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Secondary Constriction Region Variations in Individuals with Reproductive Failure

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Abstract: **To correlate the relationship between secondary constriction region variations and individuals with reproductive failure, 145 couples with reproductive failure and 75 couples with normal reproduction were studied. Karyotype analysis using Giemsa (GT) banding technique was performed. Chromosomal abnormalities were identified in 22 individuals. It included variations in the secondary constriction region and satellite, inversion in chromosome no.9, autosomal translocations and variation in Y chromosomes. The secondary constriction region variation among the individuals with reproductive failure was identified. It is suggested to carry out routine cytogenetic analysis and genetic counseling must be carried out, to rule out the carrier status.**

Keywords: **chromosome, heterochromatin, reproduction and aberrations.**

I. INTRODUCTION

Infertility is defined as the inability to conceive or produce a child after one year of unprotected intercourse [1], [30]. It is caused by many factors including change in the sperm count, morphology, motility, hormone and chromosome abnormalities [4] and tubal damage extra. Research is still pursing in the area of reproduction and its association with the secondary constriction regions of chromosomes [3]. Heterochromatin region has no coding potential and it contains the genes coding for rRNA [10]. Hence the variant is considered to be of no clinical significance. However recent studies prove that chromosomal polymorphisms are related to infertility and recurrent abortions [26], [4], [15], [16].

Chromosome inversions are a relatively common structural alteration. Pericentric inversion in the heterochromatic region of chromosome 9 has been recognized as a normal variant, generally without phenotypic effect [1]. It is not clear whether inversion in chromosome no.9 is a normal variant or an abnormal karyotype [6]. Nevertheless, this heterochromatic variant is sometimes associated with increased chromosomal instability, congenital abnormalities and cancer proneness [1].

Pericentric inversion of chromosome 9[inv (9) (p11q13)] is the most common (1–3%) type of inversion in the general population [28]. Although inv(9)(p11–q13) has been regarded as a normal familial karyotype variant, it has also been reported in various human diseases such as couples with congenital malformation, habitual abortus, mild growth retardation, malformations of the skull and facial (craniofacial) region, undescended testis, skeletal malformations, mental retardation, hermaphroditism and cardiac defects [14],[23]. In this study we have analyzed the effect of qh variations & other chromosome abnormalities such as satellite variations in patients who had abnormal reproduction.

II. MATERIALS AND METHODS

145 couples in the age group from 20 – 50 yrs with different type of abortions attending the genetic department were enrolled in this study. A detailed medical history including pedigree analysis was procured from each patient. Routine physical examination was carried out. 75 age matched couples with normal reproductive function were included as a control group. 5 ml of peripheral blood was taken from each patient.

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III. CHROMOSOMAL ANALYSIS

Chromosomal analysis of peripheral blood lymphocytes was performed based on the International System for Human Cytogenetic Nomenclature [11]. The peripheral blood lymphocytes were cultured with RPMI-1640 media along with all the supplements. After a period of 72 hrs incubation colchicines was added followed by hypotonic treatment and fixation. Metaphase chromosomes that were prepared by the standard protocols were banded using GT (Giemsa Trypsin) banding technique. At least 25 well spread metaphases were scored from each patient.

IV. RESULTS

Different types of chromosomal aberrations and frequency were studied are shown in table 1 and 2. Out of 145 couples, 22 patients showed chromosomal aberrations which included variation in the secondary constriction region of 1,9,16 chromosome, Y chromosome, satellite region of chromosome no.21 and 22 and autosomal translocations.

(Figure1,2,3,4and 5).

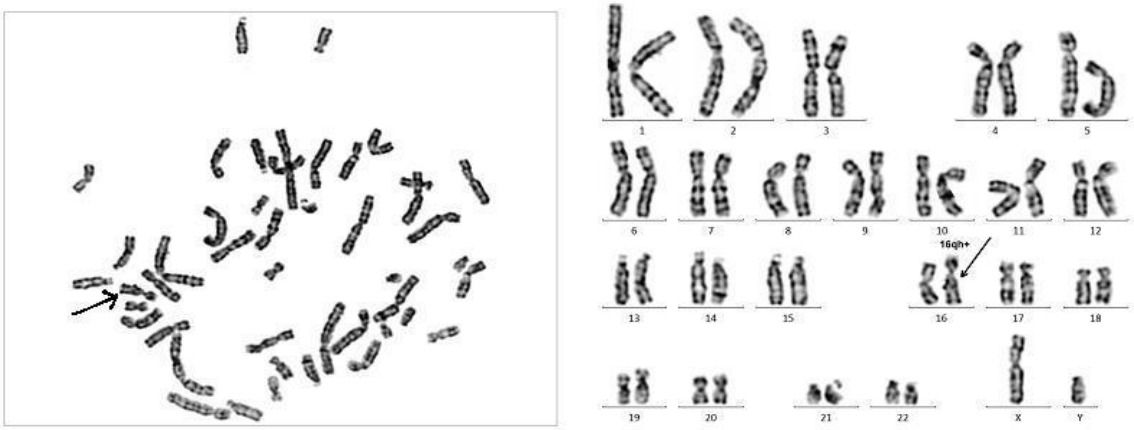

Fig. 1: 46, XY, 16qh+

"Male Karyotype with 46 chromosomes involving increase in the length of the secondary constriction region in the long arm of chromosome no. 16."

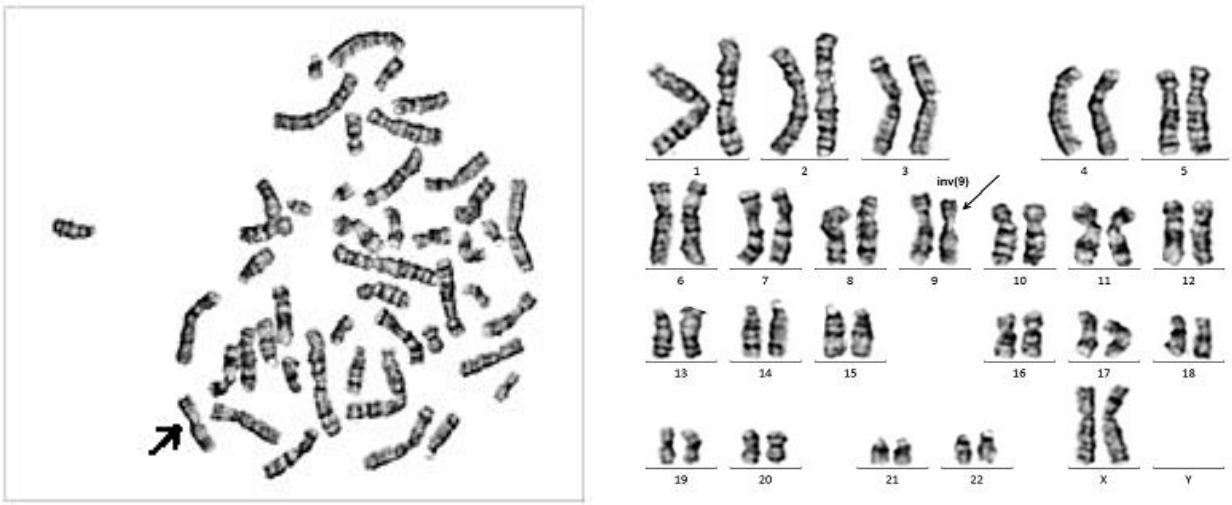

Fig. 2: 46, XX, inv (9) (p11; q13)

"Male karyotype with 46 chromosomes involving pericentric inversion in chromosome no. 9 (p11; q13)."

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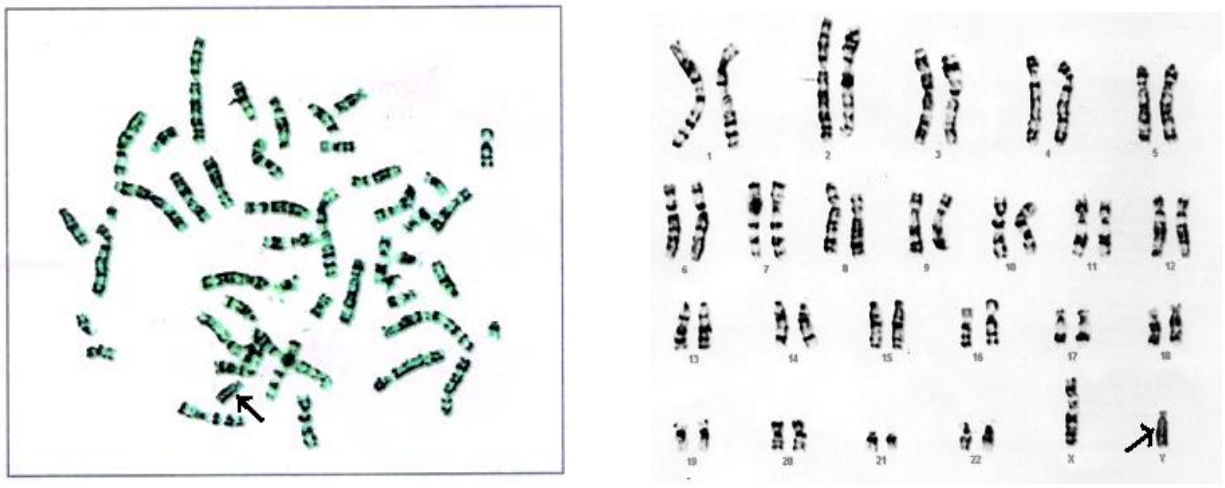

Fig. 3: 46, XYqh+

Male karyotype with 46 chromosomes involving increase in the secondary constriction region of the long arm of Y chromosome

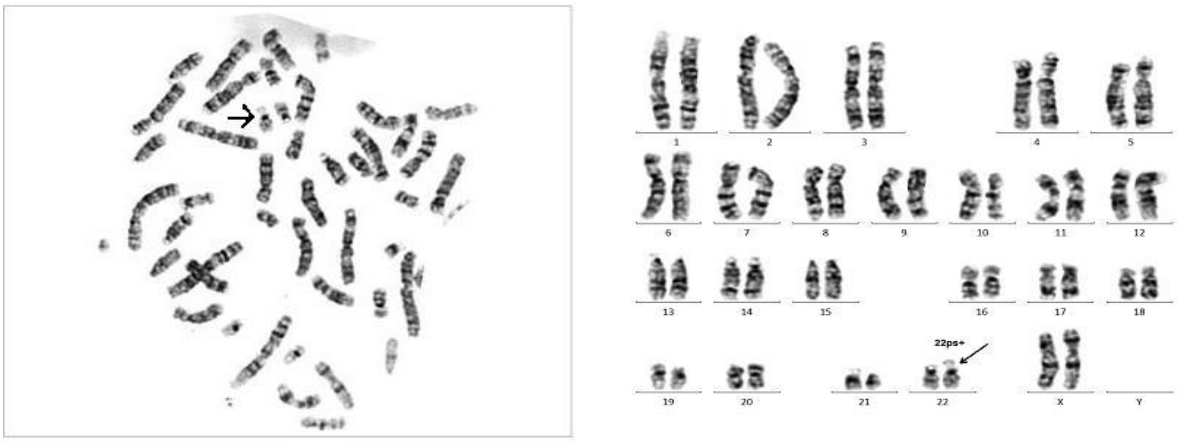

Fig. 4: 46, XX, 22ps+

Female karyotype with 46 chromosomes involving prominent satellite on the short arm of chromosome no.22

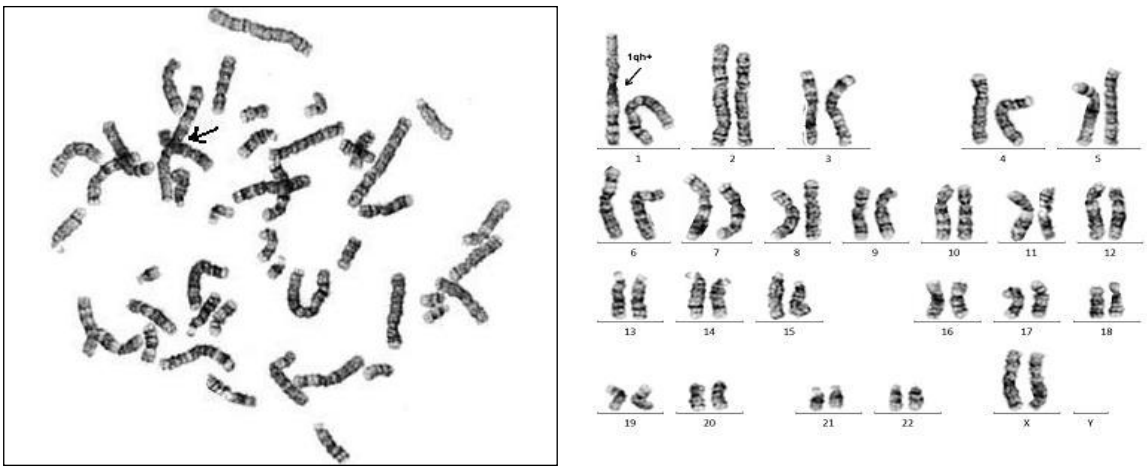

Fig. 5: 46, XX, 1qh+

Female karyotype with 46 chromosomes involving increase in the length of the secondary constriction region in the long arm of Chromosome no.1

V. DISCUSSION

Chromosome abnormalities are responsible for at least half of spontaneous abortions or miscarriages and are an important cause of congenital malformations [5],[29],[24]. The prevalence of chromosomal abnormalities is 13.8% in the general population [9] .In different studies, the rates varied between 5.2% and 13.4% [19],[13],[20].

In this study, karyotype determination was solely based on G-banding. The existence of qh variants was easily detected based on the location of heterochromatin. This limitation of secondary constriction region analysis based on G-banding established in this study was similar to that (most investigators in china)

In this study, there was one case reported with 46, XY, t (1qh+:11qh-) and his wife with 46, XX, 9qh- was led to recurrent miscarriages. Other cases with [45, XX, rob (13; 15)], [46, XX, t (4q+; 18q-)], 46, XX, t (4p+; 13q-) were reported as abortions and miscarriages. The frequency of 1qh+, 16qh+, 21s+ and 22s+ is lower. The total number of individuals with Yqh variants in our study is too small and the chance of bias therefore is greater. Some reports observed a high frequency of 9qh+ in parents of chromosomally abnormal abortuses. It cannot be concluded whether the reproductive problem of the individual with this karyotype was caused by 9qh+.

In this study, there was another aberrant karyotype 46, XX, inv (9) (p11q13). The inv (9) reported to be associated with infertility and congenital anomalies [27],[8],[19]. In 2.3% of the couples with a history of recurrent spontaneous miscarriages pericentric inversion of chromosome 9 was detected [25]. Nevertheless, most of the cytogeneticists believe that there was only one kind of breakpoint (p11q12) on the inversions of chromosome 9, which has no known deteriorated effect on carriers and does not appear to be associated with a significant risk of miscarriage or unbalanced offspring. It was therefore, generally considered as a normal chromosome variant. It has been suggested that phenotypes of inversion 9 may vary depending on the location of breakpoints [12].

VI. CONCLUSION

It was observed that secondary constriction region (qh) variations in this study showed abortions and miscarriages. It supported the reports that the abnormal reproduction was related to secondary constriction region (qh) variations, satellite variations and translocations. The present study was limited by using cytogenetic analysis. It has to be confirmed using molecular analysis.

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APPENDIX - A

Table 1: Different Type of Chromosomal Aberrations

S.No.	AGE	GENDER	PROVISIONAL DIAGNOSIS	KARYOTYPE
1.	21 yrs	F	Abortion	46,XX,21ps+
2.	31 yrs	M	Abortion	46,XY,21ps+
3.	30 yrs	F	Miscarriages	46,XX,9qh-
4.	35 yrs	M	Miscarriages	46,XYqh+
5.	30 yrs	F	Miscarriage	46,XX,9qh-
6.	32 yrs	F	Abortion	45,XX,rob(13;15)
7.	20 yrs	F	Abortion	46,XX,t(4p+;13q-)
8.	25 yrs	F	Abortion	46,XX,22ps+
9.	31 yrs	M	Abortion	46,XY,9qh-
10.	25 yrs	F	Miscarriages	46,XX,9qh-
11.	27 yrs	F	Miscarriages	46,XX,9qh+
12.	23 yrs	F	Abortion	46,XX,9qh+
13.	36 yrs	M	Miscarriages	46,XY,t(1q+;11q-)
14.	30 yrs	F	Miscarriages	46,XX,inv(9)
15.	38 yrs	M	Abortion	46,XY,inv(9)
16	27 yrs	F	Abortion	46,XX,t(4q-;18q+)
17	34 yrs	M	Abortion	46,XY,16qh+
18	34 yrs	M	Abortion	46,XYqh+,9qh+
19	33 yrs	F	Abortion	46,XX,1qh+
20	29 yrs	F	Miscarriages	46,XX,9qh-
21	26 yrs	M	Miscarriages	46,XY,9qh+
22	30 yrs	M	Miscarriages	46,XY,9qh+

Table 2: Frequency Of Chromosome Aberrations

KARYOTYPE	FREQUENCY	PERCENTAGE
46,XX,21ps+	1	0.68
46,XY,9qh-	1	0.68
46,XX,9qh-	3	1.61
46,XY,21ps+	1	0.68
46,XYqh+	2	1.37
45,XX,rob(13;15)	1	0.68
46,XX,t(4p+;13q-)	1	0.68
46,XX,22ps+	1	0.68
46,XX,9qh+	2	1.37
46,XY,9qh+	2	1.37
46,XYqh+,9qh+	1	0.68
46,XY,t(1q+;11q-)	1	0.68
46,XY,inv(9)	1	0.68
46,XX,inv(9)	1	0.68
46,XX,t(4q-;18q+)	1	0.68
46,XY,16qh+	1	0.68
46,XX,1qh+	1	0.68