

# Pedigree Analysis: An Important Diagnostic Tool for Calculating the Risk Factor in Infertile Men of Indian Population

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## Abstract

The problem of male infertility is widespread in the modern world and it is of utmost importance to look for risk factors and its early diagnosis so that corrective measures can be taken early on. The pedigree chart analysis is a very important tool in this regard which gives us the pictorial representation of the disease within the family. The research work was conducted in the Department of Research, Jawaharlal Nehru Cancer Hospital, and Research Center. Three-generation medical history of healthy control and infertile subjects were taken by preparing a pedigree chart in the form of pictorial representation. Physical examination was done for the Anthropometrical studies and other sexual inconvenience of the enrolled subjects. In the subjects enrolled for study the prevalence of infertility was found to be significantly high in families having a history of infertility and other habits in their generation line.

**Keywords:** Anogenital distance, Abortions, Infertility, Pedigree, Sperm Morphology

## 1 Introduction

Male infertility is on the rise around the globe, consequently, it is getting more consideration in numerous studies to improve its treatment management (1). In the reproductive age, 10 to 15% of couples face the problem of infertility (2). Pedigree analysis is the presentation of the family history as well as medical and genetic associations in a graphic form. For centuries it has been an essential means in medical genetics practices (3,4). For the health professionals in routine medical practices, the pedigree interpretations should be an essential tool in calculating the risk of infertility in a family. Infertility is a worldwide problem nowadays and has been increasing since the last decade or two due to changing lifestyles and environmental conditions. According to the world health organization (5), infertility has been defined as the inability to conceive after one year of unprotected intercourse. At present, infertility is a serious concern in developing countries. Infertility is affecting 13-15% of couples worldwide and becoming a common clinical problem day by day. In a study done by Polis *et al.*, (6), infertility prevalence was studied by the Current Duration (CD) (i.e. current length of time-at-risk of pregnancy) approach in developing countries and according to their study, the estimated percentage of infertile couples was 31.1% (95% CI: 27.9–34.7%). Globally infertility affects more than twenty million men and represents a major health concern. Generally, it has not been studied that males with multifactorial problems have a strong genetic basis. The present growth of the Indian population is on the rise of extraordinarily. It stands, currently, at over one billion and is expected to touch 2 billion by 2035 assuming an average growth rate of 2%. Even though increasing population growth is a major concern of the nation, in the meantime large

numbers of infertile couples in India have an equally great concern (7).

## 2 Objectives

The main objective of the current research work is to trace family history by preparing a pedigree chart of male individuals with infertility and to establish pedigree analysis as an important tool for identifying the causes and risk factors of male infertility in Indian males.

## 3 Material and methods

The present experimental work was conducted in the Department of Research, Jawaharlal Nehru Cancer Hospital and Research Center (JNCH&RC), Idgaha Hills, Bhopal from the year 2013 to 2017. It was a cross-sectional study and the subjects were enrolled from OPD, referred cases from different IVF centers of Bhopal, and volunteers from different sections of society (healthy as well as subjects not facing the problem of infertility) of age groups 18-45 years. The study was approved by institutional ethical approval (IEC 546/16.03.16).

### 3.1 Pedigree Chart Construction

Pedigree analysis was done by collecting the family history by simply asking the patient if any family members have the same illness or not. The pictorial representation of diseases was calculated in which three generations have been studied. The pedigree chart of the three-generation provides a pictographic representation of any kind of disease within a family and is also helpful to calculate the risk factor in the family if any. It is the most professional way to assess hereditary influences on disease. (a) In this study, the questionnaire approach was used for the collection of family information and construct a pedigree

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chart. (b) This approach typically takes 15 to 30 minutes. (c) Patients were provided with questionnaires about their family history information before the sample collection and physical examination. (d) Collection of three-generation pedigree family history, which then transferred to a printable standardized form. Specific questions were asked during the pedigree charting targeting adult diseases, diabetes, heart disease, and stroke, ovarian, breast, colon cancer, Infertility, Spontaneous abortions, or any Miscarriages. Visualization of the personal history in pictorial form may clarify risks to a patient that had not been appreciated earlier (8,9)

### 3.2 Physical Examination and Anogenital Distance (AGD) measurement

Before the physical examination, subjects were asked to remove the pubic hairs and wash the inguinal area to maintain the hygiene for the aseptic conditions. Physical examination was performed to find out any sexual ambiguity, scrotum disorder, undescended testis, varicocele, fungal infection, and micropenis if any. The measurement of Anogenital Distance (AGD) was taken from the center of the anus to the base of the scrotum and the center of the anus to the lower base of the penis with the help of vernier caliper (span diagnostic) or with the help of inch tape on the examination table and then the mean was calculated (10,11,12,13,14).

## 4 Results and discussion

The history of healthy control, individuals having AGD<2 inches and Infertile males, are depicted in Table 1, it was revealed that 26% (HC), 30% (AGD<2") and 53% (INF) men were passive smokers in respective groups and 0%, 12%, and 45% were active smokers respectively. Pedigree has involved both proband and consultant in which behavior, marital status, and consanguinity history signatred. The pedigree charts revealed that infertility descends from the maternal and paternal side. Table 1 revealed that in healthy control male's 6.6% having a history of infertility in their family three-generation line 7.3% abortion history, 4% radiation exposure, and 16.6% stress. Subjects with AGD<2 shows 24% infertility history, 6% abortion, 4% radiation exposure, and 70 % stress. In infertile males, it was found 58%, 43%, 21%, and 75 % respectively, which is significantly high as compared with a healthy control group. Graph 1 also shows the percentage of history with Infertility and other ailments of healthy control and infertile subjects. The present research work revealed that after the physical examination of the enrolled subjects, various physiological and anatomical disorders were found. In this study, it was also found that the percentage of these anomalies in healthy control subjects like Microphallus (1.33%), Hypospadias (0%), Varicocele (1.33%), Undescended testes (2%), Testicular Atrophy (0%), Gynecomastia (2.66%), Balanitis (0.6%) and ED (3.3%), were found significantly low as compared with Infertile subjects i.e. Microphallus (4%), Hypospadias (4.66%), Varicocele (5.33%), Undescended testes (4.66%), Testicular Atrophy (2%), Gynecomastia (3.33%) Balanitis (2%) and ED (9.6%) as shown in Table 2 and Graph 2. This study was supported by various publications. Simsek *et al.*, in their study revealed that apoptosis of germ cells is very common in men diagnosed with varicocele (15). Jarrow in his study revealed that in pubertal young boy's varicocele can cause

testicular damage (16). In another study by Aho *et al.* in their comparative study revealed that in social and sexual life there was no considerable variation between who undergo circumcision and hypospadias repair (17).

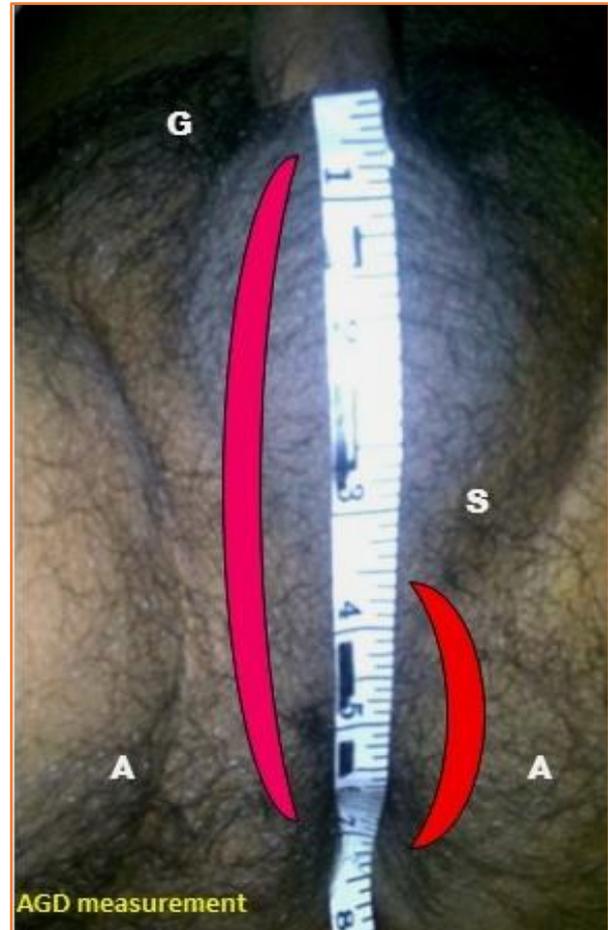


Figure 1: Showing A landmark of AGD measurement from the center of the anus to the base of the scrotum and from the base of the penis to the center of the anus. Method of measuring AGD during the present research work

In another study done by Francesco & Mario supported our work they found that in the reproductive age sexual problems occur frequently in some cases causing infertility(18). They revealed that a lack of sexual satisfaction is the most prevalent type of dysfunction in reproductive health ranging from 8.9 - 68.7%. The problems of premature ejaculation or erectile dysfunction were found 1 in 6 men having infertility. Erectile dysfunction and/or premature ejaculation, evaluated with validated tools, has a prevalence of one in six infertile men and problems of orgasm one in ten infertile men. Mescheden *et al.*, also supported our work that pedigree charting is a very important diagnostic tool for infertility in their study they revealed that by constructing pedigree chart find that 11. 8% couples were found everlasting sterility in at least 1<sup>st</sup> or 2<sup>nd</sup> degree relative i.e. Aunt, uncle, sister, brother, half-sib (19).

Table 1: Showing the Pedigree analysis of healthy control, infertile subjects, and subjects with AGD<2 inches with a family history of infertility and history of other ailments

Pedigree analysis of healthy control, infertile subjects (primary and Secondary infertility)						
Group	% Age of family history of infertility	% Age of abortion history in the family	% Age of radiation exposure	% Age of stress	% Age of the Passive smoker	% Age of the active smoker
Healthy Control	6.66 %	7.33%	4%	16.66%	26%	0%
Infertile subjects	58%	43%	21%	75%	53%	45%
Subjects with AGD<2	24%	6%	4%	70%	30%	12%

Table 2: Showing Percentage of Anatomical and Physiological anomalies found in the enrolled subjects

Percentage of anatomical and physiological anomalies found in the enrolled subjects								
Subjects	MP	HPD	Varicocele	UDT	TA	GC	BL	ED
HC	1.3%	0%	1.33%	2%	0%	2.6%	0.6%	3.3%
INF	4%	4.6%	5.3%	0.6%	2%	3.3%	2%	9.3%

Legends: HC- Healthy Control, INF- Infertile subjects, MP - Microphallus, HPD - Hypospadias, UDT - Undescended testes, TA - Testicular Atrophy, GC - Gynecomastia, BL - Balanitis, ED - Erectile dysfunction.

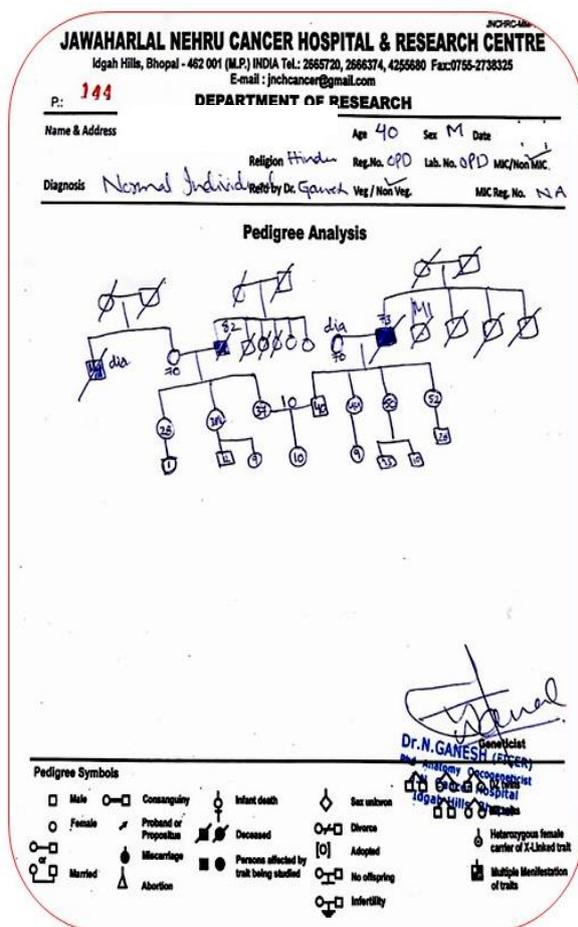


Figure 2: Showing constructed a pedigree chart of healthy control

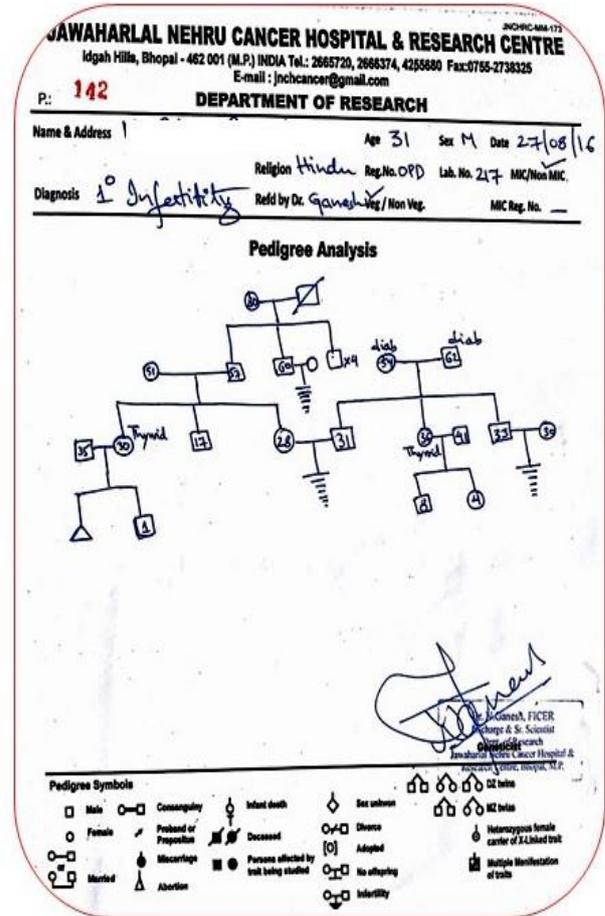
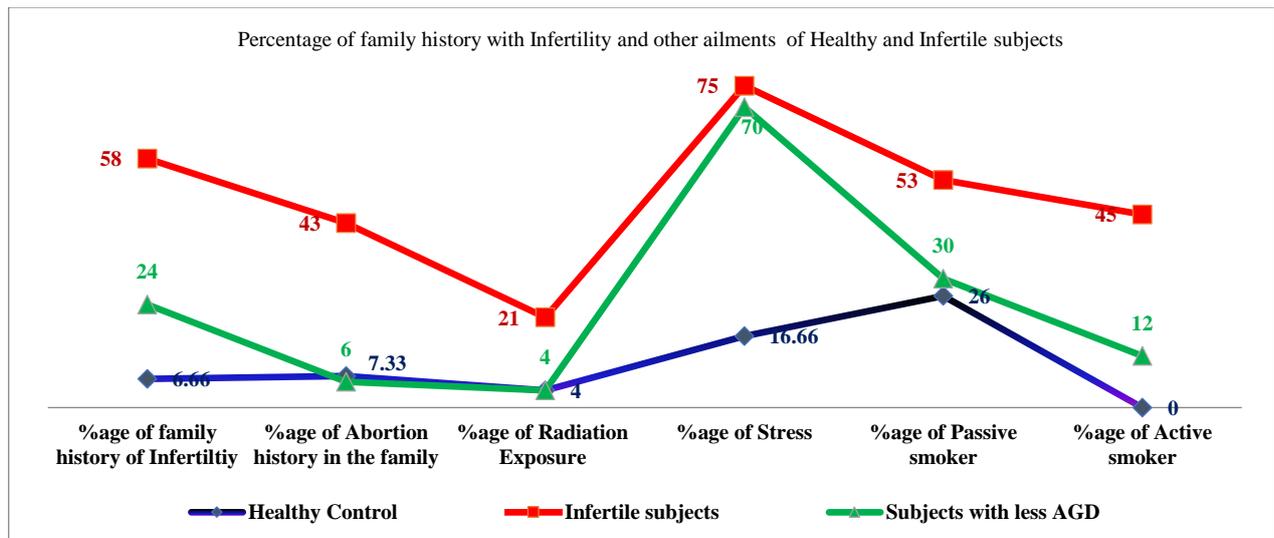
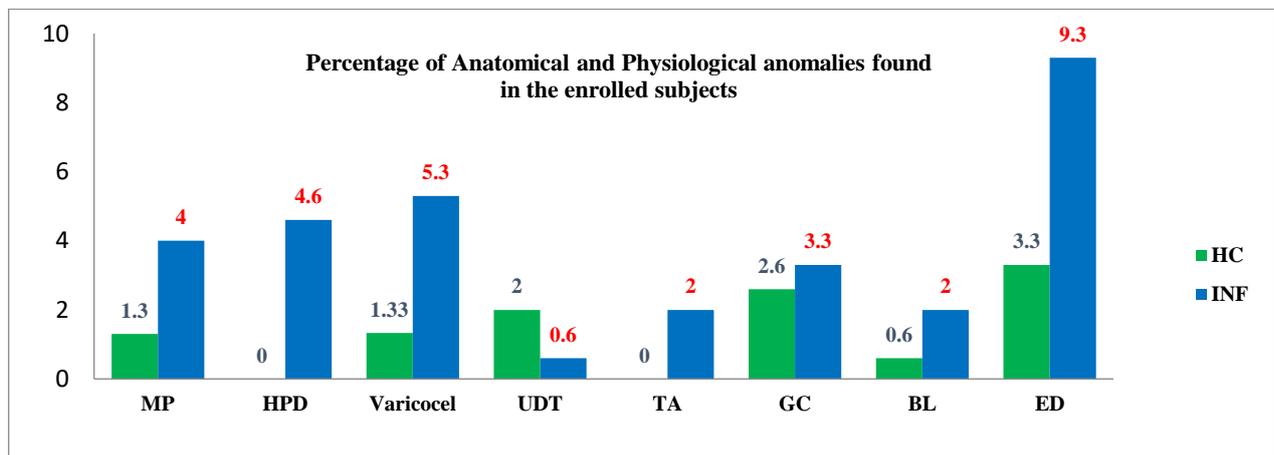


Figure 3: Showing pedigree chart constructed of an infertile male (Primary infertility) with a family history of infertility, thyroid, and diabetes



Graph 1: Showing percentages of family history of infertility and other ailments of healthy control and infertile subjects



Graph 2: Showing Percentage of Anatomical and Physiological anomalies, GC – Gynecomastia, BL - Balanitis, ED - Erectile dysfunction, HC- Healthy Control, INF- Infertile subjects

Out of these two couples from both men's and women's side had a positive history of infertility. They also found in the pedigree chart there were eight men and one woman had affected relatives the history of infertility was found significantly high in a male partner as compared to the female partner's side i.e. ( $p=0.001; \chi^2$  test). Masculine has a strong predominance of infertile relatives as compared to a woman ( $p=0.001; \chi^2$  test). In precise, our results suggest that the genetic factor plays a very important role in the diagnostic of infertility. Hence, it can be concluded that Pedigree chart analysis is a very important tool in determining infertility risk running in a family. It accesses the hereditary influences on diseases within the family very efficiently. The gathering of the three-generation medical history of the family is for the calculation of the risk assessment in the family of the rare disease or genetic problems including infertility so that corrective measures, like dietary and lifestyle measures, should be advised to young boys and girls having such history in their family to combat the problem.

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### Declaration of interest

The authors declare that there is no conflict of interest regarding this paper submission.

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