Short Communication

Indian Journal of Genetics and Molecular Research
Volume 8 Number 1, January - June 2019
DOI: http://dx.doi.org/10.21088/ijgmr.2319.4782.8119.7

Basic Guidelines of Genetic Counseling

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How to cite this article:

Divyya Raj Mohan, Hafsa Subhani, Prasanth Babu *et al.* Basic Guidelines of Genetic Counseling. Indian J Genet Mol Res. 2019;8(1):47-51.

Abstract

Genetic counseling helps people understand and adapt to medical implications about genetic disorders. It involves communication between the client and genetic counselor. Goal of genetic counseling is to provide appropriate options, testing and management strategies in the direction of the disorder and complications associated with it. In directive counseling, counselor plays a significant role by focusing on viewpoints and avoids general advises. Non-Directive counseling is where the counselor allows the client to make own decision according to their perception. Genetic evaluation methods are used to diagnose the genetic disorders, which includes ultrasound, maternal serum screening, karyotyping, FISH, cell free DNA, chorionic villus sampling, amniocentesis, chromosomal microarray, MLPA and whole genome sequencing. In India, the guidelines defined by ICMR are followed in hospitals, universities and clinics practicing genetic counseling.

Keywords: Genetic Counseling; Directive counseling; Non-Directive counseling; Risk assessment; Confidentiality; Screening.

Introduction

Genetic counseling can be defined as a procedure of communicating with an individual or couple who is affected or at risk of transmitting the genetic disease. It includes genetic aspects of the disease, information on inheritance pattern of the disease, recurrence risks, and education about screening and diagnostic tests, management and prevention of the disease [1,2,3]. The goal of genetic counseling is to avoid congenital abnormality and inherited disorders, to develop psychological health and guide an individual/a couple to choose an appropriate option by explaining them about the consequences if left unattended [4]. ICMR guidelines are followed in the process of genetic counseling.

Types of Genetic Counseling

The term "Genetic Counseling" includes different activities, by means of communication. Genetic counseling may be related to diagnostic evaluation of a child with multiple developmental disorders, related to decision making process regarding

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Received on 05.05.2019; **Accepted on** 29.06.2019

genetic testing or may be related to discussion about prenatal diagnosis where the termination of pregnancy is done only at risk of serious inherited disease [5].

The nature of discussion and the mode of counseling vary greatly which depends upon each counselor. There are two major type of counseling; Directive counseling, where the counselor plays a significant role. The counseling with the client should be rationale, instead of emotional behavior. The counselor identifies the issue and advice based on the issue; he/she will suggest or advise the clients. Counselor will influence the patients in a specific way and avoids general advises, he/she will only talk about focused and scientific viewpoints [5].

Non-Directive counseling practice has begun around 20th century, as counseling applied to decision making about reproductive and medical diagnosis [6]. In this type of counseling, the counselor should allow the client to make their own decision according to their perception. Counselors should be nonjudgmental and should not impose their decisions to avoid contradiction of the patient's choice with counselor's personal agenda [7].

Autonomy and Confidentiality

The main idea of autonomy is "self-rule", the meaning of which plays different role in different environment. A client's decision is said to be autonomous when it is not forced or manipulated by others. Genetic counselor plays an important role in clarifying the client about the test results, opportunities/choices available and later outcomes [8]. Confidentiality refers to keeping the test results data private, by not revealing it to third parties. In some cases, the results are not disclosed even to the patient if they are psychologically compromised [9]. For example, In autosomal disorder, the disclosure of results to family members/relatives is important as it gives information on severe pathological consequences that may emerge in future [10]. Thus, the balance between patient's confidentiality of his/her information and benefits of family members is still a challenge [11].

The process of Genetic Counseling involves few key aspects listed below:

- Genetic counseling should be given only by qualified genetic counselors.
- Helps diagnose the disease prenatally or postnatally.
- Helps in understanding the inheritance pattern and risk assessment.
- Helps an individual to make an appropriate decision.
- Follows principles of autonomy and confidentiality
- Evaluate the psychological status of the client before and during discussion.

Genetic Testing Methods:

Genetic testing includes chromosomal analysis, biochemical tests and DNA sequencing which may be done prenatally or postnatally [12].

Prenatal testing helps to assess the risk of giving birth to an abnormal child. Ultrasound soft markers and maternal serum screen risks are indicative of prenatal testing. Postnatal testing is done if there is any indication for anomalies such as microcephaly, abnormal newborn screen, hypotonia, intellectual disability, hearing loss etc. Tests involved include ultrasound, karyotyping, maternal serum screening, cfDNA, FISH, chorionic villus sampling and amniocentesis, chromosomal microarray analysis, MLPA, whole genome sequencing and FISH.

The sonographic examination is usually done to women at 18 to 20 weeks of pregnancy period, to examine the fetus to test for the presence/absence of soft markers, for fetal aneuploidy, cardiac defects or neural tube defects. These ultrasound markers are less sensitive for T_{21}, whereas more sensitive for T_{18} and T_{13} because of their major structural abnormalities [13]. Structural anomaly detected in ultrasound screening due to inheritance or parental choice would lead to prenatal fetal karyotyping [14].

Maternal serum screening (MSS) involves measurement of levels of biomarkers such as pregnancy associated plasma protein-A (PAPP-A), β-human chorionic gonadotropin (β-hCG) in 11 to 14 weeks of gestation and β-hCG, α-fetoprotein, unconjugated estriol, inhibin-A is offered at 15 to 20 weeks of gestation. Depending on the results and age as well as minor variables like BMI and singleton or twin pregnancy, the patient risk of carrying aneuploid fetus is identified [15].

Karyotyping is a technique done to detect numerical and structural chromosome abnormalities like monosomy, trisomy, translocation using GTG banding chromosomal analysis [14]. It is also used to evaluate infertility, history of miscarriages and mosaicism [12]. Its limitation is one where chromosomal abnormalities less than 5Mb cannot

be detected [16].

Fluorescent *in situ* hybridization (FISH) is used as an efficient method in molecular cytogenetics. It is used for detection of low level mosaicism and complex rearrangements in chromosomes. Interphase FISH with locus specific probes helps in prenatal diagnosis by identifying structural and/or numerical abnormalities [12, 17].

Prenatal screening by non-invasive method is called as cell-free DNA (cfDNA) screening which utilizes maternal blood sample to isolate cell free fetal nucleic acids for analyzing the chromosomal abnormality of the fetus. It is a screening test recommended to women with advanced maternal age. This test helps in detecting sex chromosomal abnormalities, T-21, T-18, T-13 and decrease false positive results [13,15].

CVS gives information on fetal genetic and chromosome status, which is done between 10-12 weeks of gestation (i.e.), it helps early diagnosis and directs medical termination of pregnancy in situations that warrant its suggestion. Fetal loss rate is about 0.2% due to sampling [13].Amniocentesis is done after 14-16 week of gestation. It has been offered to pregnant women greater than age of 35 because their risk to give birth to an infant with aneuploidy/abnormality. Fetal loss rate is about 0.1 to 0.2%, with experienced physicians [13].

Chromosomal microarray analysis uses either an oligoarray or single nucleotide polymorphism as a probe for testing. It helps in detecting copy number variants, deletions and micro-duplication. The limitation of this test is that it cannot detect mosaicism, single gene defects or structural rearrangements. About 98% of genome can be covered by using whole genome sequencing, which includes regions outside the exome. It helps to find structural changes, duplications, copy number variants and deletions [12]. Multiplex ligation dependent probe amplification is a polymerase chain reaction which helps to detect micro-duplication and micro-deletions [12]. It is also used in prenatal diagnosis to identify abnormalities in chromosomes 18, 13, 21, X and Y which are accurate in results [18].

Risk Assessment Based on Inheritance Pattern

It plays an important role in understanding the knowledge about Mendelian inheritance [19].

Consanguinity

Mating between two close relatives including cousins is very common in Asian population and most common in Indian subcontinent. Consanguinity influences the high risk of transmitting the genetic disorders to the offspring [20]. Studies have shown that the inheritance pattern of autosomal recessive disorder has become more prevalent [21].

The three main aspects should be considered in genetic counseling under consanguinity:

a. Know the exact relationship between two individuals.
b. Know the risk of inheritance.
c. Know about the defective gene, which might get inherited from both the individuals to the offspring [20].

Previous Child & Genetic Disorder

There are some disorders which pass from one generation to another generation. If the first child is affected with the genetic disorder, the risk of the second child is increased. The inheritance pattern may either autosomal or X-Linked. Autosomal dominant mode of inheritance has 50% chance of inheriting the trait to the next generation of every child [22]. Calculation risk for autosomal dominant disorder will be straightforward, if a clear family is characterized with a complete and reliable means of diagnosis. Factors which influence autosomal dominant disorder is age-dependent penetrance, anticipation, reduced penetrance will influence the final risk significantly.

Autosomal recessive mode of inheritance has 50% risk factor. The affected individual's parents who are heterozygous contain one defective allele and one normal. Sex linked inheritance are of classified as, X-linked dominant X-Linked recessive and Y linked. X-Linked dominant will affect the male child if mother is heterozygous carrier and father is normal. All female children will be affected if mother is homozygous and father is hemizygous. All the male children will be affected and female children will be carrier if mother is affected homozygous and father is normal [22]. Mode of Y-Linked inheritance is, the whole generation males have the chance of getting the inherited gene from father.

Family History

The major task in genetic counseling is collecting information about the client's family [20]. It is

important to collect the detailed history about the family's medical record. The complete recording of a pedigree about the proband either affected or not affected with genetic disorder should be collected [22]. Family history should be recorded meticulously, with proper location of stillbirths and miscarriages [22]. Based on the family history, the counselor can easily identify the mode of inheritance. Family pedigree is the backbone of clinical genetics. It is a useful tool for a counselor to make the decision, determine the risk and also to educate the client with proper education in genetic aspects. It helps in revealing the unselected population genetic risk [23].

Basic Risk Estimation

All the risk estimations are not of same type. They differ based on the greater or lower reliability.

Empirical Risk: It is the observed data which will be collected in unbiased manner. Unfortunately, it is becoming more complex due to the change in the specific gene or identification which results in change in the diseased frequency.

Mendelian Risk: Estimation of this risk will happen only if a clear basis of a particular inheritance, i.e., Single gene inheritance is being recognized [20].

Risk Assessment Based on Mutation and Migration

There are several types of cancers that are mostly associated with many hereditary genes due to mutation. The mutation is most commonly seen in the European and US countries. Breast cancer, prostate cancer and ovarian cancer are diagnosed with a strong family history [24]. Genetic disorders also occur due to migration which happens when the gene flow or genetic variation differs between two different populations [25].

An overview to the steps involved in genetic counseling is given in **Figure 1.**

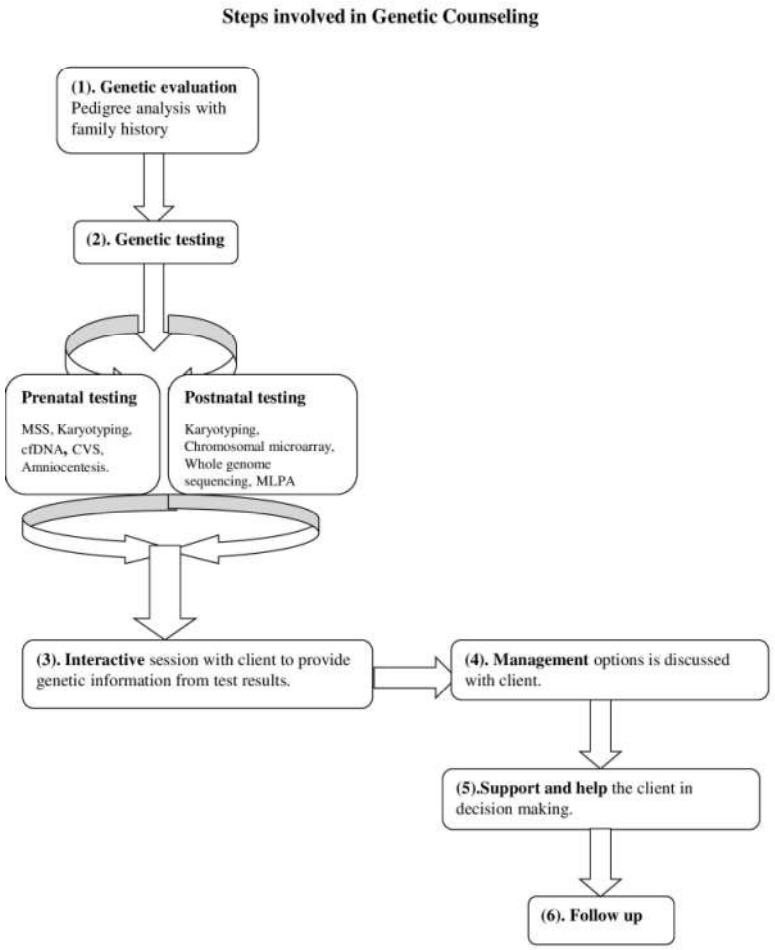

Fig. 1:

ICMR Guidelines in India

ICMR is an apex body which works under Department of Health Research, Government of India. It has formulated and promoted biomedical research with various guidelines. The aim of the guidelines is to have simplified and easily understandable rules. The principles of ICMR includes social responsibility and environmental protection which protect cultural harmony and helps to conduct biomedical and health research programmes. The guidelines that should be followed during genetic counseling include:

- Test results should be disclosed by well qualified professional who has good communication of genetic terminologies.
- When disclosing negative results, it may harm or risk the client, psychologically more like depression, emotional instability, and can also disrupt the family relationship. Thus, counselor should provide an appropriate option for his client to come up with a proper decision.
- The results about the clients should not be revealed by the counselors even to their own relatives without client's permission. Any information regarding the client should not be disclosed. Maintaining proper confidentiality is very important.
- Proper care and precaution should be taken while counseling both spouses, so that families will not be disrupted, and also minimize risk of psychological harm.
- Samples, patient record and data should be maintained properly with informed consent from the clients [26].

Discussion

Genetic counseling is the process of communication between counselor and patient/ client. This process is being practiced worldwide. Counseling should be about the genetic aspects of inherited disease, risk assessment based on inheritance, different kinds of genetic diagnostic tools and techniques. This mini review highlights on the guidelines in genetic counseling including goals, principles, steps and tools practiced. The steps involved in genetic counseling which is briefly explained in flow-chart. A brief note on ICMR guidelines for genetic counseling has also been added.

Summary

Genetic Counseling is the important technique that is being practiced worldwide. It includes the genetic aspects of inherited disease, risk assessment and different kinds of genetics diagnostic techniques. This review emphasizes on the importance of genetic counseling and its practice in Indian perspective. The awareness to genetic counseling has to be provided by medical professionals to help diagnose, care and manage genetic conditions and help parents towards better emotional stability and strength.

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