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Genetics in pediatric dentistry: A review

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Abstract
Genetics is the science of heredity and vsariation. It plays an important role in determining our individuality. The term "genetics" conveys two different concepts: genetics as the study of inherited characteristics, and genetics as the study of cellular processes controlled by DNA. Developmental defects of teeth can occur as isolated genetic traits, be associated with a chromosomal abnormality or syndrome, or be inherited as a complex trait with genetic and environmental interactions. Numerous hereditary syndromes are associated with congenitally missing teeth. Often pediatric dentists are the first health care practitioners to document dysmorphic features in a child. This article attempts to gather insight about different dental diseases and their genetic basis, the need for genetic screening and testing to avoid future problems.

Keywords: Genetics, caries, genes, Mendel, periodontitis,

Introduction
Genetics is the study of genes at all levels from molecules to population. The term gene is referred to as a basic unit of heredity lying in chromosomes; it is an entire DNA sequence that is necessary for the synthesis of a functional polypeptide or RNA sequence [1].
Each gene is responsible for a specific trait or a character of an individual; deletion or inclusion of genes gives rise to rise to certain characteristic features resulting either into a character/malformation/disease as per the situation [2].
There are hundreds and thousands of genes responsible for specific functions in an individual. These genes are located in what is known as 'chromosomes'.
Humans have 46 chromosomes that contain 100,000 genes, including numerous duplicates. Any variation is structure or form of chromosomes results in various disorders and thereby considered as functional units of heredity and evolution [3].
According to Stent (1971) the first evidence of inheritance was taught and developed by Hippocrates in fifth century BC in Greece. Hippocrates ideas can be termed as_bricks and mortar theory 'which states that hereditary material consists of physical matter. He postulated that elements from all part of the body became concentrated in male semen and then formed into a human in the womb. He also believed in the inheritance of acquired characteristics. A century later Aristotle criticized Hippocrates theory and instead proposed that heredity involved the transmission of information-_a blueprint model'. Aristotle discarded Hippocrates theory for several reasons. He pointed out that individuals sometimes resemble remote ancestors rather than their immediate parents [4].
Genetics did not develop suddenly. Instead it evolved from intellectual background of Darwin's time that dates back to 1859. Darwin proposed that a species changes as a result of generations of competition among individuals. Within a species individuals vary with respect to heritable characteristics that influence the ability to survive and reproduce [2].
Gregor Mendel (1822-1884) is appropriately called as the Father of genetics‖. His precedent-setting experiments with garden peas were published in 1866. Although Mendel devised a precise mathematical pattern for the transmission of hereditary units, he had no concept of biological mechanisms involved. August Weismann (1834–1914) gave the germ-plasm theory which stated that the germ line is the continuous element, and the successive bodies of higher animals and plants are side branches budded off from it, generation after generation [5].
Galton showed that, on the average, an individual inherits ¼ of his characteristics from each parent, 1⁄16 from each grandparent, 1⁄64 from each great-grandparent, and so on.

In 1930, G.W. Beadle, B. Ephrussi, E. L. Tatum, J. B. S. Haldane hypothesized that: The gene was at first characterized as an indivisible unit of structure, unit of mutation and unit of function with all three of these attributes considered equivalent. The concept given by them is called one gene-one enzyme concept [1].

Concept of the gene has evolved from Mendel's-unit factor‖ controlling on a phenotypictrait to the unit of genetic material specifying one polypeptide and operationally defined by the complementation test [2].

There has been no change in the concept of the gene as the basic unit of function since its discovery by Mendel in 1866. The discoveries of the mid to late 20th century defined processes that would provide the tools for molecular biology, recombinant DNA technology, and finally the biotechnology industry. Restriction enzymes were discovered and used to construct recombinant DNA molecules. The advent of protein and DNA sequencing launched a new era of phylogenetics [3]. Species could now be compared at the molecular level. The information age is essential to genomics. The electronic analysis, distribution and storage of genomic data are a hallmark of the science. The internet spawned the distribution of information from central databases. E-mail connected scientists and fostered the rapid exchange of ideas. The advent of the WWW provided a new medium for the presentation of information [5].

This article attempts to gather insight about different dental diseases and their genetic basis, the need for genetic screening and testing to avoid future problems.

Methods and criteria in genetic identification [6].

According to Neel and Chull, the roles of genetic factors are as follows.

- Occurrence of the disease in a definite numerical proportion among individuals related by a particular descent.
- Failure of the disease to spread to non-related individuals. The consanguinity effect seen often justifies the role of relatedness.
- Onset of the disease at a characteristic age without a known precipitating event.
- Greater concordance of the disease in identical than in fraternal twins.

Chromosomal aberrations are classified based upon following criterions [6, 7]:

Structural Abnormalities

1. Deletion: Breaking away or loss of a portion of chromosome. For example, Cri-du-chat syndrome.
2. Translocation: Two chromosomes break and exchange their broken segments in reciprocal translocation. For example, Robertsonian translocations.
3. Inversion: The broken fragment reattaches itself in reverse orientation to the same chromosome. For example, Increase in miscarriages.
4. Duplication: An over representation of specific chromosomal region.
5. Transverse centromeric division: Instead of dividing longitudinally, centromere divides in transverse plane forming an isochromosome, thereby resulting in duplication of one arm and deletion of another arm of the involved chromosome [6].

Numerical Abnormalities

i. Involving chromosomes sets

Monoploid
Euploid
Polyploidy

ii. Involving individual chromosomes

Autosomal derivatives
Monosomy - Missing single pair of chromosome
Trisomy
Sex linked derivatives [6].

Type of Chromosomal Abnormality

Gross chromosomal aberrations
Single gene disorders
Polygenic disorders

The genetic factors cause variations in following features of dental relation. They include:

- Variations in size, shape of jaws
- Variations in size, number, shape, form of teeth
- Malocclusion
- Periodontal conditions
- Incidence of facial clefts
- Growth and development [7]

Genetics and Dentistry

The successful completion of the Human Genome Project in 2000 led to the development of new tools for human genetic studies. These tools have been widely applied to many human traits of complex etiology, including orofacial clefts (OFCs) and dental caries, which are both of interest for pediatric oral health. Genome‐wide association studies of OFCs have been remarkably successful compared with other human complex traits, with about 13 genes showing a statistically significant association. Some of them have been extensively replicated and are estimated to account for about 55% of OFC case. GWA studies are only the first step as they represent population‐level statistical results but cannot reveal which genes/loci are etiologic in any particular individual or family [1]. Studies of the common lymphoid progenitor (CLP) phenotype in twins indicate that monozygous twins have a 35% concordance rate, whereas dizygous twins show <5% concordance; however, despite many extensive investigations, no simple pattern of inheritance has been demonstrated [1-5].

This has led to proposals for a variety of genetic modes of inheritance for CLP, including dominance, recessiveness, and gender linkage, and has led ultimately to the documentation of modifying conditions that may be present, such as incomplete penetrance and variable gene expressivity. There are three important reasons for the failure to resolve the question of a hereditary basis for clefts: (1) Some clefts are of a nongenetic origin and should not be included in a genetic analysis (such cases are seldom recognized and are difficult to prove), (2) individuals who have increased genetic liability for having a child with CLP often fail to be recognized, but because they do not have CLP themselves, they cannot be identified with certainty, and (3) CLP, although sometimes appearing to be relatively simple in origin, is undoubtedly a complex of diseases with different etiologies lumped together because of clinical disease resemblance (they all show clefting).

The three most common problems in dentistry are dental caries, periodontal problems, and malocclusion. Mainly a multifactorial etiology for all the condition are there, but most of the times genetic condition prevails [1, 3, 5].

Genetics and dental caries

Dental caries is a disease of the dental hard tissues, characterized initially by the decalcification of the inorganic portions of the tooth. Loss of the mineral content is then followed by the breakdown of the organic Matri [1, 3, 5].

Genetics in Dental Caries through Twin Studies

Studies of the etiology of dental caries suggest that both genetic and environmental factors may be concerned with the development of dental caries. Several major genes have been identified which condition defective formation of enamel or dentine leading to development of rampant caries in such teeth [6]. Twin studies have provided strong evidence for the role of inheritance. Goldberg found that identical twins showed decay in corresponding teeth and heredity affects dental decay only in as much as it controls the shape of a tooth and its pits and fissures and its position in the dental arch [7].

Bordoni concluded that there is a strong genetic component in primary teeth which affects the incidence of caries and has shown the association of TAS2R gene with caries in primary dentition [8].

Mansbridge concluded from his study that-Environmental factors clearly have greater influence but the genetic factors also contribute to the causation of dental caries [9]. This led to the conclusion of Finn and Caldwell that, Equal genetic weight should not be ascribed to both types of lesions that are smooth surface lesions and pit and fissure lesions [10].

Boraas from his study in which twins were reared apart speculated on the particular inherited traits that could contribute to the results by stating-Several genetically variable factors which may be involved in the development of dental caries and contribute to the greater monozygotic similarity in dental caries experience are, 1) Salivary factors and oral flora, 2) tooth eruption time and sequence, 3) tooth morphology, 4) arch shape, 5) dental spacing, 6) propensity for diet [13]. Klein and Palmer" [14] and Klein‘s [15] findings indicated that children have a caries experience remarkably similar to that of their parents when the susceptibility of both parents is the same (either high or low). When caries susceptibility of the two parents is dissimilar, however, the children's susceptibility tends to be more like that of the mother than that of the father. This finding was particularly evident in daughters. Li and Caulfield [16] found that mothers are the principle source of streptococci mutans to their infants, with a greater rate of transmission to female than male infants. The high degree of fidelity between strains of MS in mothers and their female infants in contrast to those isolated from male infants, indicates that the conservation of MS within mother-infant pairs is gender specific. It has been observed that infants whose teeth emerged early were significantly more likely to acquire MS from their mothers than infants whose teeth emerged later. That tooth emergence in females occurs sooner than in males is commonly accepted. Children whose teeth erupt earlier than the expected time are more advanced in other ways that might influence fidelity of acquisition, such as a more developed immune system. The obvious explanation is that mothers enjoy the most contact with their infants and, therefore, constitute the major source of MS. The mechanism may be that ntimacy between a mother and her spouse results in the appearance of an immunological recognition of the father's indigenous bacteria as non-self, and this immunological awareness is transferred to the infant through the placenta or breast milk. Mothers transfer to their infants not only maternal immunoglobulins via the placenta and colostrum, but also a complementary set of indigenous bacteria capable of co-existing with these maternally-derived or directed immunity factors [14, 15, 16].

Genetics and periodontitis

Susceptibility to periodontal disease is 50% attributed to hereditary factors as proven by different syndrome studies. The different genetic disorders such as Ehlers‐Danlos syndrome, Acatalasia, Hypophosphatasia, Chediak‐Higashi syndrome, chronic neutropenia, Papillon “Lefevre syndrome, and Trisomy 21 all are related to fragile periodontal tissue and early onset periodontitis [13]. The susceptibility study of early onset periodontitis showed that there is an increase in prevalence in women, as well as lack of a father to son transmission, indicated it is inherited as an X‐linked dominant trait. A study between identical twins confirmed the evidence of attachment loss, pocket depth, gingival index and plaque index are almost same in identical twins [14].

Gingival enlargement is characterized by overgrowth of gingival by expansion and accumulation of connective tissue. It can be also resulted from chronic gingival inflammation or drug related (phenytoin, cyclosporine, and nifedipine) induced [15]. Sometimes, there is hereditary (idiopathic) gingival enlargement that is characterized by slowly progressive benign enlargement of the gingival tissues. Hereditary gingival fibromatosis is a very rare disease of infancy occurs as a progressive gingival enlargement of normal color and firm consistency which is asymptomatic and nonhemorrhagic [15, 16, 17].

The disease may cause diastemas, malpositioning of teeth, prominent noncompetent lips [18, 19]. Hereditary gingival fibromatosis is associated with three different loci two mapping to chromosome 2 (GNGF on 2p‐1‐22 and GINGF3 on 2p22.3‐p23.3) which do not overlap, and one mapping to chromosome 5 (GINGF2 on 5q13‐q‐22) [15, 20, 21].

The genetics of cleft lip and cleft palate

The genetic evidence comes from family studies in which it can be shown that the siblings of patients with cleft lip (with or without cleft palate) have an increased frequency of cleft lip (with or without cleft palate) but not of isolated cleft palate, and that siblings of patients with isolated cleft palate have an increased frequency of isolated cleft palate but not of cleft lip [7, 22, 23, 24, 25].

This was pointed out by Fogh-Andersen (1942) and confirmed by several others. The concordance rate of cleft or palate is expected to be higher in monozygotic twins than in dizygotic pairs. In the case of CL (P), the risk for siblings born of unaffected parents increases from about 4% after one affected child to 9% after two-affected [26, 27, 28, 29].

Genetic instability in oral cancer

It can be due to mutations in proto‐oncogene (polymorphism in GST gene: GSTM1 and GSTT1 or CYP (cytochrome P450) or mutations in tumor suppressor gene (p16, 9p21, APC5q21–22 and p53) this may lead to loss of heterozygosity or failure to repair [30].

In 1971, Dr. Alfred Knudson proposed the two‐hit hypothesis. Knudson suggested that multiple “hits” to DNA were necessary to cause cancer. In the children with inherited retinoblastoma, the first insult was inherited in the DNA, and any second insult would rapidly lead to cancer. In noninherited retinoblastoma, two “hits” had to take place before a tumor could develop. This theory indirectly led to the

identification of cancer‐related genes [31]. Foulkes *et al*. found first‐degree relatives of patients with oral cancer have an RR of 3.5 times the general population and siblings had an RR of 8.6 for developing oral cancer [32]. Cancer predisposition syndromes include Werner's syndrome, Bloom syndrome, Fanconi's anemia or disorders like Ataxia telangiectasia [32].

Genetics in skeletal malocclusion

Genetic factors playing a predominant role in the etiology of malocclusion is backed up by population studies, especially family and twin studies. A literature review carried out by Lauweryns in 1993 concluded that 40% of the dental and skeletal variations that lead to malocclusion could be attributed to genetic factors [33]. Hughes and Townsend in 2001 quantified the extent of variation in different occlusal features such as interdental spacing, overbite, over jet and arch dimensions of Australian twins and indicated a moderate to relatively high genetic contribution to the observed variation [34]. Ting Wong *et al*. in 2011 suggested an association for the genes EDA and XEDAR in dental crowding present in Class I patients by identifying 5 SNPs that were significantly different in a genotype or allele frequency distribution in the Hong Kong Chinese case-control population [35]. While these studies provide evidence for the heritability of dental occlusal characteristics that contribute to malocclusion, other studies have come to the opposite conclusion. For instance, Corruccini, Sharma *et al*. could not demonstrate significant heritability for occlusal traits among Indian twins suggesting that dental patterns are environmentally based [36]. Harris and Johnson also noted almost all of the occlusal variability within their sample of untreated subjects was acquired rather than inherited [37]. These conflicting data suggest that dental variation is more dependent upon environmental factors. In a study of the association of the Pro561Thr (P56IT) variant in the growth hormone receptor (GHR) gene with craniofacial measurements on lateral cephalometric radiographs by Yamaguchi *et al*, those who did not have the GHR P56IT allele had a significantly greater mandibular ramus length (Condylion-gonion) than did those with the GHR P561T allele in a normal Japanese sample of 50 men and 50 women. The average mandibular ramus height in those with the GHR P56IT allele was 4.65 mm shorter than the average for those without the GHR P561T allele. This significant correlation between the GHR P56IT allele and shorter mandibular ramus height was P56IT allele and shorter mandibular ramus height was confirmed in an additional 80 women [38].

Theoretically, there are two general ways in which predisposing or causative factors for malocclusion could be due to heritable characteristics. One would be inheritance of a disproportion between the size of the teeth and the jaws resulting in crowding or spacing, whereas the other would be inheritance of a disproportion in the position, size, or shape of the mandible and maxilla. However genetic influences on each of these traits are rarely due to a single gene, which would be necessary for malocclusion to be due to the simple inheritance of discrete skeletal and dental characteristics. Instead they are often polygenic with the potential for environmental influence [39].

Twin studies by Lundstrom showed that heredity played a significant role in determining the following characteristics: tooth size, width and length of the dental arch, height of the palate, crowding and spacing of teeth, and degree of overbite [40]. Kraus, Wise, and Frei's cephalometric study of triplets showed that the morphology of an individual bone is under strong genetic control but that the environment plays a major role in determining how various bony elements are combined to achieve a harmonious or disharmonious craniofacial skeleton [41].

Heredity and specific Dentofacial morphologic characteristics

Lundstrom in 1949 made intensive analysis of the dentofacial morphologic characteristics in twins and concluded that heredity could be considered significant in determining the following characteristics [40]: (1) Tooth size, (2) Width and length of the arch (3) Height of the palate, (4) Crowding and spacing of teeth, (5) Degree of sagittal overbite (overjet), (6) Position and conformation of perioral musculature to tongue size and shape, (7) Soft tissue peculiarities (character and texture of mucosa, frenum size, shape and position, etc.)

Heredity also plays of part

1. Congenital deformities.
2. Facial asymmetries.
3. Macrognathia and micrognathia.
4. Macrodontia and microdontia.
5. Oligodontia and anodontia.
6. Tooth shape variations (peg-shaped lateral incisors,
7. Carabelli's cusps, mamelons, etc.)
8. Cleft palate and harelip.
9. Frenum diastemas.
10. Deep overbite.
11. Crowding and rotation of teeth.
12. Mandibular retrusion.
13. Mandibular prognathism.

Detlefsen (1928) [42] concluded that the tooth size and shape and arch size are determined by heredity. Schultz (1932) [43] identified hereditary tendency toward the elimination of upper lateral incisor, while Huskins (1933) stated it to be a sex linked recessive trait. Iwagaki (1938) [44] reported mandibular protrusion and edge-to-edge bite to be more prevalent to Japanese. Lebow and Sawin (1942) [45] published pedigrees indicating in heritance of human facial features. Moore and Hughes (1942) [46] observed that the incidence of asymmetry in the jaw size, in children with asymmetrical parents was 300 times as great as in children normal parents. Weininger (1953) [47] stated that diastema is a result of a sex linked dominant gene. Stein, Kelley (1956) [48] reported that Angle's class-II occlusion may be due to recessive factors. Asbell (1957) [49] did a study of the family line transmission of dental occlusion. Genetics of tooth size in the clinical literature statements are sometimes found suggesting that the size of teeth is basically an inherited traitthe environment has little or no effect. The "key" tooth in each morphologic class of teeth has the highest heritability. Sofaer (1971) [50] noted that with the lowest heritability erupt latest. Bader (1965) [51] reported strong genetic contribution to the size of the first and second molars (66 percent) and somewhat less to the third molar (47 percent).

Genetics of tooth eruption

The studies of heritability of tooth eruption point to multiple genes with nutrition, diseases and other postnatal factors playing minor role [52, 53].

Genetics of congenitally missing teeth

Grahnen (1956) [54] found that if either parent had one or more

congenitally missing teeth, there was an increased likelihood that their children also would be affected. Genes also influence hypodontia. The congenital absence of teeth is a discontinuous anomaly [52, 53].

Genetics of tooth morphology

The Cusp of Carabelli and shovel-shaped incisor are traits of polygenic origin with a discontinuous distribution [52, 53].

Cytogenetics

The familial form of cherubism occurs typically in an autosomal dominant trait with mutations in the SH3- domain binding protein 2 (SH3BP2) on chromosome 4p16.3. An autosomal recessive mode of inheritance has been suggested in some instances where signs of cherubism could not be found in carriers of the older generation. Point mutations in the gene coding for SH3BP2 have been identified in 12 of 15 families. All the mutations identified so far are present in exon 9 of the gene and cause amino acid substitutions within a 6-amino acid sequence [55].

Amelogenesis imperfecta

Amelogenesis imperfecta (AI) is a group of inherited defects of dental enamel formation that show both clinical and genetic heterogeneity. In its mildest form, AI causes discoloration, while in the most severe presentation the enamel is hypomineralized causing it to be abraded from theteeth shortly after their emergence into the mouth. Both the primary and permanent dentitionsare affected. Enamel findings in AI are highly variable, ranging from deficient enamel formation to defects in the mineral and protein content. The four main types of AI were described as follows: hypoplastic, hypomineralized, hypomaturation and with taurodontism [24].

The AI phenotypes vary widely depending on the specific gene involved, the location and type of mutation, and the corresponding putative change at the protein level. Different inheritance patterns such as X-linked, autosomal dominant and autosomal recessive types have been reported and 14 subtypes of AI were recognized. [56].

Amelogenin

Amelogenin, the protein product of the AMELX Xq22 and AMELY Yp11 genes, is considered to be critical for normal enamel thickness and structure. At least 14 mutations, 5 nucleotide substitutions; 7 small deletions; and 2 gross deletions have been described in amelogenin gene. This mutation destroys the function of

the amelogenin protein completely, producing enamel of normal thickness but poorly mineralized and severe discoloration [56].

Ameloblastin

Ameloblastin, also known as amelin, is expressed by the enamel-producing ameloblast cells. The ameloblastin gene is located in chromosome 4, within the critical region for local hypoplastic AI. Ameloblastinbinds specifically to ameloblasts and inhibits cell proliferation of mutant ameloblasts [57].

Enamelin

Enamelin, the largest enamel extracellular matrix protein, was initially identified by Fukae, *et al*. (1993). It is produced by ameloblasts, initially during the secretory stage concentrating near theTomes processes. Much lower levels of enamelin expression have been observed in dental pulp, presumably secreted by odontoblasts, and along the forming root. The enamelin gene mutations have been identified in autosomal dominant forms of hypoplastic AI [57].

Enamelysin (Mmp-20)

MMP-20, also known as enamelysin, was originally identified by Bartlett *et al*. (1996). This enzyme is expressed by ameloblasts and the odontoblasts of the dental papilla. Therefore, MMP-20 is considered a toothspecific metalloproteinase. MMP-20 expression was observed in pathologic tissues such as in calcifying odontogenic cysts, odontogenic tumors and tongue carcinoma [58].

Dentinogenesis imperfecta

It was probably first recognized by Barret in 1882. The first published report describing the disorder as an enamel defect was by Talbot as quoted by Witkop. The term _hereditary opalescent dentin ‘was first used by Skillen, Finn and Hodges to describe the brown translucent teeth that have an opalescent sheen and are lacking in pulp chambers. Dentinogenesis imperfecta (DGI) is a localized mesodermal dysplasia affecting both the primary and permanent dentitions. Clinically, both dentitions are affected. The color of the teeth varies from brown to blue, and is sometimes described as amber or gray [57, 59].

Radiographically, the teeth have bulbous crowns and constricted, short roots. Initially, the pulp chambers may be abnormally wide, giving the appearance of _shell teeth‘ but they progressively get obliterated [59]. DGI has been classified by Shields and co-workers into three types:

1. Type I, DGI associated with Osteogenesis imperfecta
2. Type II, DGI without Osteogenesis imperfect
3. Type III, Brandywine type.

Dentinogenesis imperfecta type I

Individuals with DGI-I also have osteogenesis imperfecta. The teeth of both dentitions are typically amber and translucent and show significant attrition. Radiographically, the teeth have short, constricted roots and dentine hypertrophy leading to pulpal obliteration either before or just after eruption [57].

Dentinogenesis imperfecta type II

The dental features of DGI-II are similar to those of DGI-I but penetrance is virtually complete and osteogenesis imperfecta is not a feature. Bulbous crowns are a typical feature with marked cervical constriction.

Normal teeth are never found in DGI-II. Sensorineural hearing loss has also been reported as a rare feature of the condition [60].

Dentinogenesis imperfecta type III

This is a form of DGI found in a tri-racial population from Maryland and Washington DC known as the Brandywine isolate. The clinical features are variable and resemble those seen in DGI-I and -II but the primary teeth show multiple pulp exposures and radiographically, they often manifest "shell" teeth i.e. teeth which appear hollow due to hypotrophy of the dentine [60].

Preventive measures for genetic disorders

The health promotional measures include eugenics, euthenics, genetic counseling, and genetic preventive measures such as avoiding consanguineous marriages and specific protection against X‑ ray, ionizing radiation, and chemical mutagens [61].

Genetic screening

Genetic screening indicates the assays undertaken on a population wide basis to identify at‐risk people. Genetic testing means assays for definitive diagnosis, these are performed due to positive screening results, family history, ethnicity, physical stigmata, or other reasons [62].

Different types of screening

a. Newborn screening: It is just used after birth to identify genetic disorders which can be treated early in life
b. Diagnostic testing: It is used to diagnose or rule out a specific genetic or chromosomal condition
c. Carrier testing: It is used to identify people who carry one copy of a genetic mutation that when present in double number causes a genetic disorder
d. Prenatal testing: It is used to detect alteration in the fetus genes or chromosomes before birth
e. Predictive and presymptomatic testing: They are used to detect gene mutations associated with disorders occur after birth or in later life
f. Histocompatibility testing: The Human Leukocyte antigen (HLA) system comprises of the major histocompatibility complex in humans. Genetic testing for HLA matching is the most important for bone marrow and less important for solid organs [63, 64, 65].

The different tests that are available for diagnosis include

1. Chronic villus sampling–it is usually done in 10–12 weeks of intra uterine life to obtain a sample of the placenta by passing a plastic tube in the vagina or a needle through the abdomen into the uterus
2. Blood for alpha fetoprotein (AFP)–this test performed in 16–18 weeks of intra uterine life and is used to measure the level of AFP, which is produced by the fetus and passed to the maternal blood
3. Amniocentesis–this can be done at 13–18 weeks of intrauterine life is known procedure of obtaining amniotic fluid from the uterus by using a needle to pass through the abdomen [66].

Genetic counseling

Genetic counseling is a communication process between health‐care specialist and individual or families affected by or at risk for a genetic disorder. The goals of the process include spreading awareness of the medical facts for the condition and understanding the contribution of heredity in the expression of the condition, its risk for recurrence. It also includes discussion of the options available for dealing with disorder and assisting families in choosing the option which are most appropriate for them [64-66].

Conclusion

Genetic disorders are attended with less importance than other diseases in public health problems. In underdeveloped countries, neonatal and infant mortality is mostly due to the lack of neonatal care units and ignorance on the part of less educated parents. There is a lack of knowledge between genetic diseases and its prevention among the general population. Therefore, better understanding of the genetic etiology of the diseases can facilitate early detection in high‐risk groups. General awareness should be raised by the government policies about cost‐effective genetic diseases and genetic counseling technique, and genetic therapy should be made affordable by the community level. To combat successfully with genetic disorders a group of equipped scientists, a greater collaboration and interdisciplinary work is required.

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