- recurrent miscarriage whereas evaluation of early genetic screening protocols will help in recurrent pregnancy loss, even in younger maternal ages.

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