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Knowledge & Practice of Genetic Counseling in Developmental Disorders

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Genetic Counseling (GC):

The term "genetic counseling" was first coined in the USA in 1947 by Prof. Sheldon Reed & later he elaborated his views in his book- *Counseling in Medical Genetics*- in 1956[1]. However, the era of 'Genetic Counseling' as a separate profession began almost 4 decades later when a book on "Practical Genetic Counseling" was written by Peter Harper in 1981 and soon spread across the globe. The definition of genetic counseling (GC) has not much changed since then and is defined as "a communication process which deals with the special health service that provides information& support to the people who have or may be at risk of genetic disorders in a family". [2,3,4]

One of the primary goals of genetic counseling is to accurately diagnose the genetic condition by advising the patients on appropriate genetic investigations based on available genetic technology & approved methods. Secondly, to prevent the happening of genetic disorders or birth defects again in that family by explaining the means & ways of preventing the specific genetic disorder [5].Considering the burden of genetic disorders in India and often association with developmental disorders (DD), the significance of genetic counseling in their early detection & prevention cannot be ruled out[6]. The primary goal of genetic counseling in any developmentally delayed child is to accurately diagnose the genetic cause after dismissing the non-genetic factors such as postnatal infection, trauma, or any other environmental factors responsible for mental or motor delay.

Genetic Causes of Developmental Disorders:

Thus, the etiology of various developmental disorders, including **intellectual disability** (ID) and **autism spectrum disorders** (ASD) is heterogeneous. It could be genetic, non-genetic, or both and it is still unknown in about 40-50 % of cases. The various genetic causes such as chromosomal abnormalities (both numerical &structural), single gene or Mendelian disorders, metabolic disorders, mitochondrial disorders, repeat disorders, and imprinting disorders are recently well described in the literature as genetic causes[6]. The experienced clinician often arrives at the suspicion of a genetic factor underneath the developmental disorder and in consultation with a geneticist team member makes further recommendationsfor essential genetic or metabolic investigations. Accordingly, karyotype (basic chromosomal genetic test),or metabolic screening (if IEM is suspected) or high-resolution

cytogenetic microarray (if microdeletion or duplication syndromes are suspected or even in unknown ID), or Whole Exome or Whole Genome sequencing (in specific medical conditions like dysmorphism, unclassified congenital birth defects, epilepsy, or unclear and unknown clinical diagnosis)are recommended in a developmental disorder. The radiological (Brain MRI, EEG, NCV, etc.) and ultrasonography investigations are always used to support the genetic diagnosis. For example, a brain MRI in Glutaric aciduria type1 or in Maple Syrup Urine Disorder (MSUD) is very informative as an additional confirmation for the genetic diagnosis.

Genetic syndromes associated with developmental delay are easily diagnosed in a few cases due to well-characterized dysmorphic features, congenital birth defects, and phenotypically correlated biochemical, metabolic& chromosomal testing. The genomic studies confirm further the inheritance or *de novo*nature of transmission. A few chromosomal and ID syndromes are common in genetic practice and can be easily identified such as Down syndrome, Fragile-X syndrome, Di-George syndrome, or some neurogenetic condition such as Tuberous sclerosis. However, the referring clinician is not expected to be equipped with genetic knowledge to suspect or identify rare genetic syndromes. Hence, the help of a medical geneticist or trained genetic counselor at this juncture is very crucial. Genetic counseling offers advice and explains to parents/couples about the nature of genetic conditions& future pregnancy planning to prevent the recurrence risk.

Several genetic conditions cause global developmental delay (GDD) - both mental & motor- in a child. Developmental disabilities in neonates & children can be caused by a number of variables including genetic factors, infections during pregnancy, prematurity, birth complications, and the mother or child's exposure to environmental chemicals as well as the mother's health & lifestyle e.g. smoking & alcohol intake[7,8].It is important to differentiate between genetic & non-genetic factors causing the developmental delay.

The various genetic disorders involve congenital birth defects, inborn errors of metabolism (IEM), neurodegenerative and behavior disorders which often manifest various overlapping signs & symptoms. Intellectual disability, GDD, Autism Spectrum Disorders(ASD), and Learning disabilities fall in this category of developmental disorders. Varying proportions of ID cases (ranging from 17% to 50%) are attributed to genetic causes[6] with approximately 40% of the excess of boys, indicating X-linked genetic disorders. The majority (50- 60%) of ID cases will manifest comorbidities, like seizures, behavioural and psychiatric problems. ASD has recently emerged as a neurodevelopmental heterogenous group having increased incidence (1in 100 to 1 in 64 as per US census) and with varied genetic factors, including lifestyle or prenatal events or inheritance. The hearing & vision impairment can also be due to genetic factors leading to further mental delay, if not detected early. The ambiguous genitalia is another diagnostic sign of clinical importance.

To arrive at the precise genetic diagnosis for appropriate & easy genetic counseling, the expert genetic counselor takes the detailed birth & family history with documentation of **pedigree charting of 3 generations** to arrive at the inheritance pattern &understand the genetic factor[9]. For example-

❖ History like advanced maternal age, recurrent

pregnancy loss/stillbirths, increased carrier risk due to ethnic background, family history of birth defects or mental retardation& abnormal prenatal ultrasound findings.

- ❖ Children born with facial dysmorphism, mental retardation, congenital anomalies and mental/ motor deficiency and / global developmental delays will require certain genetic testing for diagnosis.
- ❖ In case of any severe mental/motor delay, spasticity, neuro-degeneration or neuro-regression and muscular weakness of primary muscles neurological and genetic evaluation will be necessary with additional supportive radiological or biochemical investigations.

In the case of a developmental disorder, the genetic counselor observesthe principles & practice of genetic counseling& works on the following main aspects [10]

1. Diagnostic and clinical aspects of a developmental disorder
2. Documentation of family and pedigree information of the affected patient
3. Recognition of inheritance patterns & risk estimation of the identified genetic condition
4. Communication and empathytowards the parents/affected family
5. Information on available options & further measures in the patient
6. Support in decision-making/decisions made by the affected family

Recommendation of Genetic Investigations after Genetic Counseling:

The judicial use of only relevant genetic tests requires special genetic expertise who decides the tests after thorough clinical & familial genetic evaluation with inheritance pattern, if any. The experienced medical geneticist / genetic counselor plays a pivotal role here in explaining the nature of the genetic disorder, relevant step-wise diagnostic tests, available treatment/ management& scope of prevention[11]. The cost-effectiveness while advising the expensive genetic tests is also looked after during GC.

The explanation of chromosomal reports in the case of Down syndrome with Trisomy 21 differs from that in balanced translocation of Trisomy 21 as the recurrence risk differs in both scenarios. Similarly, explaining the future risk in autosomal recessive conditions (viz.majority of IEMs) as 25% & in autosomal dominant conditions (viz. Tuberous sclerosis) as 50% is very important and is the job of experienced geneticists to arrive at the proper conclusion and convince the parents for mode of familial inheritance. The baseline risk & empirical risk based on the observed data in the population for Mendelian, Non-Mendelian, or chromosomal disorders causing the motor or mental deficits are often used to convince the parents.

Additionally, genetic counseling takes care of confidentiality, privacy, beneficence, justice, informed consent& ethical issues arising out of carrier screening, diagnostic & prenatal genomic testing[12,13].In India, we follow ICMR Ethics guidelines[14]. The communication skills of the genetic counselor play a significant role here unlike the clinician, who probably cannot devote much time from their busy routines. The genetic counselors are trained to -1) educate parents,2) genetic testing procedures,3) develop communication skills, 4) how to provide socio-psychological support& 5) consideration of ethical, social & legal issues associated with genetic counseling[15,16].

No doubt the changing digital world such as smartphones, artificial intelligence, automation

& digital communication will certainly play a significant role in GC practice in India, especially in communicating with the rural & tribal population.

Role of A Genetic Counselor: The genetic counselor is always a team member of patient care by providing genetic communication services. Genetic counselors and genetic counseling also form a strong bridge between physicians and patients while providing all genetic-related information to both the patient and the consulting physician.

Since 1970, the special genetic training in clinical, laboratory & counseling aspects of GC to medical & non-medical graduates & postgraduates emerged, creating the 'Genetic Counselor' as a separate profession. The counselor is trained in medical genetics, diagnostics & clinical aspects of genetic conditions, documentation of family & pedigree information, recognition of inheritance patterns & risk estimation, communication & empathy towards affected family, information on available options & further measures, and finally support in decision-making/ decisions made [10]. Several countries started appointing trained genetic counselors in hospitals & clinics realizing the acute need for genetic counselors.

India has witnessed the entry of genetic counselors as a separate entity only in this decade and mostly it is confined to developmental &behavioral pediatrics and reproductive genetics. Because, the last few decades have witnessed a transitional period of public health efforts shifting from infectious to rare & common genetic disorders through rare disease policy, treatment funds for the management of affected patients, prevention of birth defects in children programs, etc.

Thus, the genetic counselor advises the patients on appropriate genetic investigations based on the available genetic technology & approved methods. Secondly, to prevent the happening of a genetic disorder/ birth defect again in that family by explaining the ways & means of preventing the specific genetic disorder by pretest & post-test GC during prenatal diagnosis. It is thus very important that a genetic counselor dealing with developmental disorders must have updated genetic knowledge& experience to accurately & reliably implement it for the patient's benefit[17].

The care, sympathy, understanding & insight into the emotional aspects of the parents of a developmentally delayed child are given the highest priority. The ability to judge whether parents understood a scientific explanation & their reactions is a significant part of this GC communication.The counselor also has the knowledge about the ancillary needs of the patients. The burden of the disease may vary from clinical \ social \ and financial toemotional factors and differs from individual to individual. Hence, the GC is always aimed to promote informed choices & adaptation to cope with a genetic condition.

Dilemmas during Genetic Counseling:At times genetic counselors may face some real dilemmas when problems like previous abortions, abnormal births, and occasional false paternity are learned. The principal obstacles to effective genetic counseling are emotional conflicts and a lack of knowledge of genetics and biology. Occasionally, disputes arise about the significance of laboratory findings, especially about the possibility of maternal cell contamination in a prenatal sample or genuine doubt of chromosomal abnormality present in the parents or revealing the findings and interpretations between professionals and parents. All these need to be tackled by the counselor with the highest efficiency & confidence. Because the parents of a developmentally delayed child are

soon going to approach in future pregnancy for prenatal genetic counselingfor the next healthy baby or relatives at risk may contact for GC [18].

The genetic counselor, hence follows systematic protocol from starting the session till ending the session. The experienced and mature genetic counselor tackles every issue with remarkable calmness & patience. It must be remembered here that the counselor's role is to support, promote& help in taking decisions by keeping professional standards of respecting goals, beliefs& cultural values[19,10].

Impact of Genomic & Digital Technology in GC Practice in India-

In the era of genomic technology, the interpretation of Microarray or Next Generation Sequencing (NGS) reporting, managing incidental findings to patients is still a complex phenomenon; not yet fully understood and universalized with consensus. The guidelines of the American of College of Medical Genetics are followed for developmental disorders as well but it may not always hold true for our genetically varied & ethnically different population. This complex genomic understanding is not expected by the referring pediatricians or neonatologists who must in coordination with a genetic counselor decide the necessary genetic investigations & further genetic counseling to answer all the queries of the patient[20].

Advances in genetic science and biotechnology have also led to the discovery of new genes for many developmental disorders and updating knowledge about it is very important.As a result, the knowledge base for genetic counseling has become important in assisting patients with accessing timely screening, adopting healthy behaviours, and making decisions about obtaining genetic testing. The new genetic technologies help in the diagnosis & further confirmation of a raredisorder. It then becomes practical to calculate the recurrence risk in the affected family[21]. Internationally, genetic testing is shifting toward gene panels and genomic testing, including cytogenetic microarray, whole exome, and whole genome sequencing to improve diagnostic yield and cost-effectiveness using different algorithms[22,23]. The parental genetic testing in a developmental disorder is essential to predict the *de novo*or inherited mutation while calculating the future recurrence risk in the parents using these advanced technologies.

Digital tools have been part of medical genetics practice for decades, such as internet or CD-ROM-based tools like Online Mendelian Inheritance in Man and Pictures of Standard Syndromes and Undiagnosed Malformations in the 1980s.Technology can help in at-risk patient identification, assist in generating a differential diagnosis, improve efficiency in medical history collection or pedigree charting and risk assessment, provide educational support for patients, and streamline follow-up.Thus, genomics & enormous data generated coupled with bioinformatics & digital technology can play a vital role for GC in developmental disorders in India,considering about 27 million births per year.

Working as a medical geneticist& counselor for more than 3 decades, the author remembers the efforts to convince initially a karyotype test in Down syndrome child -the most common chromosomal abnormality causing mental deficiency- to pediatricians& their reluctance about advising genetic tests since there is no treatment for cure. Albeit the scenario has now changed. But there is still much to be done and genetic counseling professionals can greatly contribute to awareness & education of genetic

science not only among pediatric professionals but also to the public at largeconsidering the community genetic approach[6].

Conclusion- Geneticcounselingin developmental disorders is both an art andscience involving not only the use of technical genetic knowledge and precisemedical diagnosis but also the accurate dissemination of genetic information in atactful, empathetic manner with the help of accurate tests.In case of a developmental disorder with or without behaviour problems, GC is done keeping in mind, the objectives&principles to be used, the process & steps involved, various types of counselees encountered, the knowledge about the genetic condition, genetic evaluation using different diagnostic tests, recurrence of risk estimate, prevention modalities as well as the psycho-emotional and ethical issues. In the end, it is ensured that parents /patients/family are thoroughly satisfied and must be able to take a decision instead of placing them in a state of dilemma. In India, it is a budding specialtyto do GC for developmentally delayed children and their families.

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