

## Detection of 20ph+ in a woman with idiopathic recurrent pregnancy loss

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### ABSTRACT

Recurrent pregnancy loss (RPL) constitutes a multifactorial clinical entity, often necessitating an exhaustive diagnostic approach when routine investigations yield inconclusive results. We report the case of a 23-year-old female with two consecutive unexplained pregnancy losses, in whom comprehensive endocrine, thrombophilia, and radiological evaluations were unremarkable. However, cytogenetic analysis revealed a rare heterochromatic variant, 20ph+, in the female partner, whereas the male partner's karyotype was normal. Although 20ph+ is typically regarded as a benign chromosomal polymorphism, its infrequent occurrence and detection in reproductive disorders invite reconsideration of its potential clinical significance. To our knowledge, this is the first study in India to report the presence of 20ph+ in the context of RPL. This case study underscores the importance of incorporating cytogenetic analysis into the diagnostic workup for idiopathic RPL, especially when standard investigations fail to identify a cause.

**Key words:** 20ph+, Chromosomal variant, Cytogenetic analysis, Karyotyping, Recurrent pregnancy loss

Recurrent pregnancy loss (RPL) refers to the occurrence of at least two spontaneous miscarriages before 20 weeks of gestation, as outlined in the clinical guidelines of the European Society of Human Reproduction and Embryology and the American Society for Reproductive Medicine [1]. This condition affects approximately 5% of women of reproductive age [2]. It represents a complex clinical challenge with multifactorial etiologies, including genetic, anatomical, endocrine, immunological, and thrombophilic factors. Despite extensive diagnostic evaluations, nearly 50% of RPL cases remain unexplained, necessitating the consideration of less common causes [3]. Among these, chromosomal abnormalities, both numerical and structural, are well-established contributors, often involving balanced translocations or inversions [4]. However, the role of chromosomal polymorphisms, particularly heterochromatic variants such as 20ph+, remains controversial. Traditionally considered benign, these variants have occasionally been reported in association with reproductive disorders [5-7], prompting ongoing debate about their clinical significance. Given the psychological and emotional impact of RPL, identifying subtle or rare cytogenetic anomalies may offer valuable insights into its pathogenesis.

This is the first report from India that highlights a rare case of 20ph+ detected in a woman with unexplained RPL, underscoring the importance of cytogenetic evaluation in such cases.


### CASE REPORT

A 23-year-old female presented with a history of two consecutive unexplained first-trimester pregnancy losses. She reported regular menstrual cycles of 28–30 days since menarche at age 13 and denied any use of contraception, significant weight loss, excessive physical activity, psychological stress, or chronic illnesses. There were no symptoms suggestive of hyperandrogenism, thyroid dysfunction, or galactorrhea.

On physical examination, her body weight was 51 kg, blood pressure was within normal limits, and mild pallor was noted. No other abnormalities were observed.

Baseline laboratory evaluations, including hormonal profile (follicle-stimulating hormone, luteinizing hormone, prolactin, thyroid-stimulating hormone, and estradiol), antiphospholipid antibody panel, and pelvic ultrasound, revealed no significant findings. Given the normal workup and history of RPL, cytogenetic analysis (GTG-banded karyotyping) of both partners was recommended to explore potential chromosomal causes.

In cytogenetic analysis, a lymphocyte culture was done from peripheral venous blood of both partners, and

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metaphase chromosomes were analyzed using GTG-banding at a resolution of 400–500 bands. The female partner's karyotype was 46,XX with an enlarged short arm on one of the chromosome 20 homologs, consistent with the 20ph+ variant (Fig. 1). No other structural abnormalities were identified. The karyotyping of the male partner revealed a normal 46,XY chromosomal pattern (Fig. 2). Table 1 shows the clinical parameters of the couple.

## DISCUSSION

Chromosomal heteromorphisms, especially those involving centromeric or pericentromeric regions, occupy a diagnostic gray zone in cytogenetics. The formal genetic definition of a “polymorphism” requires a variant to occur in at least 1% of the general population, whereas less frequent forms are more accurately termed “mutations” [7]. However, heteromorphisms, such as size variations in centromeric or heterochromatic regions, exist on a spectrum and often lack precise frequency data. This variability complicates their classification

and interpretation. Liehr emphasized the importance of documenting these variants systematically to better understand their clinical implications [8].

Variants involving the centromeric region of chromosome 20, such as 20ph+, are considered rare cytogenetic findings and are generally classified as heterochromatic polymorphisms. Although typically regarded as benign, their role in reproductive disorders remains uncertain due to limited available data. To date, only a few cases involving 20ph+ have been reported in the literature. The first known report described a couple with recurrent miscarriages, in which the female partner exhibited the 20ph+ variant [5]. A second case was reported as a normal variant without clinical correlation [7]. The third case involved a female patient presenting with infertility, where 20ph+ was confirmed by G- and C-banding and fluorescence *in situ* hybridization (FISH) using the alpha satellite probe D20Z1 [7]. In addition, a rare pericentric inversion of chromosome 20 heterochromatin (20 h) has been reported in a prenatal case [9].

Molecular cytogenetic studies have shed light on the complex nature of centromeric heteromorphisms. Rocchi

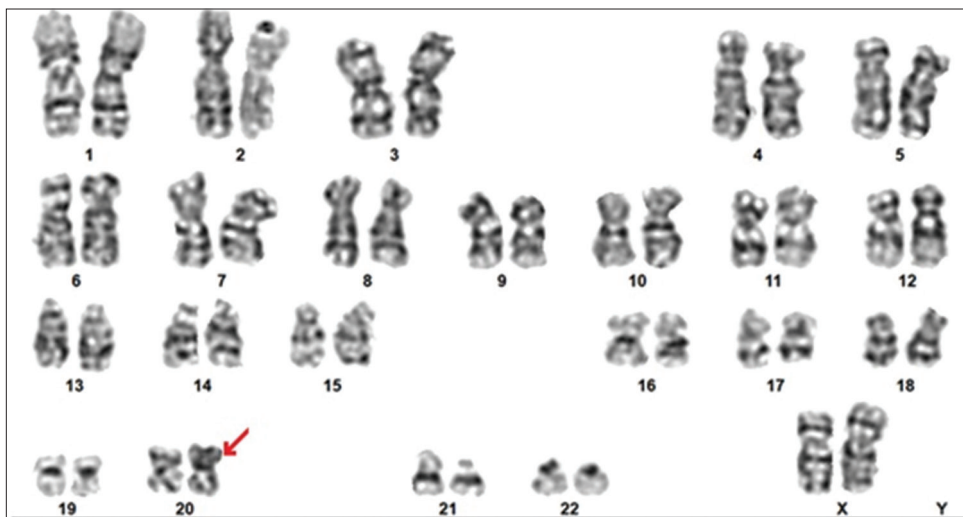


Figure 1: Female karyotype (46,XX) with 20ph+ variant indicating enlarged short arm on chromosome 20 (red arrow)

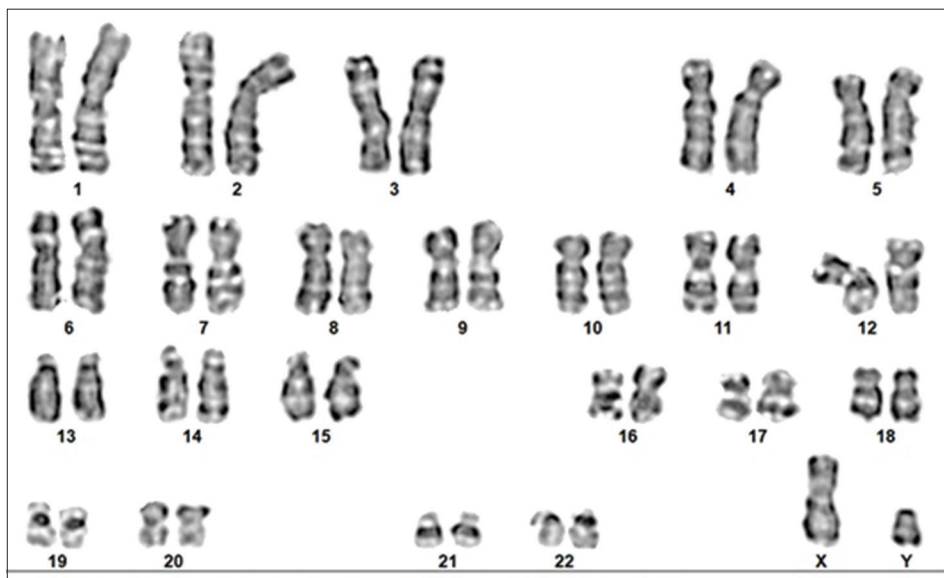


Figure 2: Male karyotype (46,XY) with normal chromosomal morphology

**Table 1: Clinical parameters of the couple**

Female partner with 46, XX, 20ph+			Male partner with 46, XY		
Parameter	Result	Remark	Parameter	Result	Remark
Hemoglobin	10.9 g/dL	Normal	Hemoglobin	12.3 g/dL	Normal
Complete Hemogram	All components show adequate value	Normal	TSH	2.54 uIU/mL	Normal
TSH	3.65 uIU/mL	Normal	Testosterone	780 ng/dL	Normal
Prolactin	21.18 ng/mL	Normal			
TORCH	All components within normal range	Normal			
Lupus anticoagulant	Negative	Normal			
Anticardiolipin antibody	12 GPL (immunoglobulin G phospholipid units) 09 MPL (immunoglobulin M phospholipid units)	Normal			
Venereal disease research laboratory test	Non-reactive	Normal			
Adenosine deaminase	Negative	Normal			
Ultrasound sonography	No significant abnormality found	Normal			

TSH: Thyroid-stimulating hormone

**Table 2: Reported cases of chromosome 20ph+ variant: Clinical contexts and detection method**

Case No.	References	Year	Clinical context	Detection method	Comments
1	Romain <i>et al.</i> [5]	1991	RPL	GTG-banded karyotype	20ph+ found in a woman with RPL
2	Wyandt [7]	2004	Infertility	G-banding, C-banding, FISH with D20Z1	Confirmed 20ph+ in a female with infertility
3	Liehr [8]	2014	NA	Conventional cytogenetics	Documented as a benign morphological variant without clinical symptoms
4	Petersen [9]	1990	Prenatal case (20h inversion)	Prenatal cytogenetic testing	Describes pericentric inversion of 20h heterochromatin; not 20ph+ directly
5	Park and Rawnsley [12]	1996	Prenatal detection (20ph+, 20ps)	Prenatal karyotype	Chromosome 20 variants detected prenatally; clinical outcome not detailed
6	Our study	2025	RPL	Conventional cytogenetics with GTG-banded karyotype	First documentation from India to report the presence of 20ph+ in RPL

RPL: Recurrent pregnancy loss, FISH: Fluorescence *in situ* hybridization

*et al.* identified specific subsets of alpha satellite DNA located at the centromere of chromosome 20, highlighting distinct chromosome-specific repetitive sequences that contribute to its structural uniqueness [10]. Building on this, Bassi *et al.* (2000) further characterized DNA sequences at the boundary between the alphoid satellite region and adjacent pericentromeric heterochromatin [11]. They discovered a particular PAC clone, dJ233C1, which spans both alphoid and non-alphoid DNA sequences in these regions [10]. Their comparative FISH analyses revealed that the pericentromeric region of chromosome 20 exhibits considerable evolutionary flexibility, with the capacity for sequence expansion and translocation events observed among primate species. This genomic plasticity may explain the presence of heterochromatic variants such as 20ph+, and it suggests that such variability could potentially affect the organization of chromatin or the assembly of the kinetochore during meiosis and early embryonic development.

Although 20ph+ has not been linked to any known pathogenic gene changes, its occurrence in multiple individuals with RPL or infertility raises the possibility of a subtle but clinically relevant effect. Structural

anomalies in centromeric heterochromatin might disturb chromatin architecture or meiotic division, contributing to early pregnancy loss through mechanisms that are not yet fully understood. Table 2 shows the reported cases of the chromosome 20ph+ variant [5,7-9,12].

## CONCLUSION

Our case adds to the limited but growing literature suggesting that heterochromatic variants such as 20ph+ may have a role in unexplained reproductive failure. This case represents the first documented instance in India linking the 20ph+ chromosomal variant to RPL. In couples with idiopathic RPL, karyotyping of both partners, including higher-resolution molecular techniques, should be considered, even when routine investigations are normal. Accumulating such data will aid in establishing whether these chromosomal variants are truly benign or represent under-recognized contributors to reproductive disorders.

In summary, while 20ph+ is usually considered a harmless chromosomal variant, its repeated association with RPL and infertility in the literature suggests it warrants

further attention. Comprehensive cytogenetic analysis and robust case documentation are essential to better understand its potential significance in reproductive medicine.

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