Review Article

Yq microdeletions and their current status in relation to Indian and Global scenario associated to male infertility: A mini appraisal

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ABSTRACT

Background: Y chromosome microdeletions provide a pivotal role in the control of spermatogenesis. These are located on the q arm of it, specifically, the azoospermia factor (AZF) region, hence named as Yq microdeletions. The mutations in this region are related to testicular pathologies such as azoospermia, oligozoospermia, and other semen categories. **Objectives:** This study was undertaken to review these microdeletions, screening, and their correlation to semen categories in relation to the Indian and Global populations in context to male infertility, future strategies, and its implications. **Methodology:** These deletions are screened using sequence-tagged sites (STS) of the European Academy of Andrology (EAAs) and Non-EAAs with polymerase chain reaction technology. The data included were Indian and Global studies obtained from research articles, abstracts, and reviews (75) indexed in Google Scholar, PubMed, and Scopus. **Results:** A number of total 45,562 Y chromosomes were analyzed. In India, this frequency contributes to 8.33% (453/5435) against the average frequency of 6.96% (3170/ 45562) worldwide. Globally, this frequency was higher (9.1%) in the North American continent. Among all types of deletions, AZFc deletions are higher followed by b, a, b+c, and others as well as are related to azoospermia than oligospermia and other semen cases/categories globally including India. In India, the data on partial deletions are scanty. Further, cases with AZFc are better suitable for assisted reproductive technologies after counseling. **Conclusion:** Evaluation of correct deletion type to a specific testis pathologic phenotype is suggested for sperm retrieval to correct the male partner. This study is hence better suitable for azoospermia with AZFc deletion around the Global and Indian scenario in association with male infertility. Future strategies are thus called for successful treatment of a specific microdeletion clinically in the male.

Key words: *Male infertility, Phenotypes, Polymerase chain reaction, Sequence tagged site, Yq microdeletions*

The Y chromosome has a definite role in sex determination and maintenance of male fertility in addition to other processes. The q arm of the Y chromosome contains the azoospermia factors (AZF) region distributed in the q long arm of it at 11, 21, 22, and 23 levels called AZF a, b, and c sub-regions which are often deleted in infertile cases [1]. The roles of this AZF region in spermatogenesis and male infertility have recently been reviewed [2-4]. The region contains three sub-regions AZFa, AZFb, and AZFc. The AZFa locus contains in proximal Yq extends 1.1 Mb encoding single-copy genes that have X chromosome homologs. Overall AZFa has 15 genes, of which three are protein-coding (DOX3Y, UTY, and USP9Y), one is a testicular-specific transcriptome unit (TTY15), and 11 are pseudogenes (Fig. 1). The AZFb region is located in the central region of Yq 11 and spans 3.2 Mb containing three single-copy regions, a Y chromosome-specific 19 satellite DNA repeat array (DYZ), and 14 multi-copy sequence units amplicons which are highly identical segmented duplications [1,5,6].

The AZFc contains 132 genes, of which 15 are protein-coding, 17 are non-coding RNA's, and 100 are pseudogenes. Among 15 protein-coding genes, there are six copies of RBMY, two copies of PRY, two copies of HSFY, one copy each of EIPIAY, KDM5D, CDY2A, RPS4Y2, and XKRY. The AZFc locus is distal to AZFb and is the most complex type and detectable region in infertile men. This locus is 4.5 Mb long containing 97 genes. Among 11 are protein-coding, 10 are non-coding RNA's and 76 are pseudogenes. Among the 11 protein-coding genes, three are four copies of DAZ, three copies of BPY, and two copies each of CDY1 and CS PG-4LY. This region also contains seven testicular-specific transcription factors [2,7] (Fig. 1).

METHODOLOGY

Genomic DNA was used for analyzing microdeletions with sequence-tagged sites (STS) based on polymerase chain reaction (PCR) technologies. Thus, we describe these AZF deletions by

adopting specific markers of the European Academy of Andrology (EAA) and non-EAA STS as suggested [8-10].

About 18 STS were essentially used for proper identification of deletions in AZF locus of infertile cases. These include SY746, SY86, DFFRY, (AZFa), SY113, SY118, SY127, RBM1Y, XKRY, SY134, SY143 (AZFb), SY153, SY148, SY157, SY255, SY254, SY158, SY160 (AZFc) in addition to SY14 (SRY), and ZFX/ZFY as internal controls. Genomic DNA was used for PCR assay with necessary reagents for detection of microdeletions in AZFa, AZFb, AZFc, AZFa+b, AZFb+c sub-regions, and others for ensuring optimal results along with positive and negative as well as blank (water) controls with primer sequences. All PCR products were analyzed on 2% agarose gels stained with Ethidium Bromide [8-10]. Testing of Yq microdeletions has many applications for correct diagnosis for the cause of infertility [8-10].

For correlation of testicular phenotypic manifestations, specific guidelines are strictly followed (Table 1) while performing spermeogram analysis [11]. Accordingly, the semen cases were grouped into azoospermia (obstructive and non-obstructive) oligozoospermia (5–15 × 106/ml), severe oligospermia, normozoospermia (normal values of sperms in the ejaculate), asthenozoospermia (low level of motility, <50%), teratozoospermia (<30% of normal sperm morphology), and aspermia. Other causes include cryptorchidism, varicocele, endocrinological, obstruction of seminal pathways, infection, alcohol, and chemotherapy in addition to genetic defects such as cytogenetic disorders, gene mutation, and Yq microdeletion [8-10]. Among genetic defects, we revealed the current knowledge of Yq microdeletions in the genes leading to infertility and their correlation to the phenotypic manifestations, implications, distribution, and prevalence in India and around the globe.

Data Collection

This information related to Y chromosome microdeletions and male infertility in India was synthesized by searching databases such as PUBMED, EMBASE, Google Scholar, and Cochrane Library from 2001 till the year 2020. Global citations/articles indexed in PubMed were 59. A total of 18 Indian studies were found, of which 15 were PubMed indexed, one was a review article, and two were abstracts (Table 2). As mentioned earlier, this information was categorized for the prevalence of Yq microdeletion, region-wise, semen categories, type of Yq deletions, and STS markers used by the PCR-STS method. The data of Yq deletions were subjected to percent values. The above-mentioned databases are readily available for the literature

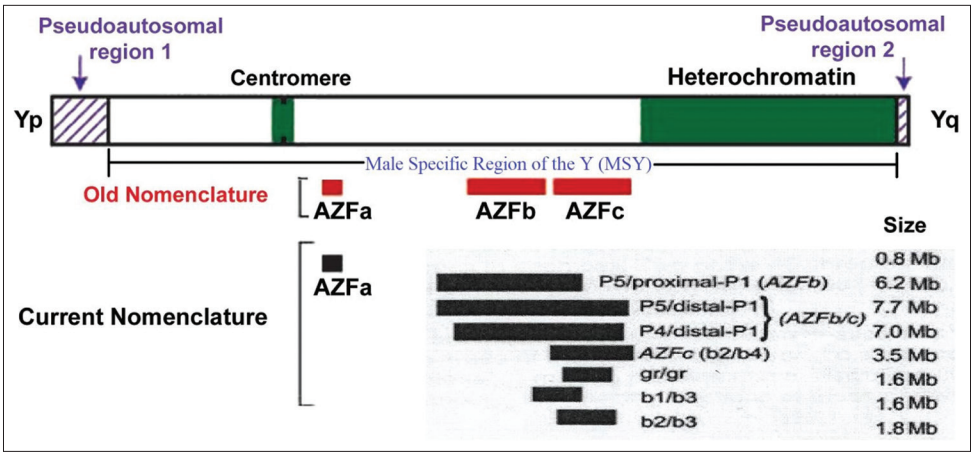

Figure 1: Old and new classification of Y chromosome in relation to azoospermia factors region [4]

Table 1: Semen variables according to the WHO [11]

S. No	Medical/Clinical Term	Condition/Definition
1	Aspermia	Absence semen upon ejaculate
2	Zoospermia	Presence of spermatozoa in the semen
3	Azoospermia	A complete absence of sperm in the semen (both obstructive azoospermia (OA) and non-OA (NOA)
4	Normozoospermia	All normal semen values in ejaculate
5	Oligozoospermia	Presence of an abnormally low number of sperm in a semen (5–20 * 10^6/ml)
6	Severe Oligozoospermia	Sperm counts fall between 0 and 5 million sperm/mL
7	Asthenozoospermia	Reduced sperm motility
8	Oligoasthenozoospermia	Combination of reduced sperm motility and low sperm count
9	Teratozoospermia	Presence of higher abnormal morphology in the semen
10	Oligoasthenoteratozoospermia	Condition that includes low number, poor sperm movement, and high abnormal forms
11	Polyzoospermia	Higher than normal values/ml
12	Hematospermia	Semen with RBC
13	Pyospermia	Semen with WBC

Table 2: Summary of our study cohort

Parameters	Global scenario	Indian scenario
Reviews	-	1[+]
Indexed[+]	59*	15[+]
Abstracts	-	02
Semen types/categories	Azoospermia, oligospermia, normozoospermia and others	Azoospermia, oligospermia, etc.
Chromosome analyzed (Y)	45562	5435
Deleted	3170	453
Percent deletions	6.96% (10–15%)	8.33% (8–10%)
Dominant deletions	AZFc	AZFc
Predominant phenotype/semen type	Azoospermia	Azoospermia
Percent partial deletion frequency	Better	Scanty
Assisted reproductive technologies suitable	Azoospermia	Azoospermia
Limitations	Gene mutation/ microdeletion traced specific to testes phenotypic manifestation to treat	Challengeable to reach the goal in future

+: PubMed, Scopus and Google Scholar. *: All articles except 4, 8, 9, 13, 14, 17–19, 24, 25, 29, 32-34, 62, 64–66. AZF: Azoospermia factors

search. Duplicate data were excluded from the study. Carefully exclusions and inclusions were permitted with respect to articles not estimated certain deletions.

Mechanism

The AZFa gene deletions involve chromosomal recombination between two human endogen retroviral (HERV) sequences. The rest AZFb and AZFc gene deletions are due to the combination between palindromes (P5P and P3P1), respectively. The complex structure of AZFc also leads to structural rearrangements [12-14]. Partial deletions occur as a result of recombination between sub-amplicons in AZFc copy number variation (CNV) results due to deletions, duplication, mutation, and others [3,7,15,16].

Statistical Analysis

The data obtained were entered into the Microsoft Excel spreadsheet and descriptive statistics were performed. No duplicate data were observed in our study as it might lead to erroneous information, meaning thereby, data in one citation/article is not duplicated in the calculation of deletion frequencies/types.

RESULTS AND DISCUSSION

Y-Chromosome Microdeletion and Male Infertility

In general, frequently AZFc is deleted in 60–70% of cases following AZFa (0.5–4%), AZFb (1–5%), and AZFb+c (1–3%) deletions. Others are partial deletions and CNVs [3]. Globally, these variations contribute to 7.5% deletions; however, in India, these relations reached around 8–10% ranging from 0.59% to 32.6 2% [17]. Rao *et al*. [4] reported an average of 8.33% (453/5435) in a range of 1.1–36% from their collections. The type of these deletions is mainly AZFa,b,c,b+c,a+b,a+b+c; AZFd; DAZ. Similarly, partial deletions in infertile cases are reported by few researchers [18].

Global estimates figure to 6.96% from the data collection (3170/45562), where North America had a high deletion frequency (9.1%), followed by South America (8.2%), and other continents (Figs. 2 and 3a) and least frequency appeared in Europe 3.33% (383/1473). In the Asian region, the highest prevalence of Yq microdeletion is among the East and South East (9.9%, 8.4%), respectively, and the lowest in South Asia (Fig. 3b) [3]. However, our subcontinent alone contributed to 8.33% (453/5435), third among the Asian region (Fig. 3b) [4]. These microdeletions are of AZF a, b, c; partial AZFc, and CNVs included other double types more than the Indian study. The cases were of azoospermia and oligozoospermia in various studies of India and worldwide. These variations could underlie differences in relation to the sample size, the methodology used, population, screened, control followed, region, and other factors. It was also suggested that the susceptibility of Yq to undergo the microdeletions is also perhaps related to race and ethnicity. An influence of haplogroups has been suggested to have an effect on partial AZFc deletions [7].

Rao *et al*. stratified the Indian population region-wise, that is, Central (Lucknow, Varanasi), Western (Gujarat and Maharashtra), Eastern (Bengal), North East (Assam), North (Delhi), and South East (Tamil Nadu, Kerala) [4]. The Western population had a low frequency of microdeletion (5.32%), followed by the Central zone (Varanasi, Lucknow). The higher frequency was observed in South East (20.52%) and North East region populations (17.77%) as shown in Fig. 4a where the total average contributed to 8.33%. This variation in Yq deletion frequency is related to Yq susceptibility to influence deletion-related genetic background, food style, size, the methodology adopted, other including geographic effect, and ethnicity in infertile men [4,8,17,19] as indicated by Colaco and Modi [3].

The worldwide data thus collected regarding Yq microdeletion frequency and prevalence were depicted in Figs. 2 and 3a where the prevalence of global estimates marginally differs from the earlier report [3], wherein, the world frequency emerged to 6.96% (3170/45562) and Asian continent 8.13% (2426/29836), respectively, and Asia occupied the third position in global frequency as found within the Asian region too, as mentioned above (Fig. 3b). AZFc deletion and spermatogenic failure in five populations of India, Poland, Tanzania, United States, and Vietnam implicated on analysis of 20,000 Y chromosomes from 20884 men and found that four of six deletions occurred in a descending manner. The order was gr/gr, b2/b3, b1/b3, and b2/b4 affecting severe spermatogenesis failure (SSF) [20]. Colaco and Modi [3,21] also reported that

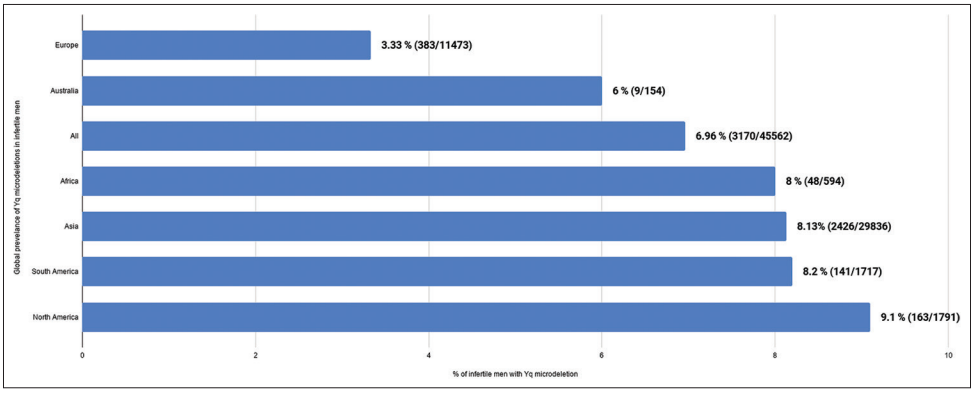

Figure 2: Percentage of Yq microdeletions across the globe modified [3]

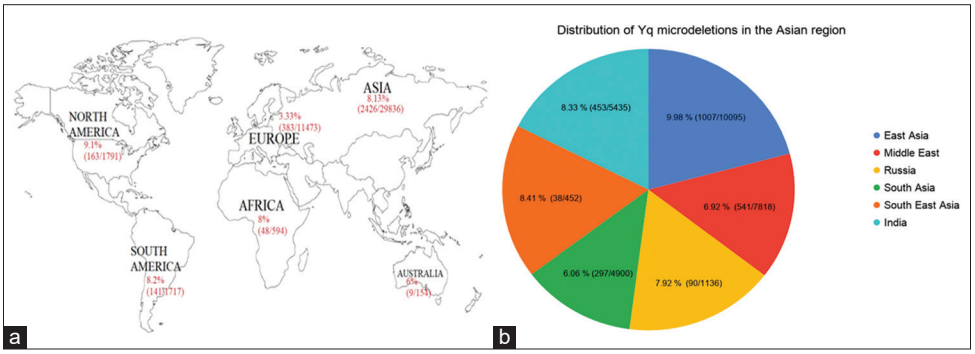

Figure 3: (a) Continent-wise percentage of Yq microdeletions in infertile men; (b) percentage of microdeletions in Asian region modified [3]

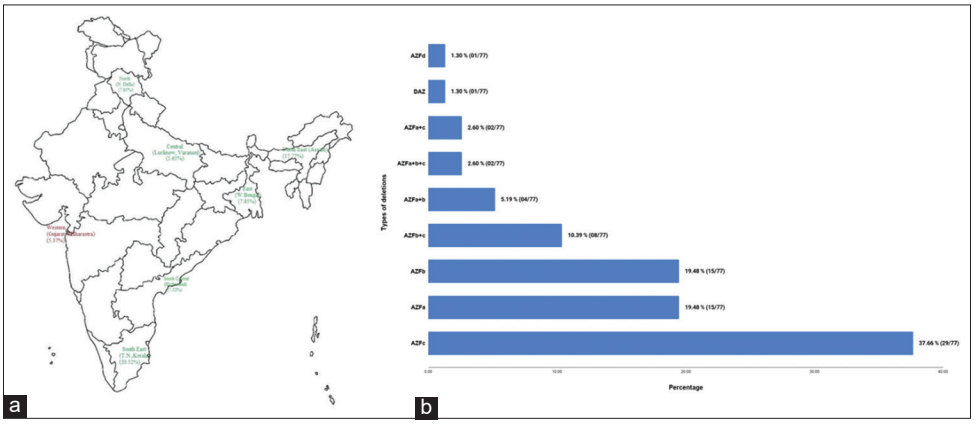

Figure 4: (a) Geographic distribution survey of Yq microdeletions in Indian infertile men; (b) Summary of percent (%) azoospermia factors sub region microdeletion types from Indian study [4]. Total microdeletions = 77

CNV frequency is dependent on race and ethnicity in addition to other partial AZFc deletions.

Yq Deletions and Phenotype Correlates

AZF deletions of Yq subregions (Yq 11.21: AZFa; Yq 11.22: AZFb; and Yq 11.23:AZFc) are specific to infertile cases. Hence, it is necessary to consider Y deletion as a cause of testicular pathologies such as sertoli cell-only syndrome (SCOS), oligo/azoospermia, and other conditions of male infertility. In general, 25–55% of infertile males were with testicular pathologies such as SCOS and hypo-spermatogenesis. Only, 5–25% of males were with severe oligospermia and others harboring Y chromosome microdeletions [4,7,18,19,22-24]. However, it depends on the number of genes deleted from the AZF locus, the phenotype manifestation varies [2,25].

AZFa Deletions

This region is necessary for the initiation of sperm production. This region in total deleted cases results in SCOS and azoospermia [3,26-30]. Few workers also believe to induce oligospermia [31]. An Indian study reported that AZFa deletions induce oligo/SCOS in certain cases at a low frequency than b and c deletions [4,19]. Waseem *et al*. [17] obtained 1.8% "a" deletions in relation to azoo/oligospermic patients. However, Dada *et al*. [32], Singh and Raman [33], and Mittal *et al*. [34] did not report these deletions in their studies. Thus, partial deletions

are associated with phenotypes ranging from azoospermia to normozoospermia [35] explaining the importance of loss of genetic content which is crucial for azoospermia. Entire AZFa deletions are not useful in infertile cases to testicular sperm retrieval for intracytoplasmic sperm injection (ICSI) purposes [28,36]. Hopps *et al*. [28] found 3–8% AZFa deletions frequency (3/78) of azoospermic cases only.

AZFb Deletions

It is involved in the progression of spermatogenic patients as this deletion has a testicular phenotype of maturation arrest; frequently at the spermatocyte stage. Hence hypospermatogenesis occurs in deleted portions of b and/b+c cases. Phenotypes are hypo-oligospermia [8]. These patients are oligospermia to SCOS in certain cases. Hopps *et al*. [28] found 14% AZFb deletions with azoospermia, comparatively more than AZFa and less than AZFc. Simon *et al*. [37] and Teng *et al*. [38] reported that AZFc is the most frequent deletion type among all followed by AZFb and AZFc with severe spermatogenesis failure (SSF).

The literature search identified a few cases of AZFb deletions in India [17]. Rao *et al*. [4] also noticed more AZFa deletions. Few reports showed lower than AZFa deletions [8] and are related to hypospermatogenesis. The chance of sperm extraction in these cases is negligible from the testis, due to heterogeneity in the extent of deletion in different patients and prevalence of partial deletions [13,36,39,40]. Hence, these cases are useful for assisted reproductive technology (ART).

AZFc Deletions

This region is the most frequent deletion type of AZF gene as it is a complex structure with more gene families [2]. Its deletions are higher in frequency followed by b and a including others [41,42] and are related to azoospermia patients. Hopps *et al*. [28] detected 53.8% "c" deletions (42/78) and the quality and quantity of these deletions decrease with age [42]. Oligospermic patients may have sperm through self-ejaculation and have next generation through *in vitro* fertilization (IVF)/ICSI. Azoospermic cases are useful for testicular sperm extraction (TESE) undergoing ICSI than those cases with a and b gene deletions [23,30]. Usually, men with these deletions are phenotype ranging from azoospermia to mild oligospermia [43-45]. In India, men with AZFc deletions have a high percentage of azoospermia followed by oligospermia and SCOS and these are of high prevalence than others such as a, b, b+c, a+b, a+b+c, d, and DAZ [4,8]. It is also reported that AZFc deletions are the most common with a high prevalence than b and a among azoospermia and oligospermic men [17]. In double deletion, b+c is in higher rate after a, b, and c in the reports of Sen *et al*. [18], Rao *et al*. [4], and Waseem *et al*. [17].

Partial Deletions

The AZFc partial deletions and their involvement in male fertility have been investigated using meta-analysis of three fully designed articles and one study of 20,000 Y chromosome analysis and published [3,10,18,46]. Irrespective of population, in individual studies, as well as pooled estimates, men with gr/gr deletions have significantly lower sperm counts and motility that occur commonly in African and Asian men (10–15%) and 5% in other population. Their association with male infertility is ethnicity-dependent [18,46]. These are stronger in Caucasian and weaker in Mongolian men, but no association was found in Dravidians and Nigro-Caucasians men. Similarly, b2/b3 deletions showed poor correlation with male infertility which is higher in the Asian population and lowest in the European population and is based on the ethnicity of the population like gr/gr. The b1/b3 deletions differ from the above two as it has the combination of b+c. All these deletions are important for only supporting the generation of male infertility.

Rozen *et al*. [10] explained the loss of SSF dependent on the prevalence of these deletions by descending manner, that is, gr/gr> b2/b3 > b1/b3 > b2/b4. These b2/b4 and gr/gr are largely responsible for AZFc region combination to SSF in the population. The prevalence varies in the population studies [47,48]. Krausz and Casamonti [49] reported that Spanish people (3.9%) have more gr/gr deletions as compared to Italians (3.3%) and Italians and Spanish mixed (3.5%) in loss of spermatogenesis. Accordingly, the treatment differs. In India, gr/gr and b2/b3 are characterized and their analysis including b2/b4, b1/b3, p5/p1, and p4/p1 is yet to be elaborated [14] for IVF treatment.

A CNVs produce phenotype through diverse mechanisms such as gene dosage, creating of the fusion gene, an unmasking of the recessive coding region, mutation, and position effect. However, no direct studies are available in the involvement of CNV with gene expression and spermatogenetic arrest [3,7]. The double AZFb+c deletions are also more prevalent in our review cohort (10–39%; 8/77). Similarly, these gene deletions contribute 1.66% lower than c (6.22%), b (3.21%), and a (4.00%) due to the loss of sperm probably for ART studies (Fig. 4b). Further studies are necessary to compare the findings around the globe.

Implications

Yq microdeletions analysis and methodologies in future: Global versus India

It is suggested that analysis of Yq microdeletions involve the use of multiple STS markers spanning various AZF loci [50]. We used the EAA and non-EAA markers of 4 to 30, but it is better to use a good number of markers to detect Yq microdeletions. Further, EAA and European Molecular Genetics Quality Network strongly recommend two STSs which are specific to the DAZ gene in the P2 and P1 Palindromes. Partial deletions cited to the b2/b4 pattern can also be analyzed using Sy 160 STS markers. Conventional PCR is to be upgraded to multiplex PCR, which is less costly, less time taking and advantageous than the former [50]. Commercial kits such as Diachem/ Bird and Euroclone are available [45].

Bunyan *et al*. [51] reported a method for the detection of partial AZFc deletions and multiplex ligation dependent probe

amplification (MLPA) probe mix (P360) known as MLPA assay. Microarray developed by Osborne *et al*. [52] for microdeletions is also recommended for these studies with better reproducible results to infertile men. It might become possible, after detailed molecular maps of the human, Y chromosome is generated using novel PCR technology with specific paired STS along the complete Y chromosome [2].

Genetic Counseling

Genetic counseling is an art of communication between a counselor and patients about the genetic disorder including microdeletions [53]. It is mandatory and now a reality in all ART centers. Today, we have a fair knowledge about the effects caused by Y chromosomal mutations. Genetic counseling should be necessary to prevent the propagation of such disorders [9]. Counseling is also essential to those couples who choose IVF and ICSI using either the sperm of the partner or the donor's sperm. In some cases, the couples opt to select female embryos for transfer after pre-implantation genetic screening [54]. Preimplantation genetic diagnosis is also a potential alternative strategy for couples dealing with Yq microdeletions [4,24,55].

Microdeletions and ARTs

Mapping of microdeletions of Yq in infertile men correlates to the phenotype of the testis which is a good predictor of sperm retrieval during TESE. Microdeletions in infertile cases carry the multi-task optimization offspring born after ICSI. Further, testing of sperm for microdeletions, which are useful for sperm banks related to ARTs. Sperm carrying higher microdeletions may lead to poor quality embryos after using ICSI [52]. Further, the patients with AZFc microdeletions presented high sperm recovery from testis than cases with AZFa and AZFb deletions who presented a poor prognosis [36]. Simoni *et al*. [56] and Nailwal and Chauhan [13] also supported that azoospermic cases with AZFc deletions are better for ICSIs. Genetic counseling is adapted to couples undergoing such ARTs. Moreover, the prediction of prognosis of male infertility with Yq microdeletion is also important for the recovery of testicular phenotypes. Testing of AZF region for deletions/CNVs may also be essential for detecting testicular tumors. In addition, microdeletions causing infertility in males undergoing ARTs through genetic counseling are also strongly associated with neuropsychiatric disorders [3,7].

Y-deletion and DNA Damage

DNA fragmentation increases with oxidative stress (OS) in a sperm cell. This OS occurs inside of sperm of infertile cases by several factors such as heavy metals, free radicals, and caspases during apoptosis. Such induced OS upsets oxido-redox ratios leading to DNA damage and mutations. Hence, it is proved that DNA fragmentation index shoots up in sperm of infertile men due to reduced recombination repair and DNA package anomaly [23,57]. Thus, OS is implicated for DNA damage in turn relating to Yq microdeletions in infertile cases. Hence, OS DNA damage and deletion in the Y chromosome are related in infertile males [20,57-60], but such couples with affected males need to be treated with antioxidants and evaluated. Such cases are also to be counseled prior to adopt ICSI and other IVF techniques in the future [31,61-63].

Y Chromosome Microdeletions in India and Global Scenario

Published data earlier showed that the frequency of microdeletions in the Indian population ranged from 3% to 29.34% with an average frequency of 8.1% [9,19,32,64,65]. Thangaraj *et al*. [66] proposed 8.5% Y chromosome microdeletion from the study of 340 azoospermia infertile cases. In another study, it was reported that it increased to 9.63% [8,32]. The frequency of deletions in the Indian population of 1636 cases is documented to be 3.4% which is significantly lower than others.

The same group had also mentioned low frequency 5.8% deletions [4], but our study cohort exhibited 8.33% deletions from 5435 Y chromosomes analyzed supporting the data of Thangaraj *et al*. [54], Pandey *et al*. [65], and Dada *et al*. [32]. Recently Rozen *et al*. [10] also reported similar data falling in the range of 8–10%. Waseem *et al*. [17] in India found that these deletions ranged from 0.59% to 32.62% with an average of 13.48%, but their own data delivered only 10.02% deletion frequency. This variation could be due to the ethnic background study protocol and other factors.

The Indian population further is affected by AZFc deletion, followed by AZFb and AZFa in most of the testicular phenotypes as reported by others [9]. The azoospermia cases are thus considered to be the most affected than oligo/severe oligospermia and others. The AZFc deletions containing such azoospermic cases are better suitable than other pathologic phenotypes as suggested above [13,17,36] for associated reproductive technologies in the present and future of the Indian scenario.

However, the global scenario also varies from various research groups. Zhu *et al*. [67] detected 8.3% Y microdeletions. Kucukaslan *et al.* [68] found only 9.6% deletions in their study. In another study by Zhu *et al*. [69], the deletion was only 2.08% with 144 infertile men. However, earlier studies ranged from 6% to 18% [70-74]. We obtained a 6.96% microdeletion frequency globally, which is marginally more than the result of 6.8% [3]. Colaco and Modi further [3] mentioned a global average of 7.5% microdeletions as compared to the frequency range of 10–15% as reported earlier [75], in comparison to the Indian subcontinent (8.33%) falling between 8 and 10% [4,9,19]. More studies are well available globally with respect to Yq microdeletions including partial types as compared to India [76,77].

Consequences of Y Chromosome Aberration Beyond Male Infertility

Three major areas have emerged for alterations in AZF genes to have effects beyond infertility. These include poor quality embryos generated in assisted reproduction when sperm from

such men having Y deletions is used, men with neuropsychiatric disorders are noticed with Y aberrations and CNV, and altered expression of AZF genes is found in men with cancers [3,7,20,21]. This area of research emerged new frontiers of research to protect the health of infertile males [7] in relation to AZF gene alterations in addition to infertility.

Limitations

The significance of Y microdeletions/partial microdeletions is to be communicated to the affected male by the clinicians. This needs to be counseled between doctors and infertile couples. An accurate methodology is to be applied for the full success of specific deletions using appropriate technologies worldwide including India to pinpoint the type of deletions and its related testicular pathologic conditions to treat the male partner clinically in the future.

CONCLUSION

The study cohort clearly indicates that Yq microdeletions are a cause of male infertility ranging from 8–10% with an average of 8.33% in India. The partial microdeletions are higher worldwide as much data are unavailable in India due to the lack of better technology and other factors. Azoospermic men are affected with a high frequency of AZFc mutations in India and around the globe. Such cases are better for chances of sperm retrieval. It also provides opportunities for counseling to couples adopting ARTs, where male partner carries these deletions.

AUTHOR CONTRIBUTION

Dr. Nidhi Shah, Dr. Parth Shah, and Dr. Mandava V. Rao are involved in review of literature and collecting of data from Indian and Abroad. Dr. Rutvik Raval and Mr. Rahul Yadav were involved in manuscript preparation, figures, and data analysis. Dr. Mandava V. Rao, Dr. Nidhi Shah, and Dr. Sandip Shah helped in finalization of the manuscript along with Dr. Rutvik Raval and Mr. Rahul Yadav.

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