



# Pros and Cons of Carrier Screening for Prevention of Genetic Disorders and Other Associated Issues: Review of Current Status

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## ABSTRACT

Genetic abnormalities cause phenotypic and clinical expressions through encoding of new or altered proteins. Such irreparable aberrations are preventable by understanding the nature of alterations and nurturing prenatal and pre-implantation diagnosis. Retrospective investigation of blood-linked relatives not only prevents the transmission of genetic aberrations to future generations but also help in understanding the impact on future health. However, more than the financial factor, psychological fear and emotion contribute as major hurdles of carrier screening. Preconception and pre-implantation genetic screening and testing are discussed with pros and cons. Carrier screening has reduced the incidences of prevalent genetic abnormalities in ethnic groups such as Ashkenazi Jewish (AJ) population. Genetic screening has been discussed at population and ethnic level with expanded carrier screening along with technological challenges and ethical and policy issues. Though there is expected trauma of stigmatization in the community, carrier screening has a pivotal role in controlling transmission of genetic abnormalities to offspring and lowering the burden of untreatable abnormalities of the genetic architecture.

**Keywords:** Carrier screening and genetic testing, Carrier screening of Jewish Genetic Disorders, Policies and ethics of genetic screening, Prenatal and preconception genetic testing, Genetic counseling, Prevention of birth with genetic defects.

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## INTRODUCTION

The balanced genetic rearrangements lead to alterations in the structure of genes, which may not pose serious phenotypic or clinical expression in carriers of

the mutations, particularly those of the first generation; whereas the unbalanced alterations result in a significant clinical outcome in children. The gametes of carriers will have four types of combinations viz. normal and balanced genetic condition in each, and 50% with two different unbalanced rearrangements.<sup>1</sup> The physically and mentally handicapped children are often diagnosed with some chromosomal anomaly, which necessitates genetic screening of the parents to understand the possibility of familial transmission.<sup>2,3</sup> Such approach for the parents and other blood-related members is called carrier screening. A carrier is a healthy individual and not affected with genetic illness; however, they may carry one copy of a recessive mutation or a balanced chromosomal translocation. When both parents carry such recessive mutation for a similar autosomal recessive disease, 25% of their pregnancies will be affected. For X-linked disorders, half of the male pregnancies of a carrier mother will be affected; however, her daughters will be unaffected but serve as carriers for the next generation. Thus, carrier screening (CS) not only helps in understanding the genetic cause in the affected proband, but also guides for suitable medical intervention, and prevents transmission of abnormalities to future generations.<sup>4</sup> Thereby, CS with known history of genetic disorders guides the blood-linked family members for introducing prevention of transmission and minimize the risk of associated and long-term clinical implications of genetic mutation in the offspring of present and future generations. Hence, CS stands mandatory for the families having a clinically affected member; however, it can be optional for people who do not have any history of genetic illness and/or risk of suspected genetic disorders in the family.

In the postgenomic era, advanced technologies have identified over 1300 recessive disorders of mild to severe form with an incidence of 25/10,000 children, which predisposes 1 to 2% carrier couples to the risk of having a child affected with at least one recessive genetic condition.<sup>5</sup> Transmission of these irreversible alterations can be prevented through CS of the prospective couples followed by prenatal diagnosis. CS could let us carry out early therapeutic interventions at fetal stage itself, which would reduce associated morbidity and mortality. However, the

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majority of the affected children are born to couples with unknown family history, and only a minority of relatives of high-risk families opt for CS. Although the parents are explained about the mutations and its impact on health and future consequences through genetic counseling, their upfront reaction to the diagnosis of their affected child involves considerable psychological trauma. This, in turn, creates anxiety and phobia towards further genetic testing of the affected proband and family members.<sup>6</sup> In this paper, we have described the attitude of the lay public towards CS, the importance of genetic counseling and screening for lowering disease-burden in ethnic groups, pros, and cons of prenatal and pre-implantation testing, the associated trauma of stigmatization and policies and ethics for CS of genetic disorders.

## POPULATION AND ETHNICITY-BASED GENETIC SCREENING

Technological advancement has made genetic screening possible at the population level for detection of a larger set of mutations and simultaneous screening of more diseases at a faster turn around time for lower costs for specific high-risk populations such as Ashkenazi Jewish (AJ), irrespective of their risk status. However, the panel of mutations is generally restricted to the most frequently occurring ones of known pathogenic values. CS is important for families carrying specific genetic conditions through generations, and at the population level for ancestral and ethnic origin. Population and/or individuals of Eastern European AJ descent are known to be carriers of Tay-Sachs disease (TSD), Canavan disease, cystic fibrosis (CF), familial dysautonomia, Fanconi anemia group C, Nieman–Pick disease type A, mucopolysaccharidosis IV, Bloom syndrome, Gaucher disease, etc., which are commonly grouped as Jewish genetic disorders (JGDs) having a frequency of 1 in 4 to 5 AJ for any of the disorders.<sup>7-9</sup> Higher incidence of TSD and almost exclusivity of familial dysautonomia might have been facilitated by genetic drift and historical and social factors.<sup>10</sup> However, all JGDs exhibit founder mutations for high-risk genetic disorders. Many of these genetic conditions predispose fetal demise, lethal childhood or significant lifetime morbidity. Nevertheless, CS of at-risk communities shall be considered with due respect to cultural and religious differences.

American College of Medical Genetics (ACMG) practice Guidelines (2008) recommended CS for individuals of French Canadian and Cajun heritage, and preconception and prenatal screening for CF for non-Hispanic Whites.<sup>11</sup> However, it is becoming increasingly difficult to assign CF to a single ethnicity since the disorder has also been detected in other populations with high carrier incidences and diverse sensitivities.<sup>12</sup> Population-based screening of

CF may also identify variants such as 5T/7T/9T in the Cystic fibrosis transmembrane conductance regulator (CFTR) gene with significant inter-individual variations. Population-based screening of spinal muscular atrophy (SMA), an autosomal recessive disorder, has also been recommended by ACMG because of its prevalence (1 in 10000 live births), high carrier frequency (1 in 40 to 60), and also for its occurrence with deletion and point mutation in *SMN* gene, which results in compound heterozygous conditions.<sup>11</sup>

## EXPANDED CARRIER SCREENING

Positive attitude of AJ population either in the form of a premarital confidential carrier matching program (ultra orthodox DorYeshorim program) or an open carrier matching program, including adolescents in high schools towards screening of “Ashkenazi Jewish Disease” has created awareness about the necessity of expanded screening.<sup>12</sup> Similar practice of expanded screening for common genetic illness such as hemoglobinopathies, SMA and fragile X syndrome has been adopted in some of the European countries owing to global migration.<sup>13-15</sup> Expanded CS is now carried out for pan-ethnic groups, which increases equity on one hand and reduces the risk of their stigmatization on the other. However, meaningful implementation of expanded screening raises many technical, ethical, legal and social questions, such as which diseases and mutations should be considered in the panels; its rationality; public and professional attitudes and preferences towards expanded screening panels; how can pre-test education and post-test counseling be optimized for facilitating informed decision-making; and so on.

American College of Obstetrics and Gynecology (ACOG) initially recommended screening for TSD, Canavan disease and CF in routine obstetric work-up for all.<sup>8</sup> Screening of TSD, established in the 1970s, has resulted in >90% reduction of the disease among the North American AJ population. ACOG committee on genetics recommended screening of familial dysautonomia due to its prevalence in the Jewish population (1 in 32). Both ACMG and ACOG have recommended CS of JGDs for 23 mutations.<sup>9</sup> Therefore, despite being less common (1 in 89 to 1 in 160), CS is made available for several diseases.<sup>11</sup> JGDs with mild to severe clinical expressions cannot be cured; however, that can be treated with limited options, which can improve the lifespan and quality of life. CS has reduced hemoglobinopathies in Cyprus, Turkey, Iran, Bahrain, Saudi Arabia, and many others.<sup>12,13</sup>

The prevalence of JGDs in non-Jewish populations is unknown except TSD and CF. The mutations may be different with variable clinical expression and morbidity

in non-Jewish populations. Thus, in the case of Jewish and non-Jewish marriage, estimation of risk to their progenies appears difficult. In such a scenario, CS of the Jewish parent may be helpful in delineating the risk and estimating the residual risk of being a carrier.

For screening general population in the absence of family history, appropriate measures should be taken in selecting disease-causing targets of specific genes and mutations. Professional guidance on targeted screening should be developed using clear criteria, instead of considering as many disorders as possible depending on the availability of technology and expertise. ACMG has recommended guidelines on expanded CS at preconception and prenatal stages.<sup>14</sup>

### ANTICIPATED ISSUES OF CARRIER SCREENING

There is fear of feeling guilty if the screen-result comes positive, or parents are blamed having a child affected by a potentially avoidable disorder.<sup>15-17</sup> Nevertheless, confidentiality of test results and genetic discrimination by insurers may cause detrimental effects, including fear of undue pressure on individual choice, particularly in socially tight communities, high schools and workplace. Also, detection of a positive carrier may devalue the lives of affected patients or impedes the search for a cure.<sup>18</sup> However, a negative test result may relieve the patients and all blood-linked members from anxiety. As there is a possibility of a small residual risk in CS at molecular level, mostly due to incomplete sensitivity of the test, compound heterozygous condition such as SMA, or incomplete penetrance of the mutation after a favorable test result, the expecting couples may thus be explained with the unexpected birth of a child with a genetic disease.

Similarly, in cases of normal karyotype in children with significant congenital malformations or their parents, there could be the possibility of genetic mutations. And without having any knowledge of a suspected genetic mutation for a clinical condition, molecular screening and/or testing, though feasible with today's technologies, would be long-term research for an affected family. Healthcare professionals thus need to explain the potential misperceptions that screening can guarantee a genetically healthy child.

### ROLE OF GENETIC COUNSELING

Screening and testing of suspected genetic illness play pivotal roles in the field of perinatology intending to reducing recurrent transmission of genetic defects. Physicians' familiarity with the available array of genetic tests, sensitivity and limitations of technological intervention, interpretation of the results, risk and associated trauma, societal stigmatization and professional discrimination, disclosure of the genetic result to the biological

relatives and their reaction, and so on, would be helpful to clear the doubts of the patients. For the AJ population, CS is a well-accepted and established practice. The positive attitude and perceptions of clinicians towards screening for individual genetic disorders have enabled prevention of transmission in such families. Pre- and post-test genetic counseling and increased genetic knowledge might reduce the psychological effects and anxiety. However, the lack of knowledge among the lay public has been demonstrated as a major concern among the healthcare professionals in many surveys and investigating screening programs for genetic diseases.<sup>19-20</sup> Also, associated expenses or lack of reimbursement facility, and supporting services appeared as major barriers.<sup>19,21</sup>

It was experienced through several study groups that counseling should be provided by a clinician for communicating the genetic information, as lay people undergoing CS are not familiar with the diseases screened for, and do not understand a positive result (abnormality).<sup>22</sup> In general, overall uptake rates for individual and/or family screening or couples of blood-lineage planning a pregnancy, are much lower, even when such screening is offered at zero cost.<sup>6</sup> Even despite efforts by the medical and Jewish communities, many Jews of the reproductive age remain unaware of the benefit of CS and thus remain at risk of bearing children with genetically transmitted diseases.<sup>23</sup> In cases of known genetic illness, prenatal diagnosis (PND) or pre-implantation genetic diagnosis (PGD) will control the birth with the prevailing genetic diseases; provided the reduction of the disease-burden or prevention may be regarded as an explicit goal of the family or the affected community.

ACOG and ACMG have recommended that every individual undergoing a genetic test or screening shall be explained about the purpose, importance and appropriateness of the tests or screening, when and which test to order, what information is expected, limitations of the tests, sensitivity and specificity, risk of false positive or negative results in light of patient's medical and family history, the options of medical management or other possible remedial actions available, facts and future consequences of mutations, possible implications of the test results, potential risks and benefits of the procedure, including psychosocial trauma of discrimination and stigmatization.<sup>24</sup> The possibility of psychological harms can be minimized through genetic counseling about the screening and consequences of being a carrier. Moreover, the public shall be educated with genetic information for creating a positive attitude, which shall be expressed on 'informed consent.' Patients should be informed about the present health status and future risk, carrier, marriage or reproductive choices, and also the uncertainties regarding test-reliability, penetrance of genes, unavailability

of efficacious interventions to reduce the consequences of the genetic diseases and its impact on blood-linked kins. The consent may also protect the inadvertent and involuntary disclosure of genetic information to kindred. The physicians may articulate the circumstances under which they would consider disclosure obligatory. The ownership of the genetic information, confidentiality, security and future access by parents and child may be clarified in the consent form. A detail description of the screening is the prerequisite for making informed decisions. Counseling should also address the anticipated use of genetic samples, when will they be destroyed, whether used for research and diagnostic test-development, state and federal regulations governing genetic information, confidentiality of information, etc.<sup>25</sup>

In the Indian scenario, CS is primarily advised by the clinicians to couples having a child affected with the identified genetic disorder. CS is mostly accepted when second pregnancy has already been conceived and rarely before planning another pregnancy. The primary issue is affordability for three tests (parents and the affected child) at one go since the concept of medical insurance is beyond the understanding of many families. Hence, many couples even directly decide for termination of pregnancy. CS for thalassemia, muscular dystrophies and autism are frequently wanted by the families. CS at the population level is still not an approach due to limited information available on prevalence and carrier frequency of genetic disorders in the country.

Nevertheless, outsourcing of genetic screening from other states or overseas creates difficulties in understanding the result or outcome of screening. Once a carrier is detected with a genetic mutation, undue fear of stigmatization and psychological trauma, blame by the spouse, affected offspring and in-laws affect the family-environment to a large extent. A positive result at pre-employment or pre-marital stage also poses a serious risk, which can be minimized by genetic counseling.

## PRE-CONCEPTION SCREENING AND PRENATAL DIAGNOSIS

Prenatal diagnosis (PND) involves a group of procedures to look for diseases and genetic mutations in a developing fetus.<sup>26-28</sup> Difference between genetic screening (which indicates likelihood) and testing (which confirms or excludes a diagnosis) must be clearly understood for proper antenatal management. ACOG and Society for Maternal-Fetal Medicine (SMFM) recommended confirmation of a genetic abnormality following chorion villi sampling (CVS) or amniocentesis.<sup>29-31</sup>

Prenatal screening is available for hundreds of recessive diseases; however, there are plenty of illnesses and conditions that can't be screened for. A systematic review on the

screening of CF stated that 80-96% of the public prefers genetic screening to be made available as a routine test, although a minority of parents and patients feel that screening should be restricted to families having the disease.<sup>32</sup> The argument lies on heterozygous mutations; if detected in an asymptomatic fetus, remain clueless on the future course of severity or treatment modalities. Healthcare professionals, however, prefer preconception screening for enabling a greater number of reproductive options. Also sooner there may be *in utero* therapeutic developments for some conditions that are currently unavailable.

Carrier status of a couple may guide them properly to conceive biologically for a parenthood status or PND and/or assisted reproduction with donors' gametes followed by PGD. Ideally, a positive screening of a partner is an indication for other partner's screening. Preconception screening would be more cost-effective and practical than a concurrent screening of the couple and PND of the pregnancy at a time-constrained situation.

Preconception and prenatal screening of CF was introduced in routine obstetrics practice owing to its prevalence in non-Hispanic Whites compared to other races and ethnics.<sup>8,14</sup> In addition to maternal screening, United States has also incorporated CF in newborn screening panel. SMA is another prevalent autosomal recessive disorder having a mutation in the *SMN* gene. The *SMN* gene has nine exons with two identical *SMN* genes located at the telomere (*SMN1*, SMA-determining gene) and centromere (*SMN2*) on chromosome 5. Understanding and interpretation of preconception CS of SMA is critical for ~5% of parents having affected children due mainly to the compound heterozygous condition exhibiting a point mutation and a deletion in exon 7 of the *SMN*. Also, the presence of two *SMN1* genes in *cis* position on one chromosome 5 and the presence of the deleted *SMN1* on the other chromosome will result in a false negative condition, which is similar to non-carriers. Thus, residual risk of being a carrier and subsequently a small recurrence of risk to future offspring affected remain in cases with two *SMN1* copy-dosages. The occurrence of *de novo* mutation is also documented in 2% of the affected individuals.<sup>11</sup> Therefore, population-based SMA-screening is recommended to identify the couples at risk. In ~95% of affected, homozygous deletion of exon 7 of *SMN1* has been reported. Replacement of *SMN1* to *SMN2* into the telomeric locus influences the severity of the SMA disease type I whereas milder type II and type III have been shown to possess more copies of *SMN2*.<sup>11</sup>

## PROS AND CONS OF PRENATAL GENETIC SCREENING AND TESTING

Overall, genetic testing facilitates certain choices in response to the probability of having a genetically healthy

or unhealthy child. Careful weigh of certain advantages and disadvantages pertaining to genetic screening and testing is important for a decision-making process. Healthcare authorities of different countries have pointed out various aspects of antenatal screening ranging from community-based population screening to families with a known history of genetic illness intending to empowering the prospective parents to make informed choices about having children, lowering the burden of genetic illness and improving the health-index. Societal discrimination, including health insurance, employment, and adoption already exists for the affected children, for those affected with a genetic disease, and/or for symptomless individuals who have a predisposition to one (risk of late onset disorders).

Conflicts on terminating the lives of inflicted fetuses lead to an argument that eliminating a human being that cannot be cured violates the principles of medicine, and thus until we come up with cures to all genetic diseases, all lives to be preserved. Medical termination of a pregnancy for an abnormal PND result raises a concern of selective breeding or eugenics, which might eradicate a genetic disease and eliminate an entire population that did not fit into society's criteria for an ideal community, and thus, a society may emerge into a supremacy in which those with bad genes will be scorned. Nevertheless, the presence of a mutant gene for a disease doesn't guarantee disease-development since many other physical, environmental and epigenetic factors contribute.

The practice of selective abortion based on PND helps to avoid the birth of a genetically impaired child is widely accepted in the USA and many other countries. Birth of a child with a severe genetic disorder may bring the mother and/or the family into distress, psychological and emotional harm and suffering, loss of a child, loss of opportunities and freedom, stigmatization or isolation, etc. all at the cost of increased financial expenses. An additional potential threat could be the relationship between parents and the affected child, since the child may be subjected to special activities because of the parents' unawareness or lack of preparation for dealing with the child. Therefore, alongside CS of all at-risk couples before conception, PND shall be considered to determine the abnormalities in the fetus.

Almost all of us are potential carriers of several deleterious recessive genes that could be lethal to our offspring if combined with another recessive allele carrying the same fate. CS will help any child suffering needlessly because of an unforeseen deleterious inheritance from the parents.<sup>8,14</sup> Thus, the pros of PND far outweigh the consequences of bringing a helpless baby who may suffer a severe and fatal destiny into this world, especially until intervention with effective treatments is established.

Pregnancies suspected carrying an affected child in which the consequences are severe and detrimental as well as something the parent and child have no control over, shall be considered for PND. PND shall be advocated as useful and necessary as that relieves parents' anxiety and unfulfilled expectations of an impaired child. ACOG guidelines recommended PND and PGD for couples who already have a child with birth defects or genetic illness, pregnant women over the age of 35 years, couples with  $\geq 2$  miscarriages, and couples concerned about specific disorders that occur more frequently within their ethnic group.<sup>29,30</sup> The PND/PGD facilitates detection of a fetal condition for termination of a pregnancy, preparation of birth and care of a potentially affected child. PGD on eggs or embryos collects information on genetic abnormalities before implantation, and thus, directs implantation of healthy embryos, and also lowers emotional attachment in case of *in vitro* abortion. However, ethically and in principle, both *in vitro* abortion of an embryo or *in vivo* termination of a fetus involves human individual 'pre-sentient' (not yet a person), though discarding affected pre-implantation embryos is preferable.<sup>33</sup>

## ETHICAL ASPECTS

Ethical issues and guidelines of genetic testing have been established for clinicians, patients, insurers and policy-makers for protecting the use of genetic information and rights of patients carrying genetic illness, especially for preconception and prenatal diagnosis towards reproductive decision-making. The present-day technologies may decipher the entire genome of a fetus long before its birth; however, genetic measurements may be confounded by other environmental triggers.<sup>34</sup> However, testing of less severe disease-conditions, future risk of adult-onset and more prominently sex-selection have brought in regulatory issues pertaining to ethics of pre-conception and prenatal testing. In any circumstances, personal preference and individual decision hold the right to deliver a child with potential or dominant genetic disorder or terminate the pregnancy.<sup>35</sup>

Some of the thorny issues of PND include paternity, sex-selection, and disclosure of familial medical conditions. The medical ethics claims the physician's obligation to pay unlimited obeisance to a patient's confidentiality unless certain circumstances are ethically and legally justified because of overriding social considerations.<sup>36</sup> The American Society of Human Genetics (ASHG) recommends voluntary disclosure by the patient, and if the harm is likely to be serious for the at-risk kindred, the healthcare providers may also disclose.<sup>37</sup> Hiding paternal identity might lead to transmission of autosomal recessive mutations on the one hand, or unnecessary amniocentesis in all future pregnancies in cases a different person is the

biological father and accordingly creating unnecessary concern for other family members. In countries with universal healthcare policy, diagnosis of a predisposing gene does not prohibit access to health insurance. The Health Insurance Portability and Accountability Act (HIPAA) prevented insurance companies from refusing healthcare based on predictive testing.<sup>38</sup> Restriction on sex-selection has been imposed in several countries except for sex-linked genetic conditions.<sup>39,40</sup>

Non-invasive prenatal testing (NIPT) based on cell free fetal DNA/RNA (cff-DNA/RNA) available in maternal blood- plasma, which is already established as direct-to-consumer products, creates serious ethical concerns about pre-test counseling and obtaining consent.<sup>41</sup> The state and country regulations have yet be framed and implemented for controlling sex-determination in cff-DNA.<sup>42-44</sup> Collectively, test regulation, professional guidelines, and policies of the advisory groups shall be implemented to meet the challenges of preconception and PND in maternal blood.<sup>30,33</sup> Nevertheless, genetic testing should be performed with particular caution and the highest standards of 'informed consent' for rendering protection against discrimination by insurance companies, family discord, psychological distress, individual privacy, etc.<sup>35</sup>

In all cases, pre- and post-test counseling by expert professionals are important. The description on the clinical significance of test, specificity and sensitivity, risk of sampling, clinical impact of mutations (if detected), possibility and seriousness of disease-development and clinical course of management, cost and payment of tests, significance of uncalled mutations, which are not understood or associated with disease-development and their future implications, if any, interpretation of the test results, etc. shall be explained to the couples in detail. The information shall also include the pros and cons of the screening/testing.<sup>8,14,30</sup>

## POLICIES AND GUIDELINES

Guidelines or policies for are not fully defined for CS in many countries, and hence, screening is only offered to individual families at the local level, or as pilot projects. However, for hemoglobinopathies and other common genetic illness, established policies and guidelines exist in the UK and USA.<sup>45</sup> ACOG and ACMG have implemented guidelines for CS at the population or ethnic levels or individual families. There are government and non-government service providers for CS; however, the screening should justify the main focus of reduction of genetic disease-burden. The Centers for Disease Control and Prevention (CDC) and National Office of Public Health and the Foundation of Blood Research, USA have defined the ACCE-framework (Analytic validity,

Clinical validity, Clinical utility, Ethical, legal and social implications) for genetic screening, which describes the consequences of screening in detail including the role of epigenetic modifiers. The positive predictive screening-value may differ across different disorders as a function of penetrance, expressivity and may be mutation-dependent. Also, a given mutation may be associated with variable clinical severity of disease-manifestation within the same family. Most of the disorders are heterogeneous with mutations in single or multiple genes such as CF.<sup>46</sup> Commercial service providers develop fixed panels of genetic screening for public as well as for targeted screening and concentrate to a limited number of mutations; and hence, cannot address molecular pathomechanism appropriately either with the spectrum of tested genes or the spectrum of mutations.<sup>47</sup>

In India, an estimated 80% of public healthcare funding comes from the states whereas policies and plans are formulated by the Ministry of Health and Family Welfare, Government of India. Furthermore, healthcare delivery managed by private sectors raises a prime concern regarding the quality and cost of healthcare. Hereditary genetic disorders and congenital malformations are steadily rising in India being the third most common cause of mortality among the urban newborns.<sup>48</sup> Variable information on a panel of genetic tests is available from individual genetic testing laboratories.<sup>49</sup> Also, variable technology is being followed for a particular genetic test by different laboratories, and in many cases, genetic testing is being carried out by diagnostic facilities isolated from the patient management system and thus, mostly lacking in genetic counseling or interpretative comments. Hence, there is a serious need for regulatory issues on consensus professional judgment and its practical implementation intending to quality control and assurances of genetic counseling and diagnostic services, irrespective of public or private services. Clear messages are essential from the regulators on what genetic testing and suitable technology are applicable or affordable for a given genetic condition. The diagnostic expenses are generally met out-of-pocket by the individuals and only 21.3% of healthcare expenditure of 6.1% of the gross domestic product (GDP) is provided by the government.<sup>50</sup> Furthermore, over 90% of the Indian medical institutions do not include medical genetics and genetic counseling for education and training.<sup>51,52</sup>

Moreover, the discovery of disease-causing genes and technological challenges in the field of medical genetics will give rise to even more debated issues. Genetic predisposition of a fetus may raise a wide array of questions and issues that must be confronted while developing policies to deal with genetic screening. To prepare citizens for informed personal decision-making, public education

and counseling will become vital to understand new genetic concepts. Although these tests are usually advised for high-risk families, nowadays, most parents are opting for prenatal genetic screening, especially for cff-DNA, to know whether their child has any abnormality or not. This has led to several debates between people who support prenatal genetic screening and those who are against it. Government intervention of standards and policies are essential for regulation of genetic screening and testing, which may truly eradicate and/or cure genetic diseases.

## CONCLUSION

By summarizing the knowledge gained from the literature on carrier screening of genetic mutations, this report intends to contribute to the awareness of public and healthcare professionals on the importance of CS, to prevent transmissible aberrations and manage affected individuals at the clinical setting. CS can be optional for people who do not have any prior history of risk of recessive disorders, but compulsory for those who have an affected member in the family; however, the decision of undergoing screening or testing solely relies on the individuals or families. Since genetic alterations are irreparable, it is advisable to investigate the type and impact of aberrations and to understand the course of appropriate clinical management accordingly. Genetic information is linked to all blood-relatives, thus, the parents should not be blamed by their children and/or close relatives. In reality, all family members will be benefited from routine screening and understanding of the genetic alterations, else many of the blood relatives will suffer from the similar illness of genetic etiology. The discussion in the present report will be helpful to reduce anxiety related to carrier screening and will educate and guide the public for participating in genetic screening and testing by eliminating fear and trauma. Prenatal and pre-implantation screening and testing and pre-/post-test genetic counseling, in spite of limitations discussed above, will help to reduce the genetic defects and/or implement therapeutic management *in utero*. Ethical issues need to be dealt with care while defining policies and guidelines for genetic screening of carrier status of an adult, embryo or a fetus.

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