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Risk Assessment and Psychological Implications of Genetic Counselling

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ABSTRACT Genetic diseases and diagnostics have now become a part of mainstream medicine. This has led to the augmentation of genetic counselling into routine medical practice as and when the need arises. The elements of genetic counselling include examination of family history, deconstructing the disease and its manifestation, risk assessment and understanding the available management options. In this review paper, the authors have extensively examined the factors involved in the risk assessment such as Mendelian inheritance, age, consanguinity and other complexities such as *denovo* mutations, penetrance, germ line mosaicism, variable expression, polygenic inheritance, multifactorial inheritance, uniparental disomy and genomic imprinting. The technological advancements that have eased the process of risk calculation have been explored. Genetic counselling often acts as a harbinger of bad news, albeit unintentionally. This leads to undue pressure on the consultant, leaving psychological implications. Hence the psychological implications of genetic counselling have been detailed.

INTRODUCTION

The field of medicine has been augmenting many emerging areas of science to bolster diagnosis, prognosis and management of diseases. Medical genetics is one such branch that has made its way into modern medicine. The many advances in genetics as a field of study have now enabled its application in health care. The scope of medical genetics expands to the detection and management of genetic diseases. Genetic diseases can classically be divided into three categories: diseases caused by single gene mutations, chromosomal abnormalities such as aneuploidy, translocations, etc. and conditions caused by a combination of genetic and environmental factors (Nussbaum 2015).

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With the advent of incorporating genetics into medicine, comes the need to collect relevant genetic data from patient, interpretation of the diagnostic tests and its communication in lay man terms. This forms an important component of medical genetics- genetic counselling.

Thus, genetic counselling effectively comprises of data collection, comprehending the diagnosis, communicating the diagnosis and various options available for the management of the disease, in addition to calculating the probability of being affected by the disease with respect to family history and inheritance. Hence by definition, it can be stated that genetic counselling aids to "understand and adapt to the medical, psychological and familial implications of genetic contributions to disease" (Resta et al. 2006).

Genetic counselling caters to (a) individuals with a known familial history of specific inherited diseases and the risk it poses to their progeny (b) parents with an unborn foetus prenatally diagnosed to have genetic diseases (c) families with affected children looking for effective management of the disorder and assessing the risk of future children that may be born with the same

disorder (Nussbaum 2015; Turnpenny and Ellard 2017). With this background, the objective of this review is to provide an overview to the elements of genetic counselling with focus on risk assessment and psychological aspects of genetic counselling.

OBSERVATIONS AND DISCUSSION

Elements of Genetic Counselling

Genetic counselling sessions aim to sensitize the counselee about the particular genetic disorder and its implications. The following can be thought to be important elements (Kelly 1980) that constitute genetic counselling:

(a) Understanding the Disease

The counselee may or may not have had prior knowledge of the disease and its manifestations. In that case it holds immense importance to lay out the details of the disease to the counselee and family of the proband as that understanding is critical to the further course of the counselling process.

(b) Family History

Family history plays a key role in understanding the inheritance pattern of the disease. Thus the counselee and counsellor often strive to collect medical history of the family which results in tracing the proband and establishing carrier statuses in the family. A well-established pedigree comes a long way in providing meaningful genetic counselling to the patient (Turnpenny and Ellard 2017).

(c) Risk Assessment

Risk assessment is often the reason for referral to genetic counselling for patients. This is especially true in case of would be parents whose foetus has been diagnosed with a genetic disease. The inheritance pattern, carrier status, family history and a host of other factors help to look at the probability of the child being affected with the disease. This forms the essence of risk assessment. This is also applicable for couples in the reproductive age who may be carriers and hence under the risk of passing on the disease to the progeny. Parents with an already affected child may be benefitted through risk assessment as it predicts the probability of their future children being affected with the same disease.

(d) Understanding Available Options

Armoured with the knowledge of the disease and the percentage risk of it being passed onto the progeny, the parents face the process of deciding the further course of action. The counsellor can aid this process through providing the available options. Recent advances in reproductive medicine has opened a plethora of options such as artificial insemination using donor sperm or *in vitro* fertilization using donor ovum and so on and so forth. The counsellor can enable the counselee to take autonomous informed decisions driving the counselling process to success.

This review focuses on factors contributing to risk assessment and the technological tools that aid in its calculation. After the assessment, it is the communication and guidance that directly affects the patients. Hence the discussion of psychological implications of genetic counselling forms an inseparable part of this paper (Fuhrmann and Vogel 1983).

Risk Assessment – Key Component of Genetic Counselling

Calculation of recurrence risk varies for each pattern of genetic disorders and also certain other variables which modify the gene expression. Thus it is imperative for a genetic counsellor to have a complete understanding on these vital aspects of risk associated with genetic disorders and factors regulating their inheritance.

Risk Assessment in Mendelian Disorders

Autosomal Dominant

Autosomal dominance is caused due to mutations on the autosomal chromosomes, resulting in disease manifestation in the individual. In this pattern of inheritance, the mutated gene is

passed on from one generation to another, affecting at least one individual in every family (Jorde et al. 2015), without any carriers for that gene.

Heterozygous condition forms the most probable case for an autosomal dominant disorder and carries a recurrence risk of 50 percent, for each of the progeny (Turnpenny and Ellard 2017). 'Bayesian Analysis' (Ogino and Wilson 2004) can be used to calculate the risk of inheriting the disease after the construction of a pedigree chart.

In addition to this law of dominance, there are other important factors which need to be considered such as penetrance, variable expression and anticipation which complicate the process of risk assessment (Young 2007). Hence on that basis, a disorder following this pattern of inheritance seemingly turns out to be more difficult during risk calculation, details of which are discussed in the subsequent sections.

Autosomal Recessive

This is a typical pattern of inheritance where the disease is manifested only in a homozygous state, that is, the parents of that affected individual are carriers for that particular disease allele. Thus, an unaffected carrier parent (both of them being heterozygous for that condition) has nearly one-fourth probability of giving birth to an affected offspring, while another one fourth will be unaffected. The remaining fifty percent would remain as unaffected heterozygous carriers (Jorde et al. 2015).

Here again recessive disorders pose a challenge, and in some case, could actually result in a dilemma as to whether it is an autosomal or sex linked [X linked] disorder which is followed in a given family pedigree. Though a counsellor could identify and categorize it as either X linked or autosomal recessive, it becomes doubtful when an affected patient has a normal mother, with one or more of his/her brother's being affected (Frota-Pessoa et al. 1968) for which counselling is essential to explain the exact pattern of inheritance which is getting exhibited, and provide the required management options. A clear distinction between these two, could be approached by using Bayesian Analysis, by calculating the joint probabilities, and then compared to derive the posterior or relative probability for each of these events (Young et al. 1968).

X Linked – Recessive

This condition, most probably results in a male being affected, with female generally as heterozygous carriers. If a woman is diagnosed to have a mutated allele on her X Chromosome, and is found to be recessive for that condition; (clinically not affected) she is considered as a carrier, in which case if she marries a normal male, each of her sons will have half of the chances of being affected and each of her daughters will have nearly fifty percent chances as carriers. An affected male when married to a normal female, will have all of his sons unaffected, and his daughters as carriers for that particular trait (Nussbaum 2015).

However certain diseases were found not to follow either X linked dominant or recessive pattern of inheritance completely, due to the differences in penetrance and expressivity amongst both the genders, accounting for several other factors for the disease to get expressed (Dobyns et al. 2004).

In situations, when an affected male appears for genetic counselling with not much of a clear family history, it would be hard enough to confirm whether he has an X-linked recessive or Autosomal Recessive trait. Under such instances, use of linkage analysis program was found to be much easier than Bayesian analysis to calculate the genetic risk for the proband. Based on that a possible pedigree is constructed, with any other relevant data, and then the ratio between these two possibilities is calculated as LOD score, which provides the pattern of inheritance. Use of such developed Software program could make the risk assessment process a simpler one, than the traditional method of Bayesian analysis (Read 1989).

X-Linked Dominant

On the basis of the dominant characteristics, fathers affected with this type of disorder will transmit the mutated allele to all of his daughters in a heterozygous condition, which results in affecting them with the disorder, whereas sons would remain unaffected. Thus, father to son

transmission is strictly not observed. When a heterozygotic female marries a normal male, there are nearly equal chances for 50 percent of her daughters and her sons to be affected. In some situations, certain disorders affect male more than female, due to the concept of X-inactivation (Young 2007; Turnpenny and Ellard 2017).

Based on gender ratio, females were observed to be affected nearly twice as that of males, as they have two copies of X chromosome in dominant conditions (except until it is a disorder with male lethality) (Jorde et al. 2015).

There are two conditions under this category as

X – Linked dominance with Male lethality [severely affected male]

In this pattern of dominance, male remain severely affected (Young 2007). When a heterozygous woman gives birth, the ratio of affected female, unaffected female, unaffected male remains as 1: 1: 1 respectively.

X -linked dominance with male sparing [unaffected male].

Under this sub context, for transmitting male, the probability that his son would be affected is trivial; however, the risk to a girl child is nearly 100 percent. For a woman affected with this type of disorder, there is nearly a 50 percent chance that, her daughters would be manifesting the disease, and that her sons will remain as an unaffected hemizygotes (Young 2007).

Complexities in Risk Assessment

Many variables modify the disease expression. For instance, in case of hemophilia the recurrence risk is easily calculated given prior evidences of the disease in the family. In some scenarios, risk assessment remains as the greatest challenge, because the proband would be the first, in his/her entire genealogy to suffer from a new disorder. In case of an affected progeny from normal parents, through genetic testing, parents will be identified as having mutation in their genes with lack of expression, which when passed onto the offspring has affected them phenotypically (Jorde et al. 2015). Therefore, there are other details which needs to be investigated during the process of counselling, in such complex scenarios, necessitating the importance of the following parameters.

De Novo [New] Mutations

When a diseased proband with no family history of the disease is diagnosed, a possible reason is the inheritance of an allele from the parent's germ cells which got mutated during DNA replication. These are known as new mutations. These new mutations are less common in disorders of autosomal recessive pattern; however, a single gene disorder which follows autosomal dominant characteristics were found appearing at a higher rate (Kosztolányi 2008).

If parents have an affected offspring due to new mutation, the risk estimate for another child would be less, as the child can inherit unaffected allele from parental germ cells. On the contrary, the affected offspring's progeny in the next generation has comparatively a very high possibility of inheriting the mutated allele and the disease is expressed phenotypically (Jorde et al. 2015).

The underlying root cause for the evolution of a new mutant gene is being studied extensively. In this context, a study conducted, came out with an estimation that, father's age is related to the variation in polymorphisms, which results in new mutations in the progeny (at time of conception) (Brown 2002; Kong et al. 2012). The knowledge of new mutation and its trace of origin are essential for a genetic counselor to confirm and assess the further risk of transmission of new mutations (Campbell et al. 2014).

Germline Mosaicism Conditions

In cases where one or more offspring, exhibit a certain pattern of disease manifestation, which did not exist in the previous generations, a probable causative behind it could be germline mosaicism in which at least more than one cell line exists in the affected individual. On that accord, if proband is identified as exhibiting germline mosaicism, then the process of risk estimation for the next generation turns out to be a sophisticated challenge in genetic counseling (Young 2007). Somatic mosaicism is a condition where more than one cell line exists in the so-

matic cells, other than germline cells of the body (Campbell et al. 2014).

In a study, considering the risk estimate in new mutations and mosaicism, it was found that the recurrence risk relies on the type of parental cell line, where the mutation results in the progeny inheriting the transmission When the source of new mutation in the genealogy is unknown, the recurrence risk was calculated by multiplication of the risk associated with each parent by the probable chance that the new mutation was passed onto the progeny, by that particular parent of origin attributing the nature of parental origin of new mutations. In that regard, the parent of origin is considered to be the key factor in determining the risk associated with developing new mutations contributing to mosaicism. (Campbell et al. 2014).

Reduced Penetrance

Understanding the mechanism of being affected with an autosomal dominant or X linked disorder, without it being inherited is complex. This complexity is often countered with generalized counseling than specific counseling due to lack of better understanding (Aylsworth and Kirkman 1979).

Reduced penetrance can be deduced by the counsellor when mutated alleles are present in the proband's parents sans the ability to cause the particular disorder (Fuhrmann and Vogel 1983). These variations may be exhibited amongst different family members due to factors such as the environmental conditions or the involvement of other genes, which can alter the expression of the mutated gene (Kosztolányi 2008).

In cases of reduced penetrance, the recurrence risk rate can be formulated, if the P(penetrance value) can be referred from the literature sources, such as for osteosclerosis disease, penetrance is 0.5 (Young 2007).

In an isolated case of reduced penetrance observed in autosomal dominant disorders, based on Bayesian analysis a derived equation was obtained to assess the recurrence risk for the progeny such as

$$P(1 - P)/ 2(1 – P.f')$$

where P represents the penetrance rate ($0<P<1$) f' represents the relative fitness ($0<f'<1$) of the individual who got affected (Hemery 1986).

Age Dependent Penetrance

This condition corresponds to the expression of the mutated gene at a later stage in life, than at the time of birth. For an autosomal dominant disorder following age dependent penetrance, an individual whose parent is affected with that disorder has nearly fifty percent chances, of inheriting the mutated gene (Nussbaum 2015). Identification of the pattern which the disorder falls into can help assess the risk calculation for the progeny of an affected individual.

Variable Expression

There are conditions in which particularly autosomal dominant disorders show varied patterns of diseased allele expression amongst the family members of same heredity .Neurofibromatosis follows this mode of inheritance. A parent possessing the mutated allele can have minimal symptoms with disease manifestation, whereas a child born to that parent, will be affected with the same disease much severely (Jorde et al. 2015; Turnpenny and Ellard 2017). For such cases, the risk for an offspring, who can inherit the mutated allele and also with the disease getting expressed phenotypically is calculated by taking the product of the pedigree risk with the incidence of complication (Young 2007).

Uniparental Disomy and Genomic Imprinting

Uniparental Disomy(UPD) is a condition where the progeny inherits two copies of homologous chromosome from a single parent, either maternal or paternal. Usually UPD is of less clinical significance, unless it results in the inheritance of two mutated alleles from a single parental chromosome, which can happen in autosomal recessive disorders. Genomic imprinting refers to the silencing of the inherited gene, which the progeny has either inherited from paternal or maternal chromosome (Jorde et al. 2015). In such conditions, the silenced gene, results in affecting the individual, as in the case of Angelman's Syndrome and Prader-Willi Syndrome (Young 2007; Jorde et al. 2015).

When such imprinting disorders prevent the normal functioning of the imprinted gene in the individual, then the recurrence risk will turn out to be 50 percent, if the mutation has been present in that particular parent. It has been observed, in some cases that microdeletions were also found to inhibit the normal functioning of one part of the bipartite imprinting center at 15q11-q13, hence knowledge on these, are required, especially while counselling for Angelman's or Prader-Willi Syndrome affected child, who might not possess these microdeletions, and therefore risk assessment would turn out to be misleading (Young 2007).

Polygenic and Multifactorial Inheritance

Many genes code for a phenotypic character and this is called polygenic inheritance. Any condition or trait that is caused/expressed due to combination of one or more factors is called multifactorial inheritance (Genetic, pattern, environmental factors etc.) (Kelly 1980; Nussbaum 2015).

Acquired disorders like late onset Alzheimer's disease, insulin dependent diabetes mellitus, are due to the result of multifactorial inheritance (Young 2007).

Polygenic Inheritance and Normal Distribution

Human characters exhibit continuous distribution which is placed in the middle of a range that closely resembles the normal curve. Few examples include the height, appearance, intelligence, blood pressure. On plotting a smooth balanced bell-shaped curve, the distribution is based on the mean which is decided by standard deviation.

Correlation(r) is used to estimate the degree of association between 2 parameters. For a polygenic characteristic, r value for first degree relatives is approximately 0.5 (that is, 50% of genes is shared in this relationship). It is true for characters determined by polygenes; a good example is finger ridge count. Correlation is slightly lower than 0.5 in the relationship where some characteristics like height where environmental role was also taken into consideration.

The quantity of the total phenotypical variance is brought out by added genetic variance which is coined as heritability (Fuhrmann and Vogel 1983; Young 2007).

where $y = \bar{y} + h^2 (x - \bar{x})$

$\bar{y}$ = Mean Offspring Height in Population

h^2 = Heritability

x = Mean Height of the Parents

y = Mean Offspring Height

$\bar{x}$ = Mean Parental Height in Population

Age as a Risk Factor

There is a strong correlation between maternal age and the risk of developing fetus with 'Trisomy 21' (Down's syndrome). As non-disjunction is more common in women of advanced age, the risk for trisomy aneuploidy increases as 90 percent of non-disjunctions happens in maternal germ cells (Jorde et al. 2015). In certain observations, advanced paternal age has an influence on affecting the progeny with genetic disorders (Brown and Catherine 2002). Thus, age is of clinical significance, especially during reproductive counseling sessions.

Maternal Age and Gestation Specific Risk

Mother's age contributes much to the risk of the baby getting affected. There is a greater risk of a baby getting affected with Down's syndrome.

A study even states that as age increases, risk of Trisomy 21 is high whereas it gets decreased with gestation. The presence in 12^{th} and 16^{th} week of gestation is 30 percent and 21 percent respectively which is higher than compared to the later stages of the gestation period. Pearson correlation analysis was done to test if there exists any change in ratio of maternal age and gestation period. For further calculation, regression analysis was performed to get a curve which shows the decrease in ratio (with respect to the gestational age) (Snijders et al. 1999).

Paternal Age -Association with Schizophrenia

Advanced age of the father is associated with diverse congenital disorders. The etiology of this association implicates autosomal dominant mutation in the germ cell line. Contemporary mutations that occurs collateral to age might contribute for high risk of Schizophrenia affecting the brain development of the fetus.

Risk of Schizophrenia gets higher as paternal age increases (Polednak 1976; Lian et al. 1986; Savitz et al. 1991; McIntosh et al. 1995; Tolarova et al. 1997; Brown et al. 2002).

Consanguinity

Consanguinity and inbreeding are terms that are commutable to describe com-mixture of couples or two individuals from a common ancestor. The increased recurrence of certain disorders, especially autosomal recessive disorders are more common amongst such people. Very rare disorders, such as Methemoglobinemia (In the case of blue Fugates of Kentucky), a recessive disorder, prevailed in their entire heredity as they kept marrying people amongst their relatives, due to being born with bluish skin. It is also an example of 'Genetic Isolation'. Thus, it was more commonly observed in those people living at the hills of Kentucky, than in the general population of the US.

Consanguineous marriages are common around the globe, especially in the South Middle Eastern countries. The probability of any extreme outcome is not an absolute number but risk that is estimated must be based on (Bennett et al. 2002) background population risk, degree of consanguinity and their family history.

Coefficient of Inbreeding(F) provides a more clearsighted degree value of inbreeding of an individual. F values are higher in offspring of incestuous than that of the first cousin relationship.

Degree and coefficient of in breeding (Snijders et al. 1999):

- First degree: Proportion of genes in common=1/2;F=1/4
- Second degree: Proportion=1/4;F=1/8
- Third degree: Proportion=1/8;F=1/16
- Fourth degree: Proportion=1/16;F=1/32
- Fifth degree: Proportion=1/32;F=1/64

There is a difference in the genetic makeup of each community and in sub communities as well because of the gene flow that is highly limited in long established societies, nearby villages might exhibit varied inherited disease profile, reverting local founder mutation and genetic drift (Bittles 2009; Bittles et al. 2010). Population stratification can be of great importance in assessing consanguineous related mortality and morbidity by comparing with progeny of first cousins and unrelated parents of doubtful validity unless the parents belong to same caste or tribes (Bittles 2008).

A change in marriage pattern will primarily result in reduction of homozygosity along with decrease in delivery of recessive single gene disorders. The less the consanguinity, there is a decline in presence of complex diseases (Bittles et al. 2010).

A study of cousin marriages in Wisconsin from 1843 to 1981 shows a rate of consanguineous marriage is about 1 in 1300 marriages (Lebel 1983). Also studies have shown there is an increased risk in pre-reproductive mortality out of which most are due to congenital defects. Calculation or concentration of absolute risk of offspring's of consanguineous union varies based on socio-demographic aspects. There is a change in counselling for a cousin union and an incestuous union. Medical family history plays a significant role in counselling consanguineous couple which serves as an important tool. It is also important that a proper follow up is maintained.

Technological Aids in Risk Calculation

With the emergence of advanced computer software programmes for risk assessment, the process has become much easier, very importantly in quite complex genetic disorders. Performing amniocentesis for elderly mother can be averted by usage of alter methods such as software analysis; in order to avoid an undesirable occurrence like fetal loss. If there is 60 percent or above risk for trisomy 21 condition (detected by maternal serum screening); then the software is used to provide us the easy way of confirmation that the foetus is actually suffering from numerical aberration. The probability of the software to anticipate false results can be ignored by comparing more than 2 software packages. To gauge the risk associated with Down's syndrome the following packages are in use: prenatal interpretive software, T21, DIANASoft, Prisca, Prenet Screen and Multicalc (Muller et al. 1999).

The software calculates the risk considering all the perspective of the couple(maternal age, gestational age, family pedigree) ; accuracy of results in all the 6 software can be achieved by

computing laboratory results into the software package in order to avoid variance in the result. Input factors that are required in software are weight, lifestyle, usage of markers, other health related problems such as gestational age. A few notable softwares presently in use are:

a) Alpha Antenatal Software

Alpha is software used for screening common birth defects like trisomy of chromosome 13/18/21 and neural tube defects. It is based on published scientific data and methodology. Alpha uses parameters like gestational age, serum markers, ultrasound markers, and other details to estimate the risk. It uses upto 12 screening markers which can include serum and ultra sound markers from 1st trimester as well as serum markers from 2nd trimester.

Alpha uses a complete different and unique approach for monitoring and improving the screening program like, with the software one can:

- Identify and correct any drift in normal median value of the screening marker.
- Obtain estimate of the expected screening performance using the age distribution of a population.

A special feature named as 'Auto monitor' has been included in the newest version of Alpha package, that is, Alpha 8. This auto monitor feature automatically screens through the information about the performance of any screening program and provides details and issues which needs further investigation. Other than this ALPHA package has features like median analysis, tabulation of serum markers with gestational age, regression of tabulated data to determine normal median equation and weight adjustment equation.

Alpha is in close agreement with the observed risk of various trisomy. Alpha is also licensed to interpret results from integrated and sequential screening.

b) PENCLAC Software

A computer program named PENCLAC is used for calculating the penetrance rate of any autosomal dominant disorder; this is achieved by the help of information like family lineage obtained from pedigree. This program is available in forms of both web based as well as executable one. Web based version has an extra feature and can calculate heterozygosity probabilities and assessment of offspring risks for all individuals in the pedigrees. The web based version was created using Active Server Pages (ASP), through the languages VBScript and Jscript. The executable one was created using Microsoft Visual Basic 6.0 (Horimoto et al. 2010).

c) Web Based Kiosk Software

It is extensively placed in most of the specialized medical centres for cancer. This software can be accessed by the patient for the questionnaires only upon the approval from the genetic staff; if not the application will be terminated by it thereby denying the access to the patient. These types of software mimic the regular paper questionnaires. If it has been approved then user should provide their name along with email, in order to obtain the risk assessment letter associated with cancer in relevance to their family history (Westman et al. 2000).

Psychological Aspects of Genetic Counselling

In the ethos of genetic counselling, communicating the assessed risk and available options of management holds as much value if not more than the diagnosis and assessment itself. It is this step of the counselling process that adds meaning to the entire exercise, for the crux of genetic counselling lies in the counselee understanding the physiological condition and taking informed decisions.

There are two schools of thought regarding the psychological aspects of genetic counselling. One side perceives that educating the patient is the primary goal of genetic counselling. Hence it is called as teaching model. The patients are referred for counselling so as to gain complete medical information and the path ahead. It is only seen as a platform to clear misconceptions and provide correct guidance. In this model of counselling, the personal issues or personality type of the patient and care giver are not taken into consideration instead the en-

tire information imparted is based on the particular genetic disease and how it implies to that individual's case (Hsia 1979). Here the patient is expected to act rational while the counsellor acts professional, impartial and non-coercive with no place for emotions (Kessler 1996).

In the counselling model, the mental state of the patient is taken into consideration while holding all the principles and goals of genetic counselling intact. The counselee is actively encouraged to engage with the counsellor and share their trepidation. Although the counsellor carriers out non directive and non-judgemental counselling, it is done with empathy and not with impassiveness (Kessler 1997). The rational behaviour of the patient is not a given in the face of adversity. Fear and anxiety over the situation can trigger unstable emotional response which can hamper the understanding and judgement of the counselee (Kallmann 1955). Background information about the consultand pertaining to socioeconomics, ethnicity, religion and related factors can provide a basis through which the counsellor can understand the counselee's perception and reaction to the given genetic information and in turn the counselling (Berliner and Fay 2007). Hence the time and space required for the patient to gain emotional stability is extended as a sign of support. Meticulous follow up is carried out to make sure the objective of counselling is achieved. A recent review about the role of genetic counsellor emphasizes on the psychological aspect stating that counselling should be empathetic and counselee-centred, enabling them to cope better with the process (Skirton et al. 2015).

The authors of this paper concur that giving forth complete medical information is imperative in genetic counselling taking in view the risk assessment and familial history. However the same must be carried out with an understating of the fragile mental and emotional state while being debilitated. Hence an amalgamation of the teaching and counselling process is the exigency.

CONCLUSION

In this review, the researchers have examined the various elements of genetic counselling with emphasis on the risk assessment aspect of genetic counselling. The various factors affecting risk assessment have been pondered upon. In addition to conventional components such as age, consanguinity and risk in Mendelian inheritance, various newfound complications such as *denovo* mutations, penetrance, variance and their likes have been explored. The use of technology has eased the process of assessment with the development of software programs and databases. As the level of understanding of the genetic data and its implications grows, the need for better communication with the consultant arises. This encompasses the psychological aspects of genetic counselling. With this review, the researchers find an underlying need to better equip the counsellor to offer a wholesome counselling experience with a comprehension of human behaviour.

RECOMMENDATIONS

Recommendations for genetic counseling are projected to offer an overview to the elements of genetic counselling with focus on risk assessment and psychological aspects for hereditary disorders. Confidentiality, autonomy, informed consent, Genetic testing, understanding test results are certain key components. The recommendations do not form absolute course of diagnosis or management and the proband must understand that the genetic counsellor provides only professional advice based on clinical and medical history and test results and such recommendations whatsoever doesn't assure a defined outcome.

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