

GENETIC COUNSELING IN REPRODUCTIVE GENETICS

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ABSTRACT:

Genetic counseling in reproductive genetics is a vital aspect of contemporary healthcare, providing essential guidance to individuals and couples confronting genetic concerns in family planning. This abstract highlights the multifaceted role of genetic counselors in preconception, prenatal, and pre-implantation scenarios, where they assess genetic risks, offer emotional support, and aid in decision-making processes. Ethical considerations, including autonomy, beneficence, and justice, are emphasized as crucial in navigating complex moral dilemmas. Ultimately, genetic counseling in reproductive genetics is depicted as a dynamic field, continually adapting to scientific advancements and diverse cultural contexts, while prioritizing the well-being and autonomy of individuals and families.

INTRODUCTION:

Genetic counseling is a medical practice that provides and supports patients/family members with inherited diseases or those who have the ability to make decisions and act on life-planning choices with appropriate genetic information.

The term "genetic counseling" was created by Sheldon Reed in 1947 [1]. Genetic counseling is a process that helps people understand and adapt to the medical, psychological and family consequences of the genetic impact of a disease.

The role of the genetic counselor is to provide information and find out the circumstances and needs of the client [2].

The National Society of Genetic Counselors (NSGC) defines genetic counseling as the process of helping people understand and adapt to the medical, psychological, and family consequences of the genetic impact of disease [3].

The first IVF child is Louise Brown, she was born in 1978. Currently, more than 1.7 million artificial reproductive technologies (ART) are performed worldwide per year, and approximately 400,000 babies are born using ART. Although ART has been performed safely, there are several genetic challenges [4].

The main reasons couples seek reproductive genetic counseling are couples suffering from infertility and couples with recurrent miscarriages. According to the World Health Organization (WHO), infertility is defined as "the inability to conceive after one or more years of unprotected intercourse"[11].

Thanks to advances in genomic medicine and genomic technology, reproductive genetic counseling is very welcome in the field of infertility treatment.

Genomic technologies have a huge impact, for example precision diagnosis helps in prevention and prediction [5]. According to some data, approximately 1 in 13 pregnancies result in a pregnancy with a chromosomal abnormality [6], with approximately 50% of first-trimester miscarriages associated with

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chromosomal defects [7]. According to some studies, about 0.2% of children are born with balanced structural chromosomal rearrangements and can have reproductive effects later in life [5]. 5.6-11.5% of stillbirths and neonatal deaths are related to some chromosomal defect [8]. About 3-4 percent of all births may be associated with a significant birth defect or genetic disorder. Some genetic disorders double before the age of 8 years, are considered late-onset or diagnosed genetic diseases [9]. About 15% of infertility is due to genetics, and genetics are also thought to account for the majority of idiopathic cases, about over 50%.

In a third of infertility cases, both sides are involved in the pathogenesis [12]. Because 5-10% of female infertility cases and 5-20% of male infertility cases are identifiable genetic problems [13,14]. Technologies such as next-generation sequencing (NGS) and the rise of monogenic causes of male and female infertility are making genetic counseling more complex. Some couples have a harder time maintaining a pregnancy than achieving one, these cases are labeled couples with recurrent miscarriage. About 5% of couples of reproductive age experience recurrent (at least two) miscarriages [15]. According to a study, 1% of couples experience the WHO definition of miscarriage (three or more miscarriages before 20 weeks of pregnancy) [13]. Most miscarriages occur in the first trimester and are mostly due to numerical chromosomal abnormalities.

Although both infertility and abortion are common in today's society, it remains a social taboo. As a result, couples facing these problems suffer mentally, so they avoid discussing the issue with their peers, which puts more pressure on them. Couples can suffer enormous emotional stress. Therefore, genetic counseling helps them open up and understand their stress and depression, including the problems they face.

According to these statistics, the genetic influence in the practice of the reproduction process is huge compared to other fields.

In the past, couples suffering from genetic problems were told about the possibility of passing on the genetic disorder to their offspring through reproduction, they only had 2 options, the option to use themselves or not to reproduce. However, promotion of pre-implantation and prenatal diagnosis is given to those couples who have offspring without effect. Thus, it greatly increased the scope of genetic counseling in the field of reproductive practice in cases where men with a history of infertility require artificial insemination (ART) and especially in vitro fertilization (IVF) and intracellular sperm injection (ICSI) .), as they may increase the transmission of genetic diseases to offspring (Yq microdeletion, chromosomal abnormalities, cystic fibrosis, unbalanced translocation, pathogenic copy number variations/CNVs) or consanguinity with a carrier state or dominant disease for a recessive monogenic disease. monogenic disorder. This showed the need for genetic counseling for every pregnant woman.

All reproductive specialists (obstetrics, gynecology, andrology, reproductive endocrinology and reproductive genetics) must have a good knowledge of genetics, especially in the age of molecular and precision medicine with high-throughput genomics/genomic techniques. It is really important to have good knowledge about genetic counseling, especially risk factors and preventive methods to avoid genetic disorders in offspring. This helps protect reproductive professionals from medical and legal consequences if they fail to prevent the transmission of genetic disorders to offspring. Genetic testing is used in all professions today. Genetic counseling has recently played a central role in reproductive medicine and has led to great advances in artificial reproductive technology [10]. This review discusses the benefits and importance of genetic counseling and the potential risks when it is not done correctly in the practice of reproductive medicine..

INFERTILITY :

According to the World Health Organization (WHO) [11], infertility is defined as "the inability to conceive even after one or more years of unprotected intercourse".

Types of infertility:

1. Primary (Couples who have never experienced pregnancy)

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2. Secondary (Failure to conceive after a previous pregnancy without contraception, breastfeeding and postpartum menstruation) [38].

Cause of Infertility :

Infertility can be caused by many different factors, male or female reproductive system or in some cases both. In addition, in some scenarios, it is not possible to explain the true causes of infertility [11].

● Female infertility can be due to:

- Tubal disorders are blockages in the fallopian tubes caused by untreated sexually transmitted infections (STIs) or complications from unsafe abortion, postpartum sepsis or abdominal/pelvic surgery. .
- Disorders of the uterus can be inflammatory in nature (eg, endometriosis), congenital (eg, uterine septum), or benign (eg, fibroids).
- Ovarian disorders such as polycystic ovarian syndrome (PCOS) and other follicular disorders.
- Endocrine disorders that cause reproductive hormone imbalances. The endocrine system includes the hypothalamus and pituitary gland. Common disorders affecting this system include pituitary cancer and hypopituitarism [16].

● Male infertility can be due to the following reasons:

- Obstruction of the reproductive track can cause problems in ejection of semen. Obstructions are caused by genital injuries or infections.
- Hormonal disorders can cause disturbances in the hormones produced by the pituitary gland, hypothalamus and testicles. Hormones such as testosterone regulate sperm production. Disorders that cause hormonal imbalance are, for example, cancer of the pituitary gland or testicles.
- Failure of the testicles to produce sperm, for example due to medical treatments that improve sperm-producing cells (such as chemotherapy).
- Abnormal sperm function and quality. For example, the use of anabolic steroids can lead to abnormal sperm parameters such as sperm count and shape [17].

EXAMINATIONS AND DIAGNOSIS CARRIED OUT:

● Gynecological examination to determine a fertility defect:

It begins with the personal history of the patient (female partner), which includes genealogical information, pedigree information (anamnesis), followed by a clinical and laboratory examination. They help to deal with pubertal development, a sign of hypogonadism or excess cortisol. Vaginal sonography adequately detects abnormalities of the internal genital organs. The main components of the endocrine system include luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid-stimulating hormone (TSH), prolactin, testosterone, progesterone, dehydroepiandrosterone sulfate (DHEAS), sex hormone-binding globulin (SHBG), free androgen index, free androgen index and anti-Müllerian hormone (AMH).

NORMAL HORMONE RANGE

- LH : 5-25 IU/L
- FSH : 4.7-21.5 mIU/mL
- TSH : 0.4-2.5 mIU/L
- Prolactin : < 25 ng/ml
- Testosterone : 15-70 ng/dl
- DHEAS : 13 - 380 ug/dl
- SHBG : 18 - 144 nmol/L
- Free Androgen Index : 6 - 86 ng/dl
- Estradiol : 30 - 400 pg/ ml

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- AMH : 1.5 – 4.0 mg. /mL

Table 1 : Female hormones

- **Andrological examination to detect a decrease in fertility:**

It begins with the personal and family history of the patient (male partner), followed by a physical, hormonal examination. profiling, exclusion of malformations of the urogenital system, ultrasound of the scrotum, semen analysis. According to WHO guidelines [18], semen analysis should not only include sperm count and concentration, but should also assess sperm morphology and motility.

LIQUEFICATION	: 30-60 min
VOLUME	: > 1.5
pH	: 7.2-7.8 (alkaline)
COLOR	: Grey opaque
SPERM CONCENTRATION	: $16 \times 10^6 / \text{ml}$
MOBILITY	: > 40 %
MORPHOLOGY	: > 4 %

Table 2 : Sperm analysis

- **Genetic diagnosis in women :**

After a gynecological examination and hormonal evaluation, genetic algorithms can be determined. About 40% of women with fertility problems have menstrual irregularities that indicate ovarian dysfunction. Karyotyping reveals a gonosomal aberration in 10-13% of women with ovarian dysfunction such as Turner syndrome (45,X, structurally abnormal X chromosome or 46,XX / 45,X mosaic) or trisomy X (47,XXX). It is really important to have knowledge about abnormal karyotype to manage the abnormal karyotype because women with primary amenorrhea due to Turner syndrome have only a small chance with ART (assisted reproductive technology). Women with trisomy X usually have normal fertility, but may develop POI (where a woman's ovaries stop working before age 40).

- **Genetic diagnosis in men:**

After an andrological examination and hormonal evaluation, genetic algorithms can be determined. Example: Chromosome analysis is recommended in men with azoospermia, severe oligozoospermia or hypergonadotropic hypogonadism. The most common chromosomal abnormality causing azoospermia or severe oligozoospermia is Klinefelter syndrome (47, XXY), which occurs in 1 in 500 men in the normal population, 15% of men with azoospermia [19]. Correct cytogenetic diagnosis has direct therapeutic consequences for the patient.

KARYOTYPING :

For couples facing unexplained infertility (disease undetected by clinical diagnosis), carrier typing of both partners is recommended. Infertile couples are at high risk of chromosomal abnormalities, especially infertile couples more structurally balanced chromosomal abnormalities such as translocations or inversions are seen. In most cases, infertile couples have a balanced translocation, carriers of the translocation have a high risk of having children with unbalanced chromosomal abnormalities.

This condition is believed to cause severe syndromic conditions, including malformations and intellectual disability. To avoid these conditions, affected couples (infertile couples) should be recommended genetic counseling and prenatal or preimplantation genetic diagnosis [20].

DIAGNOSTIC WORK-UP IN RECURRENT MISCARRIAGE :

In couples who are facing recurrent miscarriages, the attention of medical examinations usually lies on the female side, but it is preferred that both the partners undergo cytogenetic evaluation. Congenital malformations of the uterus and acquired conditions such as adhesions, polyps and myoma might lead to slightly increased miscarriage risk and warrant ultrasound examination or hysteroscopy. Endocrine dysfunction that could also cause miscarriage are apparently showing hyper- or hypothyroidism, while latent hypothyroidism (increased TSH, normal T3 and T4 values) is not a proven risk factor to cause miscarriages.

The risk of recurrent miscarriages is in correspondence with maternal age, while paternal age does not have a major role. Around 60-70% of first trimester miscarriages are due to numerical chromosomal abnormalities. Around 4-5% of couples with a minimum of 2 miscarriages, 1 partner might have a high chance of being a carrier of balanced structural chromosome abnormality, compared with 0.7% in the normal population and 1% in couples after miscarriage[21]. Due to this, conventional karyotyping is recommended to both the partners. Earlier pregnancy loss is contributed by numerous genetic and environmental factors.

GENETIC DISORDERS :

Genetic Disorder is an inherited or developed medical condition caused by DNA abnormality, it might get transfer to the offspring of the affected person. It might also interrupt with fertility and might cause negativity to positive pregnancy.

Genetic disorders can be monogenic, polygenic multi-factorial (many genes interacting with environmental factors), chromosomal (including microdeletion), mitochondrial, genomic disorder (copy number variations) and epigenomic disorders. A carrier patient with a carrier dominant gene has a 50% chance of transmitting it to the offspring, both the sexes are at equal risk. Isolated cases in a family may represent new mutation.

GENETIC COUNSELLING :

Genetic counselling is a field handled by experts who are trained genetic counselors. The National Society of Genetic Counselors (NSGC) defines genetic counselling as the process of assisting people with understanding and adapting to the medical, psychological, familial implications of genetic contributions to disease [3]. This is a process of interpretation of family and medical history to assess the chances of diseases occurrence or recurrence. Genetic counselling provides education about inheritance, testing options, diseases management and prevention. Genetic counselling also promotes informed choices and adaptation to the risk or condition [3]. Genetic counseling usually has a specific therapeutic concentration like prenatal, pediatric, psychiatric, cancer genetic counselling etc.,

Individuals seek genetic counselling for numerous reasons. People who have questions about origins of diseases or traits in their family might seek genetic counselling. People who have or are concerned they might have an inherited disorder or birth defect could seek genetic counselling. Physicians also recommend pregnant women whose ultrasound examinations or blood tests indicate that their pregnancy might have risk for complications or disability, as well as women over the age of 35 who are pregnant to undergo genetic counselling. Couples who already have a child with genetic disability or who have given birth to infants diagnosed with a genetic disease by routine newborn screening may also seek genetic counseling [23].

The aim of genetic counselling is to support individuals in their ability to make an informed decision regarding genetic testing and the implications of such testing [22].

GENETIC COUNSELOR :

Genetic counselors are health professionals with specific education training and experience in medical genetics and counselling [24]. Usually genetic counselors work as part of the healthcare team, they provide information and support to families who have members with birth defects or genetic disorders and families

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or individuals who may be at risk for a variety of inherited conditions [24]. Genetic counselors interact with clients and other healthcare professionals in an assortment of clinical and nonclinical settings, like university-based medical centers, private hospitals, private practice and industry settings [25]. Now-a-days primary care practitioners are providing aspects of genetic counselling and genetic services, demanding a need to train nurses, social workers and physicians. Genetic counsellors have a critical role in educating providers and developing standards of practice. Genetic counselors also afford health professionals and patients the opportunity to communicate with others, like policymakers and the media, about new genetic services [26].

QUESTIONS GENETIC COUNSELOR MUST ANSWER :

- What is the Disease ? (clinical and laboratory diagnosis)
- How severe it is ? (prognosis and therapeutic possibilities)
- How it is caused / inherited ? (risk of recurrence)
- What can be done to avoid or prevent the disease ? (prenatal diagnosis) [53]

TYPES OF CONDITIONS THAT COULD BE INCLUDED IN THE GENETIC COUNSELOR CASELOAD:

- Genetic disorders may be detected at any time during the life span usually, most disorders are detected during the gestational period or soon after a child is born. Results during the gestational period may reveal Down syndrome or Spina bifida, while postnatal testing may reveal phenylketonuria or hypothyroidism.
- It was stated that genetic counselors could provide care for families affected by or concerned about the following conditions : familial cancer [27-31], neurodegenerative conditions [27] (include offering presymptomatic testing), chromosomal abnormalities [27-31] (including the sex chromosome [29,31]), multiple miscarriages [27,28] and single-gene disorders [29,31] including haemoglobinopathy [27,28], cystic fibrosis [27,30], metabolic disorders [28,30], neurofibromatosis [28,29], muscular dystrophy [28,29], haemochromatosis [30] and Huntington disease [32,28,30]. Counselling for neural tube defect [29,30], advanced maternal age [28,29,31] or abnormal prenatal screening [28,31] results, were also explicitly mentioned by several authors.

PSYCHOLOGICAL FACTORS AND GENETIC COUNSELLING :

Anxiety :

It is a normal human feeling that occurs when a person faces threat, danger or stress. When people get anxious, they typically feel upset, uncomfortable and tensed. [47]

Depression :

It is a mental disturbance that causes due to depressed mood, loss of interest or pleasure, decreased energy, feelings of guilt or low self-worth, disturbed sleep or appetite and poor concentration [48]

Psychological Factors in Infertility :

When women's exceed the rate of natural anxiety and depression, it results in extreme negative outcomes of pregnancy [49]. Psychological stress usually negatively associated with a positive pregnancy [50, 51, 52].

APPROPRIATE ROLES AND RESPONSIBILITIES FOR GENETIC COUNSELOR :

Role of genetic counselors include family history taking [27,30], pedigree drawing [30] , risk assessment [27,30] , discussion of natural history of the condition [27], psychosocial impact of the diagnosis [30], provision of patient education [32,29,30], discussion of options [27], addressing ethical issues [32], making a psychosocial assessment [27] and providing psychosocial support [32]. Other responsibilities that are considered to be appropriate for genetic counselors included providing professional and public education [29,31] and conducting newborn screening programmes [31].

GENETIC COUNSELLING CONSIST OF :

Genetic counselors assess the risk of occurrence or recurrence of a genetic condition or birth defect using a variety of techniques, including knowledge of inheritance patterns, epidemiologic data and evaluation of

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clinical data. They obtain and review (medical and family histories) then explain the nature of genetics evaluation to clients. They explain medical information regarding the diagnosis, potential occurrence of a genetic condition or birth anomaly [24]. Also potential treatment options, possibilities, limitations of tests, assessments in determining the genetic status are discussed with client. Prenatal diagnosis using cytogenetic or biochemical analyses of fetal cells, amniotic fluid or mother's blood can provide distinct answers to genetic questions [33]. In particular, populations where the probability of genetic disorders, such as Tay-Sachs disease or sickle cell anemia, is found to be high, screening programs have been organized to counsel clients before they start families. The discovery of disease and susceptibility genes brought forth by the sequencing of the human genome has brought challenges to the field of genetic counseling. The traditional role of genetic counseling has significantly widened to address a diversity of developing needs, ranging from individuals looking for disease susceptibility testing to those looking to find out if a therapeutic treatment option is the right one for them [26].

REPRODUCTIVE GENETIC COUNSELLING :

Reproductive genetic counselling is a process of communication in regard to the occurrence and the risks of recurrence of reproductive genetic disorders within a family. This aims to give a clear and defined understanding of all important implications and possible options of the disorder to the patients to facilitate deliberate decisions [9]. It is must that the decision is taken by the counselee and not by the counselor. Genetic counselling aims to help the individual or family as follows :

- Comprehend the medical facts including diagnosis, cause, probable course of disorder, available management including precision, prediction & prevention in the family
- Appreciate the way heredity contributes to the disorder and the risk of recurrence in relatives
- Understand the options for dealing with the risk of recurrence
- Choose the course of action, which seems appropriate to them in view of their risk & family goals and act in accordance with that decision
- Make the possible ways of adjustment with the disorder in an affected family member and/or to the risk of recurrence of that disorder in the family

GENETIC OF INFERTILITY PRACTICE :

Infertility is defined as ' inability to achieve pregnancy even after one or more year(s) of unprotected intercourse' according to the World Health Organization (WHO) [11].

Genetic abnormalities are in the range of 15-30% of male and 10-15% of female infertility, including chromosome aberrations and single gene mutations. Genetic variability and epigenetic factors affect reproduction and fertility from gametogenesis to birth. Genetic research has expanded in the last few years, and more and more genetic causes are coming up. This is changing previous estimates of the genetic contribution of infertility. Genetics has become more important following the development of *in vitro* fertilization (IVF) and intra cytoplasmic sperm injection (ICSI). The use of ICSI has raised major concerns about safety for the offspring, since it bypasses (penetrate) the physiological protective mechanisms (by injecting sperm into the egg directly with the help of micro infection) related to normal fertilization. Natural selection prevents the transmission of mutations causing infertility. This protective mechanism is bypassed by using assisted reproductive technology (ART). The risk for genetic causes of infertility will increase in future generations [34]. There are enormous tests now available to explore the genetic causes of infertility. There are several genetic etiological factors underlying infertility (Table) and examples of chromosomal abnormalities are : Yq microdeletion, CNVs, monogenic, multi factorial, epigenomic, mitochondrial, etc,. Sperm chromosomal alterations [35] are also highly prevalent in spermatogenic impairment but not with necrozoospermia [36]. Infertile males with oligo/astheno/teratozoospermia (with normal blood karyotype) have ten-fold increase of chromosomal abnormalities in their sperms, including diploidy, disomy and nullisomy. Based on prevalence data routine karyotyping of infertile men within explained spermatogenic failure is widely recommended before ART. Sperm fluorescent in situ hybridization (FISH) is commonly used to determine the proportion of aneuploidy present in sperms of

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infertile men. Testicular sperm from men with non-obstructive azoospermia display a higher rate of aneuploidy in spermatozoa than ejaculated sperms. Increased sperm aneuploidy increases the risk of IVF/ICSI failure and fetal aneuploidy. Indications for sperm FISH are repeated in vitro fertilization failure, oligospermia, nonobstructive azoospermia (testicular sperm), teratozoospermia, necrozoospermia, Klinefelter's syndrome (mosaic and non mosaic), translocations, exposures to gonadotoxins, chemotherapy, pesticides exposure, etc,. Various Y chromosome microdeletion / azoospermic factor (AZF) are predominantly found in non-obstructive azoospermia or severe oligospermia. Testing of AZF has a prognostic impact for sperm extraction, since no sperm can be retrieved in AZFa and AZFb, while there is a fair chance in AZFc. Copy number variations (CNVs) have not yet been defined as a cause of male infertility, but that seems inevitable.

GENETIC COUNSELLING IN INFERTILITY :

Reproductive genetic counselling is a process of communication in regard to the occurrence and the risks of recurrence of reproductive genetic disorders within a family. This aims to give a clear and defined understanding of all important implications and possible options of the disorder to the patients to facilitate deliberate decisions [9]. In general, decisions should be taken by the counselee and not by the counsellor. This should be a non-directive & unbiased manner. The ideal genetic counselling avoids a direct approach and concentrates on the medical, psychological and social circumstances so that couples can make decisions that are appropriate for them. The nondirective decision-making approach may sometimes prove unattainable, especially in situations where ambiguity in decision making. Shared decision-making can then provide a complementary approach when trying to balance the tensions between evidence-based guidance and the need to respect patient choice. Counselling provides help in areas of psychological assistance, technical explanations and discussing relationships. Genetic counsellor should be sensitive for infertility diagnosis as it carries social taboo, inferiority complex, familial disharmony/anxiety and ethics of various treatment options. Where genetic risks are related to the cause of infertility, genetic counselling is always required. There are several options available to couples avoid having an affected child, having no children, having no genetic testing, having prenatal/preimplantation genetic diagnosis, using donor gametes or adoption. For prenatal/preimplantation genetic diagnosis (PGD) or use of donor gamete the genetic counselling should be provided by trained professionals. Counselling should begin with the history of both the partners, including the medical, social, reproductive and genetic histories of both partners. In situations where both partners are known to carry genetic defects (causing infertility) there can be a high chance of transmitting the disease to the child. In this situation, to the clinicians and infertility clinic personnel it might feel that it is not ethical to proceed ART to the couple unless followed by preimplantation and/or prenatal diagnosis. In some countries, there are laws for these matters but, in the absence of law, it makes the doctor's role very difficult. In this situation the interests of a future child should take importance over the interests of a couple. In this situation preimplantation genetic diagnosis is helpful to have a normal baby. Indications of genetic counselling are advanced age of couple, parent with known genetic disorder/carrier (chromosomal, Yq microdeletion, cystic fibrosis, etc), before offering assisted reproduction & preimplantation genetic diagnosis, gonad/gamete cryopreservation, donor gamete use, etc,. Traditionally genetic counselling in infertile couples is done before offering assisted reproduction. Pre ART counselling is important in identification of risk factors, disease states as well as to discuss preventive measures through carrier screening, preimplantation screening and prenatal screening. This provides anticipatory guidance. The patient's ethnicity, medical history and genetic family history are key elements in this evaluation.

Preconception period is considered as the optimal time to review the importance of preventive measures of transmitting genetic disorders in offspring. It also provides the opportunity to address the risks associated with environmental hazards and medications, general risk of congenital anomaly or chromosomal abnormality associated with parental advanced age. Preconception counseling clinics have progressively become an integral part of modern reproductive care. This should cover risk associated with advanced age,

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ethnicity, individual with balanced chromosomal translocations, risk of fetal malformations associated with drugs/radiation exposure, etc.,. The couple can make choices here. The couple may choose for ICSI and PGD to have a normal daughter. This is an appropriate use of PGD and couples should be encouraged to consider this option. If the couple decides to have an AZF (Azoospermia Factor) microdeleted son, they will need to be aware of having knowledge/interventions that may help their son preserve or optimize any future fertility options sperm/gonad cryopreservation around pubertal age.

Genetic counselling not only provides health care, but also provides emotional support and helps the couples/ family/ individual to overcome the social taboo.

ETHICS AND GENETIC COUNSELLING :

Genetic counselor must inform about the risks of prenatal testing and also the significance of such testing and the potential for therapeutic intervention [3]. Most people have limited knowledge about disabilities and prenatal decision making during the screening process occurs within a limited timeline, while requiring families to learn new medical information [45]. These choices are laden with uncertainty and raise challenging ethical, legal and social issues [3]. Genetic counselors are trained to make possible decisions to promote informed choices. Genetic information can have profound psychological implications for consumers, especially family members with genetic disorders[3].

CONCLUSION :

Genetic Counselling is preferred to be taken by couples , before getting pregnant , which might help them to not pass on any genetic defects to their offspring. Especially for infertile couples, not only to identify the reason for infertility, but also to get some emotional support. This emotional support could help family/ couple/ individual to overcome social taboo. In some cases infertility might increase stress and lead to depression , which might also cause physical weakness. Thus, Genetic counselling provides support and help the affected person to escape depression. It is recommended to couples whose blood related person have genetic issues or couples who have a previous child with genetic issue or couples of age more than 35 years to have a genetic counselling to avoid genetic issues passing to their offspring. Genetic Counselling could help the family / couple / individual to understand what they are going through and also gives them a wide knowledge of their issue so that they could take a decision that would be beneficial for them without affecting the next generation. Genetic Counselors' are formally trained medical genetics allows them to address genetic-related issues and indications in the fertility field. Here the genetic counselor will only provide information and suggest most of the ethically possible ways, but the decision is taken by the counselee only. Hence it gives freedom of choice but with ethics. Genetic Counselors in the fertility clinic improve quality of care according to fertility practice.

BIBLIOGRAPHY :

1. Resta RG: Defining and redefining the scope and goals of genetic counseling. *Am J Med Genet Part C Semin Med Genet* 2006; 142C: 269–275.
2. Skirton H, Patch C, Voelckel M-A: Using a community of practice to develop standards of practice and education for genetic counsellors in Europe. *J Community Genet* 2010; 1: 169–173.
3. National Society of Genetic Counselors (2012). Genetic counseling as a profession.
4. Adamson GD, de Mouzon Z, Chambers GM, et al. International Committee for Monitoring Assisted Reproductive Technology: world report on assisted reproductive technology, 2011. *Fertil Steril.* 2018; 110:1067-1080.
5. Milunsky JM and Milunsky A. "Genetic counseling in perinatal medicine". *Obstetrics and Gynecology Clinics of North America* 24.1 (1977): 1-17.
6. Plachot M., et al. "Chromosome analysis of oocytes and embryos". *Human Reproduction* 3.1 (1998): 125-127.
7. Boue J., et al. "Retrospective and prospective epidemiological studies of 1500 karyotyped spontaneous human abortions". *Tera- tology* 12.1 (1975): 11-26.
8. Alberman ED and Creasy MR. "Frequency of chromosomal abnormalities in miscarriage and perinatal deaths". *Journal of Medical Genetics* 14.5 (1977): 313-315.

GENETIC COUNSELING IN REPRODUCTIVE GENETICS

9. Milunsky A. "Genetic disorders and the fetus: diagnosis, prevention & treatment". *The American Journal of Human Genetics* 77.5 (1992): 896-897.
10. Simpson JL and Elias S. "Prenatal diagnosis of genetic disorders". In Creasy RK, Resnik R [eds.]: *Maternal fetal medicine: Principle & practice*. WB Saunders, Philadelphia(1994): 61.
11. WHO | World Health Organization. Sexual and reproductive health – Fertility and infertility – Assisting couples and individuals. WHO.
<http://www.who.int/reproductivehealth/topics/infertility/en/>. Published 2017.
12. Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. *Reprod Biol Endocrinol*. 2015;13:37.
13. Ferlin A, Raicu F, Gatta V, Zuccarello D, Palka G, Foresta C. Male infertility: Role of genetic background. *Reprod Biomed Online*. 2007;14:734–45.
14. Deutsche Gesellschaft für Gynäkologie und Geburtshilfe e. V. Diagnostik und Therapie vor einer assistierten reproduktionsmedizinischen Behandlung. <https://www.awmf.org/leitlinien/detail/ll/015-085.html>. Published 2019.
15. Carrington B, Sacks G, Regan L. Recurrent miscarriage: Pathophysiology and outcome. *Curr Opin Obstet Gynecol*. 2005;17:591–7.
16. Rutstein SO, Shah IH. Infecundity infertility and childlessness in developing countries. Geneva: World Health Organization. 2004
17. Gore AC, Chappell VA, Fenton SE, et al. EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine - Disrupting Chemicals. *Endocrine Review* 2015; 36 (6): E1 -E150.
18. WHO | World Health Organization. Examination and Processing of Human Semen. Fifth ed. Published 2010.
19. Lanfranco F, Kamischke A, Zitzmann M, Nieschlag E. Klinefelter's syndrome. *Lancet*. 2004;364:273–83.
20. Rudnik-Schöneborn S, Tüttelmann F, Zschocke J. Genetische Diagnostik vor assistierter Reproduktion – Empfehlungen der neuen S2k-Leitlinie 2019. *Gynäkologische Endokrinologie*. 2020;18:97–107.
21. Braekeleer M De, Dao TN. Cytogenetic studies in couples experiencing repeated pregnancy losses. *Hum Reprod*. 1990;5:519–28.
22. Sequeiros, J., & Guimaraes, B. (2007). Definitions of genetic test- ~ ing. EuroGentest Network of Excellence Project. Retrieved from
<http://www.eurogentest.org/web/files/public/unit3/DefinitionsGeneticTesting-3rdDrafl8Jan07.pdf>
23. March of Dimes (2012). Genetic counseling. Retrieved from
http://www.marchofdimes.com/pregnancy/trying_geneticcounseling.html
24. National Society of Genetic Counselors' Definition Task Force. (2006). A new definition of genetic counseling: National Society of Genetic Counselors' Task Force report. *Journal of Genetic Counseling*, 15(2), 77–82.
25. American Board of Genetic Counseling (2012).
26. National Human Genome Research Institute. (2012).
27. Hannig V, Cohen M, Pfothner J, Williams M, Morgan T, Phillips J 3rd: Expansion of genetic services utilizing a general genetic counseling clinic. *J Genet Couns* 2013; 23: 64–71.
28. Kromberg JGR, Wessels T-M, Krause A: Roles of genetic counselors in South Africa. *J Genet Couns* 2013; 22: 753–761.
29. Kromberg JGR, Parkes J, Taylor S: Genetic counselling as a developing healthcare profession: a case study in the queensland context. *Aust J Prim Health* 2006; 12: 33–39.
30. James C, Worthington S, Colley A: The genetic counseling workplace—an Australasian perspective. A National Study of Workplace Issues for Genetic Counselors and Associate Genetic Counselors. *J Genet Couns* 2003; 12: 439–456.

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31. Powell KP, Hasegawa L, McWalter K: Expanding roles: a survey of public health genetic counselors. *J Genet Couns* 2010; 19: 593–605.
32. Hines KA, Veach PM, LeRoy BS: Genetic counselors' perceived responsibilities regarding reproductive issues for patients at risk for Huntington disease. *J Genet Couns* 2010; 19: 131–147.
33. Zych, K. A. (2008). Genetic counseling. In E. Fletcher-Janzen & C. R. Reynolds (Eds.), *Encyclopedia of special education* (3rd ed.). Hoboken, NJ: Wiley.
34. Faddy M., et al. "Intra-cytoplasmic sperm Injection and Infertility". *Nature Genetics* 29 (2001): 131.
35. Halder A and Tutschek B. "Analysis of meiotic segregation in human nondecondensed interphase spermatozoa by multicolor rapid direct FISH". *Indian Journal of Medical Research* 107(1998): 94-97.
36. Halder A., et al. "Absence of sperm meiotic segregation error of chromosomes 1, 9, 12, 13, 16, 18, 21, X and Y in a case of 100% necrozoospermia". *Asian Journal of Andrology* 5.2 (2003): 163-166.
37. Roberts, C. D., Stough, L. M., & Parrish, L. H. (2002). The role of genetic counseling in the elective termination of pregnancies involving fetuses with disabilities. *Journal of Special Education*, 36(1), 48–55
38. Magdum M, Chowdhury AT, Begum N, Riya S. Types of Infertility and Its Risk Factors among Infertile Women : A Prospective Study in Dhaka City. *J Biosci Med* (2022;10:158-68).
39. Gaff CL, Clarke AJ, Atkinson P, et al. Process and outcome in communication of genetic within families: a systematic review. *Eur J Hum Genet* (2007; 5: 999-1011).
40. Holden J., (2015): Depression and Anxiety in the Workplace
41. Timothy J., (2017): What is depression and what can I do about it? .
42. Feijing Zhou & Yuezhi Dong, (2016): Psychological stress is related to treatment outcome in women undergoing in-vitro fertilization and Embryo transplantation, *Int J Clin Exp Med*, : 9(4):7478—7488, Reproductive Medicine Center, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China.
43. Constantini-Ferrando M., Joseph-Sohan M., Grill E., Rauch E., & Spandorfer S., (2016): Does stress affect in vitro fertilization (IVF) outcome? Reproductive Medical Associated of New Jersey, Cornell Medical College, New Your, NY.
44. Gourounti K., Anagnostopoulos F., Vaslamatzis G., (2011): The relation of psychological stress to pregnancy outcome among women undergoing in-vitro fertilization and intracytoplasmic sperm injection. *Women Health*; Jun 21; 51(4):321-39.
45. Li X., Ma Y., Geng L., Qin L., Hu H., & Li S., (2011): Baseline psychological stress and ovarian norepinephrine levels negatively affect the outcome of in vitro fertilization, *Gynecol Endocrinal J*; 27 (3), PP 139-143.