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"Chromosomal Analysis in Patients of Recurrent Pregnancy Loss"

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Abstract-
Background and Objectives - The advancement in genetics has shown that recurrent pregnancy loss is associated with chromosomal abnormalities. The main objective of this study is to find out the percentage of underlying chromosomal abnormalities in cases of recurrent pregnancy loss.
Result - Out of 50 patients (16 males and 34 females) studied for karyotyping, 7 (14%) were found positive for chromosomal abnormality leading to RPL. The 4 females and 3 males with abnormalities had structural chromosomal variations; 4 heteromorphism and 3 inversion types. Chromosomes 9, 21, and Y were associated with the abnormalities, with chromosome 9 being the most frequent. The age group 26-35 years and patients with more than 4 previous abortions had a higher prevalence of chromosomal abnormalities leading to RPL. Hypertension, consanguinity, and asthma may also have some associations with RPL.
Conclusion- Chromosome 9 was the most commonly affected chromosome in both male and female patients with RPL, showing heteromorphisms and pericentric inversions. Of the 7 patients with chromosomal abnormalities, 4 were female and 3 were male, highlighting the importance of cytogenetic testing for both parents and offering alternative options for future offspring.

Introduction:

The pain of seeing their progeny die within the uterus consecutively is torture beyond imagination for a lot of couples. Pregnancy loss is defined as the spontaneous loss of clinically established intra-uterine pregnancy before the foetus reaches viability, that is up to a maximum of 24 weeks of gestation. [(1)]

Spontaneous Recurrent recurrent. when particularly challenge, medical a pose to continue abortions spontaneous consecutive more or two of occurrence the as defined is RPL)) loss pregnancy .abortions [(3)] .world the over all pregnancies of %3-1 in occurs It [(2)]

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Spontaneous abortion is the natural way of screening the embryos without which the incidence of infants born with birth defects would be far greater. [4] Clinical risk factors of RPL in the mother may include endocrine abnormalities, chronic debilitating diseases, use of drugs or intake of environmental toxins, infections, immunological factors like autoimmunity, uterine defects, incompetent cervix, inherited thrombophilia and physical trauma. [5]At least 50% of the Recurrent pregnancy loss cases are idiopathic since no abnormality is found in the diagnosis. [3,6,7] There is growing evidence that RPL has genetic susceptibility. Even maternal and paternal age has also been linked to RPL.[8] The standard RPL evaluation in a genetic lab includes testing for chromosomal translocations and abnormalities in each parent as well as maternal testing for endocrine disorders like thyroid abnormalities and autoimmune disorders. [9] It is seen surprisingly that almost 50 percent of all first-trimester spontaneous abortion cases are due to the derangement of one or more chromosomes. [10]

As cytogenetics can explain abortions caused by chromosomal anomalies and identify couples at risk of having a baby with unbalanced chromosomal translocations, so this study was carried out to find out the relation of recurrent pregnancy loss with chromosomal abnormalities.

Materials and methods :

The retrospective case-control study was performed by collecting and analysing data from a total of 50 patients including male and female parents facing RPL who were referred to the Anatomy department's genetics lab from the Civil Hospital, Ahmedabad.

Inclusion criteria -

- Females who are facing recurrent pregnancy loss and having pregnancy less than 24 weeks, referred by Obstetrics and Gynaecology department. The couple, as well as the female parent individually in case the male parent refuses to participate in the study.
- The female with at least two spontaneous abortions in the past with no history of TORCH infections or physical trauma during pregnancy.

Procedure-

Informed consent was taken from the patients. The patients were comfortably settled in the lab, and their medical history was taken before karyotyping was conducted in the Genetics lab. Blood was collected from the vein, cultured, and treated with colchicine, followed by a series of treatments until chromosomes could be analyzed using GTG banding. Karyotypes were prepared and analysed using GenASIs. If chromosomal abnormalities were found, proper genetic counseling was given. Statistical data was recorded for each patient.

Result :

A total of 50 patients comprising of 16 males and 34 females were studied for karyotyping.
Out of 50 karyotypes studied-

- 7 patients (14%) were found positive for chromosomal abnormality leading to RPL.
- 4 patients (57%) who were found to be positive were females and 3 patients (43%) were males.
- .All the chromosomal abnormalities were of structural variety

- 4 chromosomal abnormalities out of 7 are of heteromorphism type while 3 were of inversion type.
- Out of 7, 4 chromosomal abnormalities were associated with chromosome 9, 1 abnormality with chromosome Y and 2 abnormalities with chromosome 21.
- In males, chromosomes 9, 21 and Y abnormalities account for 1 case each. Chromosome Y was associated with pericentric inversion while chromosome 21 was associated with heteromorphism in the short arm and chromosome 9 was associated with heteromorphism in the long arm.
- In females, abnormalities in chromosome 9 account for 3 cases of RPL while chromosome 21 accounts for 1 case of RPL. Chromosome 9 was associated with both pericentric inversion and heteromorphism involving long arm while chromosome 21 was associated with heteromorphism involving long arm.
- Chromosomal abnormalities were more prevalent in the age group 26-35 years in both males females and.
- Patients with more than 4 previous abortions were found to have chromosomal abnormalities leading to RPL.

Discussions-

Recurrent pregnancy loss (RPL) is a challenge for couples trying to conceive, and karyotyping has made it possible to determine chromosomal causes even when there are no clinical signs of abnormality.

- 14% of cases in the study had known chromosomal abnormalities, with structural abnormalities being the most common. Studies conducted by Turki, R.F. et al. and by Elhady. et al. obtained 7.6% [(12)] and 11.6% [(13)] of the population to be having chromosomal abnormalities leading to RPL respectively. This means the locality under study has more population getting tested in the genetics lab for chromosomal anomalies that could lead to RPL. This could be due to the availability of genetics lab within the Civil Hospital campus where varied RPL patients including those from the poor socioeconomic class were tested at minimal costs.
- Chromosomal aberrations are more frequent in females but males also significantly contribute to RPL. In a study conducted by Elhady. et al., chromosomal aberrations were more frequent in females [7.14%] compared to males[5.35%], although the difference was not statistically significant.
- Age groups of 26-35 years in both males and females have a higher chance of chromosomal abnormalities. In a different study by Elhady. et al. no increase in the number of abortions with advanced maternal age was observed. [(13)] This means that the relationship between advancing age and RPL varies depending on the physical and socio-economical environment as well as the genetic constitution.
- Patients with more than 4 previous abortions constitute over 50% of cases facing RPL due to chromosomal anomaly. A study conducted by Elhady. et al. under similar circumstances found

that more than 50% of couples having 4 or more spontaneous abortions had a chromosomal anomaly that was leading to it.[13] Chromosomal abnormalities are the reason for multiple consecutive abortions and genetic counselling of such cases is critical and very important.

- Consanguinity may also play a role in accumulating variations leading to chromosomal abnormalities causing RPL. Hypertension and asthma may also have some associations with RPL.

Education about cytogenetic testing is thus important, especially for poorer and uneducated sections of society.

Conclusions-

The most commonly affected chromosome in patients of RPL was chromosome 9 in both sexes. It showed heteromorphisms-: {+XX,9HQ,46},{+XY,9HQ,46}; as well as pericentric inversions -:{,46 (INV(9)(P11Q13 XX,},{(P11;Q11) INV(9) XX, ,46}. All the aberrations found were structural in nature. With increasing age, the tendency of having RPL was also increasing. Hypertension, consanguinity and asthma may also have some associations with RPL. Out of 7 patients which were having chromosomal abnormalities, 4 were females and 3 were males which meant cytogenetic testing of both male and female parents is crucial in detecting such abnormalities and providing alternate options to the couple for future progeny.

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TABLES-

Tables- Table 1- Percentage of RPL patients with chromosomal abnormalities-

Aetiology of RPL	Percentage
Non chromosomal causes	86%
Chromosomal abnormalities	14%

Table 2- Age group of males and females with normal and abnormal karyotype-

Age group	Males with No chromosomal abnormalities	Males with chromosomal abnormalities	Total	Females with no chromosomal abnormalities	Females with chromosomal abnormalities	Total
18-25	2	1	3	17	1	18
26-35	11	2	13	13	3	16
36- 45	0	0	0	0	0	0
>45	0	0	0	0	0	0

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Table 3- Correlation of the number of abortions with chromosomal abnormalities- (write percentage)

No. of consecutive abortions	No. of cases with chromosomal abnormalities	No. Of cases with no chromosomal abnormalities	Total
2	2	21	23
3	2	2	4
4	0	3	3
>4	3	1	4

Table 4- Different chromosomal abnormalities found in patients-

Gender	Chromosomal abnormalities found	No. Of cases	Structural (S) / Numerical (N)
Male	46,X, INV Y (P11.2; Q11.2)	1	S
	46, XY, 21PS+	1	S
	46,XY,9HQ+	1	S
Female	46,XX, 21PS+	1	S
	46,XX,9HQ+	1	S
	46, XX, INV(9)(P11Q13)	1	S
	46, XX, INV(9) (P11;Q11)	1	S

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Table 5- Other factors associated with RPL-

Associated Factors	No. Of cases	Normal chromosomal findings	Abnormal chromosomal findings
Hypertension	2	1	1
Consanguinity	2	1	1
Diabetes	2	2	
Tobacco	1	1	
Asthma	1		1
Still birth	1	1	
Polyhydraminos	2	2	
Intraplacental hematoma	1	1	