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Genetic Counselling: A Tool to Resolve Ethical and Social Issues Related to Birth Defects

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ABSTRACT Genetic counselling serves the society with its potential communication tools in clinical diagnosis and therapeutic interventions. India is one of the leading countries in birth defects so far been reported with 64.3 congenital anomalies in every 1000 live births. Environment, genetics and a strong association between both impart significant effects on birth defects. Patients' education about reproductive rights, managing birth defects severity and reducing the prevalence of congenital malformations are at its need. This study reviews how genetic counselling can brace the society in order to achieve maximum healthy live births and eliminate social and ethical constraints related to this. The concept for designing mobile genetic counselling services in India is one of its kind introduced in this study. This could hope for early detection of congenital abnormalities before or at birth and treat the conditions promptly to pledge newborns with a healthy and nourished livelihood.

INTRODUCTION

Genetic counselling is a tool that spreads the knowledge of genetic diseases. It assesses the risks for an individual or families, analyses the medical and family history, identifies the pattern of inheritable diseases and braces the society providing appropriate genetic services. The transition from genetics to genomics, the relevance of molecular evolution fulfils the success of human genome project and supports the advancement of medical genetics. As the curve of genetic disorders is sloping high in a great significance, the urge of genetic counselling is at its field to serve the society at the earliest. In a global scenario, visit to a genetic counsellor has almost become routine, whereas in India a huge effort is still needed to combat the large spectra of genetic diseases. The Indian Council of Medical Research has organized various multi-centric studies that have provided information on genetic causes of mental retardation, genetic counselling and antenatal diagnosis, possibility of introducing genetic services in district hospitals and periconceptional folic acid usage for preventing the recurrence of neural tube defects in India (Verma et al. 2003). In the present scenario, genetic counselling is an essential aspect of molecular diagnostics to deal with clinical diagnosis, laboratory investigation, prognostication and treatment of genetically determined disorders.

The major components of genetic counselling involve pre and post-test counselling, where the genetic counsellor plays a major role in abiding all the four principles of bioethics. Pre-test counselling consists of the ultimate genetic tool, gathering family history that helps in documenting the accurate information about the proband and family and helps in assessing risk for a particular trait in a family, identifying the inheritance pattern, probable disease onset. It further helps in decision making whether a genetic test is needed or recommends medical management to the patients (Uhlmann et al. 2011). From the beginning of the counselling session till the declaration of genetic results, the fundamentals followed are autonomy, beneficence, non-maleficence and justice. Autonomy describes the patient's will and preferences in decision making. It is an extensive section of medical ethics that contains a huge number of literatures (Stiggel-

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bout et al. 2004; Varelius 2006; Entwistle 2010). The principle of beneficence defines the way of doing good to the patients in a clinical set up. This portrays the role of a counsellor in delivering the right information to the proband, the physician's role to disclose the appropriate diagnostics and test results and the patients or the family being filled with exact information about the management of certain clinical conditions. In the terms of third party interference with one's genetic information and results, with all the complexities of the principle, the patient's confidentiality is given priority and the data is being protected to ensure the benefit of the patients (Mawere 2012). Beneficence is well balanced with the ethics of non-maleficence, where the basic is to do no harm. Providing right information, helping a patient in decision making, performing the right evaluation, potential medical treatment are the tools involved in this principle. Patient's justice is widely defined as the right of choice. It distributes the medical information among the patients, prioritises the right of a proband to know about his clinical condition, the right of a family to understand their risk and utility of medical resources in managing the condition (Chagani 2014). All these principles are carefully taken care in the context of genetic counselling as it involves lot of dilemmas, conflicts, social interference and legal concerns. Post-test genetic counselling narrates the test results, discloses the possible risk in the proband or for a family, guides the proband for decision making in set ups like reproductive or adult counselling, defines the possible inheritance of any genetic disorder and sometimes break the bad news balancing sympathy and empathy at the same time (Haecke and Montgolfier 2015). In India, genetic counselling is evolving greatly and its usefulness is being accepted by the physicians overall. Incorporation of genetic counselling in multidisciplinary hospitals is a value added in their speciality services. In R&D companies, the research unit leading molecular diagnostics and translational research is including counselling as a major tool to defect molecular targets rapidly by identifying a disease trait that helps them providing the patient with targeted therapies in the date of personalised medicines. Literatures from India on counselling reflect various aspects of genetic services, its advantages and challenges as well. Among the vast field of clinical set ups, this review focuses on the congenital anomalies that covers genetic counselling in the aspects of reproductive, pre and post-natal counselling, genetic testing in perinatal, neonatal and foetal care as well as paediatric genetic counselling. Recent studies have shown an extensive improvement in the counselling and screening of haemophilia in India. A study by Jadav et al. (2014) have highlighted the ethical issues related to haemophiliacs in India, where patient's autonomy and justice is mentioned as the key principles. The counselling needs for the rare genetic disorders and the importance of raising the awareness of such conditions are summarised in the article. Another study by Muthuswamy (2011) have reflected similar concerns in hemoglobinopathies in India. Although the screening programme have been difficult in the beginning, it became easy as the increase in awareness programme and one to one counselling has been continued in states like West Bengal and Assam (Muthuswamy 2011). Earlier study on genetic counselling of 3500 cases from New Delhi have underlined 12.4 percent of the cases been counselled for recurrent abortions, 12.1 percent for identifiable syndrome, 11.3 percent for chromosomal anomalies and 11 percent for mental disorders. The study reported 28.7 percent of prenatal diagnosis cases, 13.7 percent mental retardation plus multiple congenital anomalies, 11.5 percent cases of thalassemia, hemophilia and leukemia and 8.5 percent of malformations and neural tube defects (Verma et al. 2003).

OBSERVATIONS AND DISCUSSION

Ethical and Social Constraints

The ethical, legal and social aspects of genetic counselling in India reports diverge issues, out of which stigmatization is a common term. The growth of genetic advancements with medical excellence and prognostic values is escalating new techniques in genetic testing and gene manipulations. Although sex determination, in vitro fertilization, assisted reproductive technologies include certain risks and limitations, the success rates of the sophisticated reproductive technologies are compelling them to go for it. The conflicts of donor and/or surrogacy, predictive testing, genetic screening, prenatal testing, foetal tissue transplantation have raised significant ethical concerns. Here the genetic coun-

sellor faces real challenge in counselling the proband considering all the four principles of bioethics (Muthuswamy 2011). Another obstacle for counselling a genetic condition is the risk assessment based on the pattern of inheritance. In case of multifactorial disorders, polygenic inheritance or complex genetic traits, the counsellors may enter into dilemmas regarding risk assessment and inferences.

Confidentiality holds the crucial role in genetic counselling. The counsellors are trained to maintain the patient's privacy. In certain cases, it becomes mandatory for the physician to disclose the results to a proband's family members, whereas the individual does not consent for the same. A role of a counsellor is critical in such cases, when to prefer patient's autonomy, or to follow law of beneficence for the at risk family. If the family is not informed about the probable risk, it could support non-maleficence to them. Such ethical issues are dealt carefully by the counsellor. Sometimes the genetic counsellor may adopt nondirective methods, expressions and gestures to help in the decision making process rather than directly make a decision for an individual or family.

Ethical concerns arise greatly in case of predictive testing. The individual or a family may or may not come with known history of genetic disorders. After genetic testing, new information about faulty alleles may raise concern about disease predisposition. This may in turn affect the whole family, increase anxiety of inheriting or predisposing the genetic condition (Fulda and Lykens 2006). Predictive testing has always been a fear of discrimination. The result, if disclosed to society may appreciate interference of third parties, insurance companies, family affairs and may violate the act of non-discrimination being harmful to the patient. It greatly affects the psychological aspect and may invite uneventful situations. In case the proband is negative of a disease's trait and his or her other relatives are affected, it may provoke guilt feeling in the consultee. Sometimes a person blames himself for undergoing gene testing and putting their family in great psychological stress. Apart from predictive testing in mutation analysis, prenatal testing sometimes generates psychological issues. An example by Muthuswamy (2011) explains the dilemma in the sonography that shows an irregularity of the foetal head where the amniotic fluid is normal for á-fetoprotein. The issue indicates parental psychological distress even if the finding is of small significance. Similarly, males and females with normal phenotypes and XX or XY chromosomal complement may raise such conflicts. It is critical to resolve parental psychological stress just to inform about the condition which may put them in to social stigma and make them feel grief about their life.

Birth Defects Perspective

Another field that utilizes genetic counselling as a potential tool to educate society is the prenatal set up. Extensive study reports have focused on the benefits and limitations of prenatal testing, counselling, ethical and social issues related to this.

Congenital anomalies are the structural or functional malformations identified in infants or neonates that could lead to one or more moderate to severe phenotypes. The conditions may occur during intrauterine life and could be identified prenatally, at birth or even later in life. The prevalence of birth defects increases proportionately with the incline in environmental exposures. This supports the report of 2.76 million deaths during the neonatal period of 2013 due to large spectra of congenital anomalies worldwide (WHO 2015). The global report from March of Dimes, 2006 highlights India with 64.3 birth defects per 1000 live births which accounts around 1,613,502 congenital anomalies every year (March of Dimes 2006; WHO Regional Report 2011). This contributes 9.6 percent to the neonatal mortality, 19.5 percent to perinatal mortality and 9.9 percent stillbirths (Table1).

Table 1: Presentation of birth defects prevalence in India

India	*Rate/1000 live births (%)*	*Source*
Congenital anomalies	64.3	WHO, 2011; MOD 2006
Neonatal mortality	9.6	Samnas et al. 2013
Perinatal mortality	19.5	Samnas et al. 2013
Stillbirths	9.9	Samnas et al. 2013

Source: MOD 2006; WHO 2011; Samnas et al. 2013

Congenital anomalies may result in physical and mental disabilities, short or long term effects and even death depending on the severity

of the malformations. According to the reviews, birth defects commonly reported in India are neural tube defects (NTDs), Down syndrome, metabolic disorders, blood disorders like hemoglobinopathies, thalassemia, congenital heart defects (CV) and duchene muscular dystrophy (Samnas et al. 2013; Sharma 2013). Around 110,000 infants were diagnosed with congenital rubella syndrome, whereas other significant anomalies include Club foot (2.7/1000 live births), cleft lip and palate (1.9/1000 live births), gastrointestinal tract abnormalities and defective diaphragm (Table 2).

Table 2: Representation of common congenital anomalies incidence in India

India	*Rate/1000 live births (%)*	*Source*
NTDs	4.7	WHO, 2011; MOD 2006
Down syndrome	1.6	WHO, 2011; MOD 2006
Pathological Hb	1.2	WHO, 2011; MOD 2006
CV system	7.9	Samnas et al. 2013
Club foot	2.7	Samnas et al. 2013
Cleft lip and palate	1.9	Samnas et al. 2013

Source: MOD 2006; WHO 2011; Samnas et al. 2013

The causes of birth defects include both genetic and environmental counterparts. Genetics have influence on foetal development, where environmental exposures increase the chance in certain folds that triggers genetic alterations leading to change in the phenotype of the new-borns. There are more than 700 birth defects identified till date, among which 30-40 percent has genetic origin, 5-10 percent have environmental influences and around 50 percent cases are unknown due to lack of reporting, limitations in identification of the disease origin and insufficient data for clinical diagnosis (Sachdeva et al. 2014). A community based survey on 12.8 million rural children from Tamil Nadu has reported 1.3 percent of the them born with some kind of visible anomalies, where the causes involve presence of family history (9%), drugs during pregnancy (5%) and mostly consanguineous marriages of about 32 percent (Sridhar 2009). A review by Kar (2014) have portrayed the causes of neonatal mortality in India which states that congenital anomalies account 9 percent of the total statistics, where preterm birth complications cover the major portions having 35 percent of the total incidence. Risk factors for birth defects include advanced maternal age, smoking, alcohol consumption, medical condition and nutritional status of the mother, exposure to teratogens, low birth weight, positive family history, consanguinity, unplanned pregnancies, lack of antenatal care and parental carrier status of certain genetic trait as per classified in Table 3 (Kallen et al. 2000; Sharma et al. 2006; Barness 2010; Shamnas et al. 2013; Sharma et al. 2013). A study by Reefhuis et al. (2015) reported the effect of medications during pregnancy that increases the frequency of certain birth defects. Extensive researches on virus such as Cytomegalovirus and Zika virus causing birth defects were reported recently (Butler 2016; Mysorekar and Diamond 2016).

Table 3: Risk factors for congenital anomalies

Genetic	*Environmental*
Family history	*Teratogenic exposure*
Consanguinity	Smoking
Affected parents	Alcohol consumption
Inheritance of genetic trait	Induced genotoxicity
Presence of mutation	Maternal age
Chromosomal anomalies during fetal development	Occupational exposure

Source: Sridhar 2009; Kallen et al. 2000; Barness 2010; Samnas et al. 2013; Sharma 2013; Sachdeva 2014

Birth defects in India greatly sustain ethical, legal and social issues. Ethical dilemmas, issues related to privacy, patient's autonomy are the common segments of reproductive counselling, birth defects, prenatal and neonatal genetic counselling. Issues related to congenital anomalies substantially involves dilemma in prenatally detected chromosomal errors, or physical deformities, clinical diagnosis at birth, genetic testing after birth or even a recurrent pregnancy loss which elicits social stigma and burdens the patient and family members.

Ethical and Social Issues in Birth Defects

The primary concern begins at data gathering where the proband and family is aware about their medical history noted by the counsellor. This needs confidentiality as the information carries personal and family history, genetic profile, risk for genetic diseases in the family, pres-

ence of lethal mutations, pattern of inherited trait and can be used to identify risk for future generations (Muthuswamy 2011). An individual may not prefer their reproductive choices to be investigated by third parties, or they may hesitate to reveal results of genetic tests from the fear of genetic discrimination and social stigma. Moreover, in case of large scale mutation analysis, as the data may identify the study subjects, it is necessary to maintain the confidentiality of the data (Jenkins et al. 2008). The next step often involves decision making and consent to a genetic testing. This may include several dilemmas as the outcome of the genetic tests might have impact on the family. In such scenario, the counsellor prefers to avoid biases by being non-judgmental and guides the family in decision making about the test. In prenatal cases, it is often related to the risk status of the foetus and leaves the parents with uncertainty of their newborn's genetic profile, where they express anxiety. Moreover, the patients have right to know about the genetic test, its benefits and risks, results and impact on their family at the same time while sharing their medical data with the counsellor. After explaining the details, the test begins with informed and written consent from the patients or their family members. Ethical issues are raised in case of inadequate information about abnormalities of sex chromosomes, results of paternity testing, consequences of predictive testing, and results of mutation analysis not explained at the time of pre-test counselling (Bove et al. 1997). The fear of genetic discrimination comes from the genetic test results which may lead to unemployment, insurance denial, family affairs that in turn affect the life of a patient.

Focusing the prenatal diagnosis and genetic testing, the major issues raised are the risks of the genetic testing and the foetus being tested for. Related issues highlight social interference with pregnancy loss, abortions, giving birth to an abnormal child and gender selection. During prenatal genetic testing such as amniocentesis, chorionic villi sampling and chrodocentesis, there are at least 1 percent of risks for miscarriages associated to the test. As these tests are invasive, genetic counselling helps in decision making, being transparent about the aim of the test and is unable in ruling out the outcome of the chromosome abnormalities for every case and only to reduce the risk for a malformed foetus (Wieacker and Steinhard 2010). In the view of ethical considerations, prenatal testing, sex selection are encouraging the parents to adopt advanced technologies and decide to abort a foetus based on its gender and without any developmental disabilities that underlines the value judgements. Abortion choices are often given in prenatal diagnosis, where the moral values are in conflict and the women often face social discrimination (Kaushal 1999). However, prenatal diagnosis may be useful in cases like metabolic disorders, where the foetus can be treated inside the mother's womb by vitamins and controlling the mother's diet (Smolska 1996). Justification of selective abortions supports the fact that the foetus is aborted because of severe phenotypic complications that would ultimately lead to death or chromosomal abnormalities that needs to terminate the pregnancy and protects the mother's autonomy and right to a healthy birth. The ethical aspect includes the counsellor's duty towards the decision making step where moral values of two individuals are involved, the mother and the foetus (Anderson 2009).

One of the major applications of genetic testing, the new-born screening, also invites ethical and social arguments. Newborn screening not only unveils the genetic status of the child but also puts the family in psychological distress as different diseases do not have the same onset. Also the severity varies among new-borns (Macer 1998). One advantage of new-born screening on foetal or prenatal screening is to early diagnose a defect and treat to extend the lifespan of children which may bear a positive impact on the society, rather a foetal or prenatal screening where the status of the embryo carries dilemma, genetic discrimination, psychological burdens and social affairs.

Genetic Counselling

Genetic counselling incorporates awareness for preventing birth defects. It helps in early diagnosis of the congenital anomalies and manages the conditions to add life to years. Earlier studies have highlighted the role of a physician in overseeing deliveries with congenital anomalies. However, genetic counselling is an effective tool to resolve such critical stages of clinical interventions. The basic tenets of genetic counselling aim to reduce the incidence of ge-

netic disorders, where the society accepts the evolution in genetic studies, eugenics, as to determine the faulty traits at the right time and to treat the condition soon (Andrews et al. 1994). It is considered as an essential tool in reproductive genetics, prenatal, perinatal and postnatal or neonatal clinics as it serves the patients and family members with several diagnosis options to improve their livelihood. Reproductive genetic counselling session often includes preconception counselling where the expert guides the couple in order to achieve a successful pregnancy. In case the consultees have personal or family history of birth defects, recurrent pregnancy loss, still births or any other reproductive issues, the counsellor may assess the risk for the expected pregnancy and provide them with options to attain a successful pregnancy. Here, the counsellors have to guide the patient in decision making being completely non-judgmental. The options may include artificial reproductive technologies, where the benefits and risks of the techniques, its validation is clearly explained to the consultees before obtaining informed and written consent (McGowan et al. 2009). Genetic counsellors are trained in maintaining the confidentiality and privacy of the patient's data. The way of communication helps to build up a belief of the consultand on the counsellor in sharing their medical history and genetic data. Disclosure of genetic result may hamper a child's future employment or insurability and thus the parents favour a healthy way of maintaining privacy and confidentiality in data gathering (Jenkins et al. 2008; Haecke and Montgolfier 2015). Pedigree analysis is the most effective tool of genetic counselling till date after family history taking. The counsellor assesses the risk for a foetus to be affected with certain genetic determinants based on the family history provided. This needs high privacy as the pedigree not only carries the risk for the newborn but it contains the medical and genetic data of the entire family (Uhlmann et al. 2011). When the foetus is in the womb, genetic counsellor helps the parents in identifying its condition. This is recommended when the parents have a personal or family history of similar or different birth defects, carrier for certain traits, history of miscarriages or any other multifactorial diseases running in the family. An example illustrates the advanced maternal age related to higher incidence of birth anomalies in the neonates. Presentation of such risks during the counselling session in a nondirective way makes the parents understand the possible test outcomes. Likewise, the counsellor helps the consultand to be prepared to adopt the situation resulted from a genetic testing (Wieacker and Steinhard 2010). Prenatal testing results may sometime put the counsellor in dilemma in how to disclose it to the consultee. This may be due to the gender of the foetus, false paternity or any pathological findings. Here the role of genetic counselling is to disclose the result to the consultand in a transparent way so that they understand the outcome of the birth and prepare themselves for accepting the fact (Kaushal et al. 1999). In prenatal counselling set up, if assisted reproductive technologies (ART) are suggested to bypass the risk of congenital anomalies, counselling session often demonstrates the pictorial view of understanding, where the guidelines for reproductive testing are sketched in order to achieve pre-implantation genetic diagnosis (PGD). In such scenario, the couple are well aware about the manipulations made to achieve a successful pregnancy. In India, countryside families are still under the darkness of education. Awareness of reproductive health and childbirth is lacking in those parts and thus the incidence of congenital anomalies is inclining. To control such situations, genetic counselling is a best tool to educate the villages about reproductive health, perinatal, neonatal and antenatal care. Patient education is the major initiative taken by every genetic counsellor, where the consultand and the family members receive flawless information about the birth. The pros and cons of in vitro fertilization, overview of prenatal screening, pre-implantation diagnosis and possible test outcomes, risks and benefits are well explained by the genetic counsellor to educate the society toward a healthy birth (McGowan et al. 2009). As India represents a significant percentage of congenital anomalies per year, genetic counselling is a need to raise awareness and educate the society about the environmental teratogens, its effects in reproductive health and child birth. Moreover, consanguineous marriages in India are seemed to be higher compared to the rest of the world. This facilitates the need for genetic counselling to prevent abundant pregnancy loss, congenital anomalies and genetic disorder in the new-borns. Genetic counselling not only guides the society with early diagnosis

and prevention of congenital anomalies, but also serves with the possible management options for newborns or children with birth defects. This in turn saves the affected individuals from social stigma, discriminations or related psychological states. Lifestyle or surgical managements are recommended based on the severity of phenotype. Genetic counselling helps in managing the metabolic syndromes throughout the life and nourishes one's life with healthy therapeutic interventions (Grundy et al. 2005). In order to manage less severe phenotypes of congenital anomalies, genetic counselling guides the consultee for surgical interventions such as in cases of cleft lip and palate (Nahai et al. 2005). Genetic counselling helps in managing the chromosomal disorders leading to congenital birth defects such as Downs, cri du chat, Turners and Klinefelter syndromes (Marder and Dennis 2001; Morgan 2007; Gies et al. 2014).

In order to reduce the ethical and social concerns of birth defects, this study presents a schematic diagram of genetic counselling setup as a potential tool. A novel way of serving the society could be *mobile genetic counselling* services, where the trained counsellor can visit district hospitals and arrange village camps to educate people about reproductive health and healthy childbirth, as well as counsel individuals by home visits wherever needed (Fig. 1).

CONCLUSION

Birth defects are neither always caused by only genetic determinants nor purely environmental. It is a result of the interaction of environment with genetic factors that either introduces DNA adducts in the cells or causes chromosomal damage. The error may be pre-conceptual if purely genetic, or may arise during foetal development due to enormous intra and exogenous stimulants. India has presented an incline in the rate of annual congenital anomalies, where around 1,613, 502 newborns are born with defects every year. To diminish the incidence of birth defects in India, it is urgent to look upon the exogenous constraints. In order to achieve such goal, India needs more practice on genetic

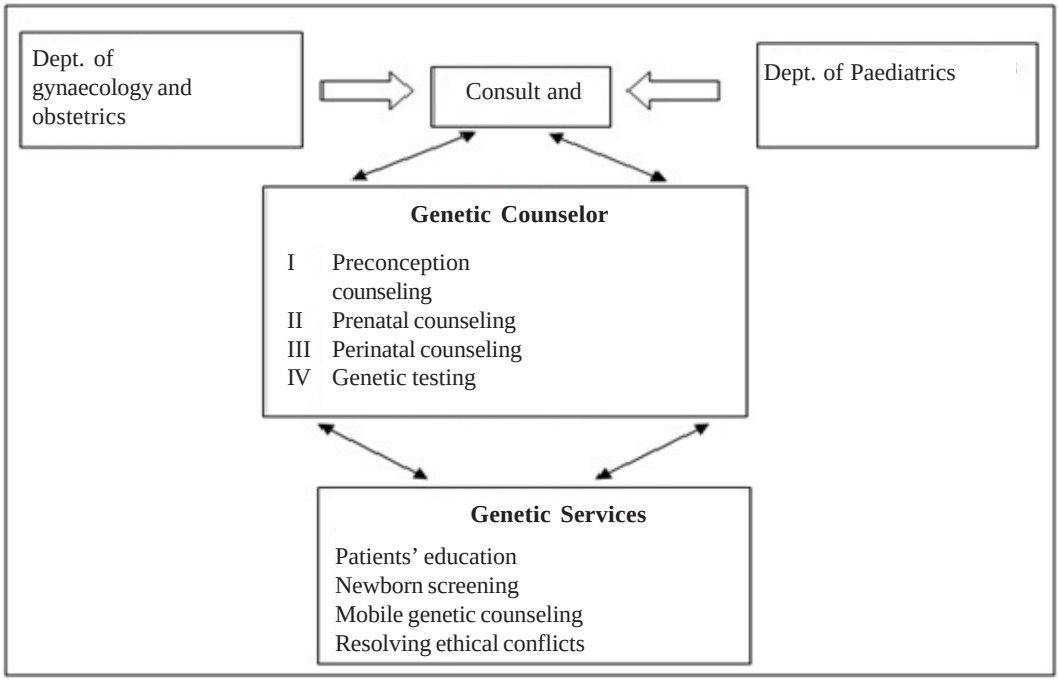

Fig. 1. Schematic representation of a genetic counselling setup in managing birth defects
Source: Authors- Manjima Chatterjee and Radha Saraswathy

counselling to serve the society underneath the shadow of birth defects. Mandatory genetic counselling services for each district may help in reducing the social burden of congenital malformations. The malpractices can be alleviated focusing more on the ethical issues and genetic discriminations. Mobile genetic counselling services can be introduced where the professionals could visit the hospitals or public health centres. The counsellors may even provide one to one counselling at patients' home with the help of medical excellence and advanced genetic diagnostics. This may in turn help India in recovering the rate of birth defects per annum and serve the society with a healthy proportion of childbirths each day. Genetic counselling may likewise prove its effectiveness as a routine tool in the context of birth defects and help the society to be free from ethical and social controversies.

REFERENCES

Anderson RR 2009. Religious traditions and prenatal genetic counseling. *Am J Med Genet Part C Semin Med Genet,* 151C: 52–61.

Andrews LB, Fullarton JE, Holtzman NA, Motulsky AG (Eds.) 1994. *Assessing Genetic Risks: Implications for Health and Social Policy.* Volume 1. Washington DC, United States: National Academies Press.

Bove CM, Fry ST, MacDonald DJ 1997. Presymptomatic and Predisposition Genetic Testing: Ethical and Social Considerations. In: WB Saunders (Ed.): *Seminars in Oncology Nursing*. May 31, 13(2): 135-140.

Butler D 2016. Zika raises profile of more common birth-defect virus. *Nature,* 535(7610): 17.

Chagani SMI 2014. Telling the truth - A tussle between four principles of ethics. *Journal of Clinical Research & Bioethics,* 5(2): 172.

Christianson A, Howson CP, Modell B 2005. March of Dimes: Global report on birth defects, the hidden toll of dying and disabled children. *March of Dimes: Global Report on Birth Defects, the Hidden Toll of Dying and Disabled Children*. USA: March of Dimes.

Entwistle VA, Carter SM, Cribb A, McCaffery K 2010. Supporting patient autonomy: The importance of clinician-patient relationships. *Journal of General Internal Medicine,* 25(7): 741-745.

Fulda KG, Lykens K 2006. Ethical issues in predictive genetic testing: A public health perspective. *Journal of Medical Ethics,* 32(3): 143-147.

Gies I, Unuane D, Velkeniers B, De Schepper J 2014. Transition in endocrinology: Management of Klinefelter syndrome during transition. *European Journal of Endocrinology,* 171(2): R67-R77.

Gilbert-Barness E 2010. Teratogenic causes of malformations. *Annals of Clinical & Laboratory Science,* 40(2): 99-114.

Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH 2005. Diagnosis and management of the metabolic syndrome an American Heart Association/ National Heart, Lung, And Blood Institute scientific statement. *Circulation,* 112(17): 2735-2752.

Jadhav U, Mukherjee K, Lalwani A 2014. Ethical issues in the care of persons living with haemophilia in India. *Indian Journal of Medical Ethics,* 11(4): 223-227

Jenkins MM, Rasmussen SA, Moore CA, Honein MA 2008. Ethical issues raised by incorporation of genetics into the National Birth Defects Prevention Study. In: *American Journal of Medical Genetics Part C: Seminars in Medical Genetics*. USA: Wiley Subscription Services, Inc., A Wiley Company, 148(1): 40-46.

Källén K 2000. Multiple malformations and maternal smoking. *Paediatric and Perinatal Epidemiology,* 14(3): 227-233.

Kar A 2014. Birth defects in India: Magnitude, public health impact and prevention. *Journal of Krishna Institute of Medical Sciences (JKIMSU),* 3(2): 7-16

Kaushal P, Malaviya DR, Roy AK 1999. Ethical aspects in genetic counselling. *Current Science,* 77(10): 1236-1238

Macer DR 1998. Ethics and Prenatal Diagnosis. In: A Milunsky (Ed.) *Genetic Disorders and the Fetus: Diagnosis, Prevention and Treatment*. Baltimore: John Hopkins University Press, pp. 999-1024.

Marder E, Dennis J 2001. Medical management of children with Down's syndrome. *Current Paediatrics,* 11(1): 57-63.

McGowan ML, Burant CJ, Moran R, Farrell R 2009. Patient education and informed consent for preimplantation genetic diagnosis: Health literacy for genetics and assisted reproductive technology. *Genetics in Medicine,* 11(9): 640-645.

Morgan T 2007. Turner syndrome: Diagnosis and management. *Am Fam Physician,* 76(3): 405-410.

Mawere M 1937. Critical reflections on the principle of beneficence in biomedicine. *Pan African Medical Journal,* 11(1): 29

Muthuswamy V 2011. Ethical issues in genetic counselling with special reference to haemoglobinopathies. *The Indian Journal of Medical Research,* 134(4): 547.

Mysorekar IU, Diamond MS, 2016. Modeling Zika virus infection in pregnancy. *New England Journal of Medicine,* 375(5): 481-484.

Nahai FR, Williams JK, Burstein FD, Martin J, Thomas J 2005. The management of Cleft Lip and Palate: Pathways for treatment and longitudinal Assessment. In: *Seminars in Plastic Surgery*, New York: Thieme Medical Publishers, Inc., 19(4): 275-285.

Reefhuis J, Devine O, Friedman JM, Louik C, Honein MA 2015. Specific SSRIs and birth defects: Bayesian analysis to interpret new data in the context of previous reports. *BMJ,* 350: h3190.

Sachdeva S, Nanda S, Bhalla K, Sachdeva R 2014. Gross congenital malformation at birth in a government hospital. *Indian Journal of Public Health,* 58(1): 54.

Shamnas M, Arya PS, Thottumkal VA, Deepak MG 2013. Congenital anomalies: A major public health issue in India. *International Journal of Pharma-*

ceutical Chemical and Biological Sciences, 3(3): 577-585.

Sharma R, Kapoor B, Verma U 2006. Drug utilization pattern during pregnancy in North India. *Indian Journal of Medical Sciences*, 60(7): 277.

Sharma R 2013. Birth defects in India: Hidden truth, need for urgent attention. *Indian Journal of Human Genetics*, 19(2): 125.

Smolska A 2006. *Selective Abortion on the Basis of Prenatal Genetic Diagnosis: Ethical Problems faced by the Doctor*. Master Thesis. Linköping: Centrum för Tillämpad Etik, Campus Linköping, Linköpings Universitet.

Sridhar K 2009. A community-based survey of visible congenital anomalies in rural Tamil Nadu. *Indian Journal of Plastic Surgery*, 42(3): 184.

Stiggelbout AM, Molewijk AC, Otten W, Timmermans DRM, Van Bockel 2004. Ideals of patient autonomy in clinical decision making: A study on the development of a scale to assess patients' and physicians' views. *Journal of Medical Ethics*, 30(3): 268-274.

Uhlmann WR, Schuette JL, Yashar B (Eds.) 2011. *A Guide to Genetic Counseling*. New York: John Wiley & Sons.

Van Haecke DDA, de Montgolfier S 2015. Genetic test results and disclosure to family members: Qualitative interviews of healthcare professionals' perceptions of ethical and professional issues in France. *Journal of Genetic Counseling*, 25: 483–494.

Varelius J 2006. The value of autonomy in medical ethics. *Medicine, Health Care and Philosophy*, 9(3): 377-388.

Verma IC, Saxena R, Lall M, Bijarnia S, Sharma R 2003. Genetic counseling and prenatal diagnosis in India—experience at Sir Ganga Ram Hospital. *The Indian Journal of Pediatrics*, 70(4): 293-297.

Wieacker P, Steinhard J 2010. The prenatal diagnosis of genetic diseases. *Deutsches Aerzteblatt International*, 107(48): 857.

World Health Organization 2016. *Report on Regional Review Meeting: Neonatal-Perinatal Database and Birth Defects Surveillance*. New Delhi: WHO.