The human Y chromosome is very much essential not only for sex determination, but indeed required for the control of spermatogenesis. In infertile conditions such as, azoospermia, oligozoospermia, the Y chromosome partial deletions eliminates the azoospermia factor (AZF) regions (AZFa, AZFb and AZFc) are often observed and it is considered as the second most frequent genetic cause of spermatogenic failure. Given that the ethnic background, geographic location and the Y haplogroups influence the occurrence of different AZF deletions, but the effect of AZF specific type of deletion on spermatogenesis is still unclear. In Western countries prior to intra cytoplasmic sperm injection (ICSI) procedure the infertile couples undergo AZF deletion assessment in addition to semen analysis. However, in Indian context the molecular and genetic diagnosis based approach for male infertility is very limited. Thus, the current study has been initiated to elucidate the association of different types of AZFc partial deletion patterns and spermatogenesis in admixture population of Southern and Western Karnataka, India.

Current study has recruited Siddi tribes, normozoospermic controls and infertile individuals for comprehensive and systematic examination of semen evaluation and AZFc partial deletion analysis. Interestingly, in comparison to control samples higher percentage of abnormalities is observed in the infertile group with an increase in morphologically defective sperm and an overall reduction in sperm vitality, count and motility. In addition, age-wise analysis revealed the inverse relationship between the semen variables and subject’s age. However in the present study, due to strong traditional and religion faith, it was not possible to collect the semen samples from Siddi tribal individuals to carryout systematic semen analysis and sperm function assay to correlate with the AZFc partial deletion.

Furthermore, the present study records the higher frequency of b2/b3 AZFc partial deletion in normozoospermic controls with negative effect on spermatogenic impairment and on contrary, severe reduction in the sperm count, motility and vitality are observed in infertile subjects. Additionally, infertile individuals also exhibited higher frequency gr/gr partial deletion with variations in sperm dysfunction, thereby
showed a significant association with the deletion. Surprisingly, out of 200 Siddi males only one individual displayed b2/b3 partial deletion, whereas the rest of the subjects showed no deletions for other markers that are employed in the current study. Taken together, our data suggests that b2/b3 deletion followed by gr/gr deletion or combination of gr/gr; b2/b3 deletion may be considered as a risk factor for spermatogenic impairment and male infertility in the study population.

Next, the single nucleotide variants (SNV) analysis demonstrated that the loss of DAZ and CDY1 specific gene copies in our study subjects with AZFc partial deletions. Specifically, DAZ3/4 + CDY1a deletion patterns are predominately observed in all the three groups, whereas, DAZ3/4 + CDY1b deletion combination are recorded in normozoospermic controls and infertiles. Further, the individuals with b2/b3 and gr/gr partial deletions showed higher frequency of DAZ3/4 + CDY1a and DAZ3/4 + CDY1b deletion patterns, which is associated with significant impairment in semen parameters.

In conclusion, this pioneering Y chromosome AZFc partial deletion analysis report from Southern and Western part of Karnataka demonstrate the association of AZFc partial deletions as a high risk factor for spermatogenic impairment in our study cohort. Specifically, b2/b3 and gr/gr deletion with absence of DAZ and CDY1 gene copies results in poor semen quality, which in turn affects male fertility. Thus, our study suggests that understanding the AZFc deletion patterns, altered semen characteristics and their association in different populations/ ethnic groups may be useful for appropriate clinical assistance to the infertile couples.