



Review Paper

Genetic Diseases in Cattle: A Review

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Abstract

Genetic disease is an illness caused by inborn abnormalities in genes or chromosomes, which are quite rare. The genetic diseases in dairy and beef cattle are tissue specific viz; Skeletal, central nervous system, blood, skin, muscle and ophthalmic. Some genetic diseases like Bovine leukocyte adhesion deficiency (BLAD) are breed specific and affecting significantly on economics of dairy farming. The various scientists had reported the frequency as 3.33% and 4.0% in Iranian Holstein-Friesian and Chinese Holstein cattle respectively. However, in India BLAD carrier was estimated as 3.23% in pure and crossbred Holstein-Friesian only. The details of these genetic diseases with special reference to its definition, genetic cause (DNA mutation) and its clinical symptoms are discussed in the review. In the modern era of animal breeding, Veterinary doctors, animal scientists, cattle breeders and livestock stakeholders should have the awareness of genetic diseases and their implications. The DNA testing is currently available for some of the genetic diseases; however it is necessary to develop it for all the genetic diseases so that breeding sires can be effectively screened for undesirable alleles and culled to avoid further propagation in breeding population. The information in the review can aid in investigating, reporting, treating and suggesting strategies for elimination of undesirable genes from breeding population.

Keywords: Genetic diseases, Dairy, Beef, Cattle.

Introduction

A genetic disease is an illness caused by inborn abnormalities in genes or chromosomes, which are quite uncommon and affect one animal in every several thousands or millions. A genetic disease may or may not be a heritable disease as some genetic disorders are passed down from the parent's genes, but others are always or almost always caused by new mutations or changes to the DNA. Most of them occur rarely and are of minor concern, but some increase in their frequency to the point that they become a significant economic concern and need to be selected against. The genetic diseases occur in all breeds of cattle however some defects are strongly associated with certain breeds ('Weaver Syndrome' in Brown Swiss). Around 200 different genetic defects have been identified in cattle. Genetic abnormalities contribute to poor animal performance, structural unsoundness, semi-lethal disease, or lethal disease etc.

The most common inheritance pattern of genetic disease is as a simple recessive trait. The defective calf receives a recessive gene from its sire and dam. A few inherited defects are known to be caused by genes with incomplete dominance and a few are caused by two or more sets of genes¹.

In cattle breeding, artificial insemination is widely used, carriers of genetic diseases are likely present within the population of breeding sires. It is suggested to screen breeding sires for

genetic diseases in order to avoid an unnecessary spread within the population². Currently DNA tests are available for genetic diseases like Citrullinemia and BLAD which can be diagnosed at very young age of animal based on PCR-RFLP marker which can aid to identify suspect cases and for screening of potential sires with undesirable alleles. Thus the testing of genetic diseases at young age will help in avoiding heavy economic losses which may have occurred due to the spread of faulty semen from breeding sires. Therefore it is necessary to study all the genetic diseases with its definition, genetic cause/base, clinical symptoms and frequency of occurrence in general to find out possible strategies to counter them and avoid economic losses due to these diseases in dairy and beef industry.

Classification

In depth review of available literature in public database helped in classifying genetic diseases in dairy and beef cattle. The genetic diseases are classified based on its frequency of occurrence in dairy cattle and beef cattle. The genetic diseases in dairy and beef cattle are tissue specific viz. Skeletal, central nervous system, blood, skin, muscle function disorder and ophthalmic tissues. The details of these genetic diseases with emphasis on its definition, genetic cause (DNA mutation) underlying the disease and its clinical symptoms are described as given below.

Table-1

Sr. No.	Specific Tissue	Dairy Cattle	Beef Cattle
1	Skeletal	a. Chondrodysplasia b. Complex Vertebral Malformation c. Osteogenesis Imperfecta d. Osteopetrosis e. Syndactylism	a. Osteopetrosis b. Arachnomelia c. Arthrogryposis Multiplex d. Congenital Contractural Arachnodactyly f. Syndactylism
2	Central Nervous System	a. Weaver Syndrome b. Spinal Dysmyelination c. Spinal Muscular Atrophy	a. Ideopathic Epilepsy b. Neuronal Ceroid Lipofuscinosis c. Hydrocephalus d. Spastic Paresis
3	Blood	a. BLAD b. Hereditary Zinc Deficiency c. Citrullinemia	Nil
4	Skin	a. Epitheliogenesis Imperfecta b. X-Linked Anhydrotic Ectodermal Dysplasia	a. Hypotrichosis
5	Muscle Function Disorder	Nil	a. Congenital Pseudomyotonia b. Crooked Tail Syndrome
6.	Ophthalmic	a. Anapthlmos and Microphthalmos b. Congenital Cataract c. Optic Nerve Colobomas	d. Anapthlmos and Microphthalmos e. Congenital Cataract f. Optic Nerve Colobomas

Genetic Diseases of Dairy Cattle

Skeletal Tissue: Chondrodysplasia: Chondrodysplasia is a congenital anomaly related to defects of the genes that control the chondrogenesis³. This disorder has been reported in many cattle breeds and around nine different genetic types have been recorded⁴. Three types of morphologically different forms on genetic basis have been recorded in Danish cattle: chondrodysplasia in the Dexter breed, chondrodysplasia in the Danish Red Dairy breed related to the sire *Thy Skov*, and chondrodysplasia in Danish Holstein related to the sire *Igale Masc*.

Clinically this disorder may show wide variation, but the main feature is reduced length of bones with an endochondral growth pattern. Some time death of the foetus and abortion also observed. This disease is further categorised into three different forms.

Complex Vertebral Malformation: The complex vertebral malformation (CVM) syndrome is a congenital disorder. The CVM is a lethal malformation syndrome, also observed in late term aborted foetuses and perinatal calves. This characterized in growth retardation and bilateral flexure of the carpal and metacarpophalangeal joints along with rotation of the digits⁵.

With the help of genomic analysis, it has been identified a single base substitution (guanine to thymine) at position 559 in the gene *SLC35A3* as the cause of CVM⁶. Affected calves possess this mutation in both alleles, indicating autosomal recessive nature of the disorder. This gene *SLC35A3* codes for a nucleotide-sugar transporter in which the base mutation is

reflected in an amino acid substitution at position 180 (valine to phenylalanine), hence it inhibits the function of the transporter. The nucleotide-sugar transporter plays an important role in mechanisms controlling the formation of vertebrae from the unsegmented paraxial mesoderm. Therefore, the defective transporter molecule leads to vertebral malformations^{7,8,9}. The genomic analysis has formed the basis for the development of commercially available genotyping tests.

Britt Berglund observed that Complex vertebral malformation (CVM) is an autosomal recessive inherited disorder in the Holstein breed¹⁰. It causes intra-uterine mortality through the entire gestation period leading to repeat breeding and involuntary culling of cows and thereby economic losses.

Berglund et al. observed 23% prevalence of CVM carriers in HF bulls. Ghanem and co-workers (2008) observed the frequency 13.0% were carriers in HF cattle. Schütz et al. (2008) reported 8.3% in 2002 and in the year of 2007 it is observed 2.3% CVM carriers¹¹. Meydan and co-workers (2010) observed the mutant allele frequencies were 0.017 with corresponding carrier prevalence of 3.4% CVM².

Osteogenesis Imperfecta: Osteogenesis imperfecta (OI) is a congenital collagenopathy of type I collagen. This is the most abundant and ubiquitous collagen which constitutes an important component of bone, tendons, ligaments, skin and teeth in mammals.

This type I collagen is a heterotrimer protein made by the two α 1(I) and one α 2(I) chains, which are coded by the *COL1A1* and *COL1A2* genes, respectively.

The OI in cattle is mainly observed by joint instability due to weakened tendons, ligaments and joint capsules leading to subluxation or luxation. A prominent impairment of bone strength causes foetal fractures as well as multiple acute fractures in newborn calves. Also, the hardness of the dentine is reduced, predisposing the animals to tooth fractures. Reduced strength of skin is not a major sign in bovine cases. Severely affected calves are growth retarded. The OI disorder is a lethal disorder^{12,13}. Biochemical changes have been found in Australian and North American cases, but the molecular basis has not been identified for any bovine cases¹⁴.

Osteopetrosis: Osteopetrosis (OS; Marble Bone) is a fatal autosomal recessive genetic defect previously identified in humans and a long list of animals. Affected known cattle breeds are Black and Red Angus, Hereford, Simmental, and Holstein. A deletion mutation in SLC4A2 gene located on chromosome 4 has been attributed to this disease manifesting in Aberdeen Angus¹⁵.

The affected calves with OS are born 10 to 30 days early. Usually they show the head abnormalities that consist of brachygnathia inferior, impacted molars, and a protruding tongue. The long bones are shorter along with marrow cavities are filled with unreabsorbed bone (primary spongiosa), but are very fragile and can be easily broken¹⁶.

Syndactylism: Syndactylism ('mulefoot') is a congenital malformation of the distal parts of one or more limbs characterised by complete or partial fusion or nondivision of the functional digits. The defect is due to the deletion and insertion of c.4863-4864delCGinsAT (p.Asn1621Lys; p.G1622C) and point mutation c.4940>T (p.Pro1647Lys)^{17,18}.

Typical cases of syndactylism are externally recognised by the presence of a single hoof-like structure instead of the normally paired claws. Sometimes dorsal midline groove may be present. The morphological variation reflects the underlying skeletal malformation. Thus, cases observed which shows narrow interdigital cleft and fusion of only the most proximal part of the claw capsules. This type of cases may remain unrecognised unless the digits are carefully inspected. Some extra morphological abnormalities, such as synostosis, may develop in other parts of the distal appendicular skeleton of affected limbs, for example, in metacarpal/ metatarsal bones and carpal/tarsal bones. Concomitant adaptive changes are found in the muscles, tendons, nerves and vascular supply of the distal limb¹⁹.

Central Nervous System Tissue

Weaver syndrome: Weaver syndrome is also known as bovine progressive degenerative myeloencephalopathy. It is most commonly observed in brown Swiss cattle. Mutations in EZH2 (Histone-lysine N-methyltransferase) cause Weaver syndrome.

Cattle experience weakness and a lack of coordination in all four limbs. The disorder is known as "Weaver Syndrome" because the animals have an odd weaving gait when they try to walk. The disease affects cattle when they are around six months of age and becomes progressively worse until the animal either dies or is killed. There is no treatment for the disease.

While Weaver has previously been mapped to *Bos taurus* autosome (BTA) 4:46–56 Mb and a diagnostic test based on the 6 microsatellite (MS) markers is commercially available²⁰.

Spinal Dysmyelination: Spinal dysmyelination is a disease which was reported to affects American brown Swiss cattle. The disease is apparent as the calf is born. The SPAST gene (BTA11), encoding the spastin protein is the affected gene of this disease. The defect is due to the missense mutation c.560G>A (p.Arg560Glu).

Sometime gross lesions are absent at necropsy, but some calves may shows muscular atrophy, and the cervical and thoracic spinal cord segments might seem decreased in size on transverse section. Main clinical findings are lateral recumbency with slight opisthotonos and spastic extension of the limbs^{21,22}. Occasionally, swollen axons and a few neurons with central chromatolysis are seen in the brain stem. Variable degrees of denervation atrophy may be present in the skeletal musculature²³.

Spinal Muscular Atrophy: Spinal Muscular Atrophy is a progressive lethal autosomal recessive disease. It is reported mainly in advanced backcrosses between American Brown Swiss and European Brown Cattle but it is also observed in Holstein-Friesian calves. The gene AFG3L2 respective for this disease was physically mapped to chromosome 24q24 using fluorescence in situ hybridization. Due to their different localizations AFG3L2 is not a positional for BSMA²⁴.

The condition is characterised by severe muscular atrophy, progressive quadriparesis and sternal recumbancy. The preliminary signs observed at 3rd to 4th weeks of age like symmetric weakness of the rear legs, locomotive difficulties and slight dyspnoea- appear. Animals usually look alert and have a good appetite and normal suckling reflex. Death occur after 2-4 weeks, usually as a consequent as a respiratory failure due to atrophy of the respiratory muscles. Bovine SMA is inherited as an autosomal recessive disorder and its gene has been mapped to distal part of chromosome 24. Now marker assisted tests are available in order to detect carriers of this undesirable gene.

Disorder related with Blood

Bovine Leukocyte Adhesion Deficiency (BLAD): Bovine leukocyte adhesion deficiency (BLAD) disease is immunological disorder. The disease is due to a single base

substitution of adenine with guanine at nucleotide 383 in the CD18 gene (*ITGB2*), which subsequently leads to replacement of aspartic acid with glycine at position 128 in the corresponding protein (D128G).

Clinically such individuals are more prone to recurrent and prolonged mucosal and epithelial infections^{25,26}. These animals shows signs of immunodeficiency, but the appearance of affected animals varies. The haematological changes in combination with stunted growth may be the only clinical sign of BLAD, at least at certain stages of disease development. Widespread ulcerative and necrotising, stomatitis, periodontitis, loss of teeth and alveolar periostitis are frequent lesions in the oral cavity. Extensive dermatophytosis may occur. Multifocal chronic ulcerative and necrotizing enteritis also observed, rhinitis and suppurative bronchopneumonia are frequent additional necropsy findings².

The perusal of literature regarding BLAD genetic disease in cattle has revealed the detailed information regarding BLAD defect in cattle. Nagahata H, (2004) studied about the genetic cause and nature of this disease and reported that BLAD is an autosomal recessive congenital disease reported in Holstein cattle and characterized by frequent bacterial infections, delayed wound healing and short growth, and is also accompanied with persistent marked neutrophilia.

The various scientists has worked on the BLAD and reported that the frequency in Iran Holslein-Freizan (HF) cattle is 3.33%²⁷, in Turkey the mutant allele frequency in HF were 0.02% and carrier prevalence were 4.0%, in Chinese Holstein cattle it is 0.49%²⁸. However, in India BLAD carrier was estimated as 3.23% in pure and crossbred HF²⁹ and 1.59% in AI bulls³⁰.

Congenital Erythropoietic Porphyria: Congenital erythropoietic porphyria (CEP) in cattle is an hereditary enzyme deficiency in the pathways of haeme biosynthesis. Haeme, which is a essential part of haemoglobin, is synthesised by a number of successive enzymatic steps, starting with the formation of d-aminolevulinic acid from glycine and succinyl-CoA, which is further metabolised to porphobilinogen. Porphobilinogen is consequently synthesised to uroporphyrinogen III by the action of two enzymes, uroporphyrinogen I synthetase and uroporphyrinogen III cosynthase^{31,32}.

The affected gene is UROS gene (BTA 26). This gene encodes the enzyme uroporphyrinogen III synthase³³. Clinically, the most prominent lesion is photosensitization, which may cause subepidermal blistering and dermal necrosis of unpigmented areas. These lesions are produced because of the photodynamic properties of the porphyrins deposited in the skin. These porphyrins absorb energy when exposed to ultraviolet light and become unstable. A typical lesion of CEP is diffuse systemic brown discoloration of bones and teeth.

Hereditary Zinc Deficiency: The “hereditary zinc deficiency” (HZD) refers to a fundamental aspect of this disorder and has been used in recent publications. This disease is generally caused by impaired intestinal zinc absorption due to abnormal function of a protein belonging to a family of zinc-uptake proteins. The molecular basis is a single nucleotide substitution in the gene *SLC39A4*. In acrodermatitis enteropathica, a human analogue of bovine HZD, defects in the gene *SLC39A4* have also been identified³⁴.

Clinically the lesions are mainly characterised by parakeratosis and dermatitis, and occur in areas of continual skin flexion or in regions particularly subjected to abrasion. Lesions are most wide around the mouth, eyes, base of the ear, joints, and lower parts of the thorax, abdomen and limbs³⁵.

Citrullinemia: Bovine citrullinemia is a unusual Holstein and Holstein-Friesian-specific metabolic genetic disorder of cattle worldwide^{36,37}. Similar to leukocyte adhesion deficiency and uridine monophosphate synthase deficiency, this inherited disease is autosomal recessive and breed specific³⁸. The inherited disorder results in a deficiency in argininosuccinate synthetase, leading to enzymatic disruption of the urea cycle. The mutation involves a single-base substitution (C-T) in exon 5 of argininosuccinate synthetase (ASS), which converts the CGA codon that codes for arginine-86 to TGA, a translational termination codon. This results in a shortened peptide product (85 amino acids instead of 412) depressed the functional activity.

Clinically, citrullinemia causes ammonemia (increased circulatory ammonia) and related neurological signs. Affected calves present with ataxia, aimless wandering, blindness, head pressing, convulsions and death.

The various scientist worked on the Citrullinemia and found the various frequencies like in U. S. an incidence of 0.3%; DNA sequencing showed that this bull was heterozygous for the translation-termination mutation described as the cause of bovine citrullinemia^{28,39} observed that Citrullinemia carrier frequency was 0.16 % in tested Chinese Holstein cattle.

Skin Tissue

Epitheliogenesis Imperfecta: Epitheliogenesis imperfecta (EI) is a inborn malformation characterized by local agenesis of the skin. Many types of this disorder are known. The classic form (type 1) is lethal and characterised by lack of skin on the distal parts of the limbs, deformed ears due to auricular epithelial defects, defects in the integument of the muzzle, and a defective oral epithelium. This defect may be related with defective metabolism of fibroblasts impairing the nutrition of the epithelium⁴⁰.

Clinically typical lesions present in the distal parts of the limbs, the muzzle, nostrils, and oral cavity. Also lesions were found at the base of the ear and the teats. The ears were not malformed.

X-Linked Anhydrotic Ectodermal Dysplasia: The X-Linked Anhydrotic Ectodermal Dysplasia is the X linked recessive disease. This disease is located on sex chromosome. The mainly affected gene is EDA gene, which encoding ectodysplasin A. It is a protein involved in the formation of hair follicles and tooth bud during fetal development. Also it is caused by a 19bp deletion in Exon 1⁴¹.

The major clinical findings in this particular disease are diffuse hairlessness and tooth abnormalities. Also reduced number of sweat glands are observed. Since the disorder follows the X linked recessive transmission, only males present the full form, whereas heterozygous females (carriers) are asymptomatic or show slight symptoms such as hypotrichosis and reduction in number of teeth^{42,43}.

Ophthalmic Tissue

Anophthalmos and Microphthalmos: It is the condition in which animals are born without eyes. And even when ocular tissue get devoid of an orbit, almost a vestigial ocular tissue can be found; these are some examples of extreme microphthalmos.

It is relatively a common disorder in the Japanese brown cow breed in which an ophthalmos is seen⁴⁴. Affected animals are born with a remnant of pigmented tissue situated deep in the orbit and also with caudal sacral and tail abnormalities. In such affected animals the orbit normally fails to develop. Thus an ophthalmic or severely microphthalmic animals have abnormally small orbits.

Congenital Cataract: Several reports have been documented of Congenital cataracts in cattle. The observed prevalence with as high as 34% in some herds⁴⁵. Cataracts related to the genetic defects and also some other ocular abnormalities such as retinal detachment, aniridia, microphakia, and hydrocephalus are observed. The microphthalmia and cataracts with retinal dysplasia have reported in calves exposed to bovine viral diarrhea in utero. Oxidative stress is a key feature of many forms of cataract, with oxidation causing cross-linking of thiol groups of lens crystallins with subsequent protein aggregation and cataract formation.

The association between cataract and proximity to telephone mast and electromagnetic field strength was statistically important, as was the association between cataract and intraocular oxidative stress as determined by the concentration of the protective antioxidant enzymes superoxide dismutase, catalase and glutathione peroxidase⁴⁶.

Optic Nerve Colobomas: Optic nerve coloboma was first described by Barnett and Ogien in 1972 in Charolais cattle and consequently reported by others also⁴⁷. The genetics of these lesions is somewhat curious: the autosomal dominant inheritance of the condition is completely penetrant in the bull but only incompletely penetrant (52%) in the cow, in fact recessive in F₁ crossbred animals⁴⁸.

Animals not seem to be particularly affected with regard to their vision, although clear assessment of bovine visual acuity is not readily accomplished in a farm environment. The colobomas are related with an abnormality in optic cup fissure closure, as demonstrated by their predominantly typical (i.e. ventral) appearance, but this occurs with the formation of a cystic defect, as often seen in optic nerve colobomas in other species⁴⁹.

The genetic diseases exhibited in ophthalmic tissue are also observed in beef cattle.

Genetic Diseases of Beef Cattle

Skeletal Tissue: Osteopetrosis: Osteopetrosis (OS; Marble Bone) is a fatal autosomal recessive genetic defect previously identified in humans and a long list of animals. Affected known cattle breeds are Black and Red Angus, Hereford, Simmental, and Holstein. A deletion mutation in SLC4A2 gene located on chromosome 4 has been attributed to this disease manifesting in Aberdeen Angus¹⁵.

The affected calves with OS are born 10 to 30 days early. Usually they show the head abnormalities that consist of brachygnathia inferior, impacted molars, and a protruding tongue. The long bones are shorter along with marrow cavities are filled with unreabsorbed bone (primary spongiosa), but are very fragile and can be easily broken¹⁶.

Arachnomelia: This disease is generally found in breeds like Brown, German Fleckvieh-Simmental cattle. The main cause of this defect is due to SUOX gene (BTA5) encoding molybdohemoprotein sulphite oxidase in Brown and deletion c.1224-1225delC (frameshift p.His24fsStop73). The defect is due to single base insertion c.363-364insG in exon 4 leading to premature stop (p.Ala124GlyfsStop42) in Brown cattle and deletion c.1224-1225delC (frameshift p.His24fsStop73) in Simmental cattle breed.

Facial deformities (short lower jaw and concave rounding of the dorsal profile of the maxilla), legs longer and thinner than normal (dolichostenomelia), severe angular deformities in the distal part of the hind legs (marked bilateral hyperextension of the fetlocks)^{51,52}.

Arthrogryposis Multiplex (Curly Calf Syndrome): This disease is generally found in Angus cattle. This defect caused due to autosomal recessive gene. Exact cause of the disease is due to the deletion of a section of DNA (at least 38,000 bp) that encompasses two different genes. The mutation results in no protein being produced (loss of function mutation).

The main clinical symptoms of this disease are bilaterally tibia (twisted rear leg with ankylosed joints). Some time abdominal hernia and cranial defect (cranioschisis with meningocele) are found⁴⁹.

Congenital Contractural Arachnodactyly (Fawn Calf Syndrome): This defect is found in breeds like Angus cattle. This type of syndrome is caused due to deletion of ~54,450 bp. The affected gene is not specified⁵³.

Clinically inherited proximal limb contracture, inherited distal limb hyperextension are observed. Along with that congenital kyphosis are observed. This findings decreases as calves grows and mature. The joints of newborn Congenital Contractural Arachnodactyly (CA) affected calves are actually hyperlax and the distal joints are hyperextensible. No neurological or neuropathological abnormality has been detected in CA affected calves.

Syndactylism: This disease is also found in beef cattle like Angus and Simmental. It is a congenital malformation of the distal parts of one or more limbs. This disease characterised by complete or partial fusion or nondivision of the functional digits. The main cause of the defect is point mutations 5385+1G>A at the first nucleotide in the splice donor site of intron 37 in Angus and two point mutations c.241G>A (p.Gly81Ser) + c.3595G>A (p.Gly1199Ser) in Simmental cattle breed.

Clinically this disorder observed by the presence of a single hoof-like structure instead of the normally paired claws. A dorsal midline groove may be present. The phenotypical structural variation shows the underlying skeletal malformation. The fusion or non division of the two developed digits of the foot are observed^{17, 18}.

Central Nervous System Tissue

Idiopathic Epilepsy: Idiopathic Epilepsy (IE) is a convulsive disorder caused by an autosomal recessive genetic defect and is incompatible with life. The IE is predominately seen in horned Herefords, but can be seen in polled Herefords with horned animals in their pedigrees. The first convulsion in affected calves can be observed anywhere from birth to several months of age and they have a “normal” phenotype when they are not seizing. Environmental stressors (heat, cold and weaning) can trigger the seizures and the seizures can last from minutes to more than an hour⁵⁴.

Neuronal Ceroid Lipofuscinosis: This disease is observed in Australian Devon cattle and the defect is due to single base duplication (c.662dupG in exon 4) causing a frame shift and premature termination (p.Arg221GlyfsStop6) which was predicted to result in a severely truncated protein.

Major signs of the disease are blindness, ataxia, seizures and accumulation of lysosome derived fluorescent storage bodies in neurons and most other cells. The vision defects observed in this disease may be due to degeneration of the retina or CNS⁵⁵.

Hydrocephalus: Hydrocephalus, or water in the brain, is a common inherited brain defect in beef cattle. The calves with hydrocephalus have excess fluid in their brain cavities. Neonatal calves are unable to stand or nurse, and most of them die either at birth or shortly afterward. They sometimes have domed heads and eye defects as well. The disease is prohibited by keeping carrier bulls from breeding with carrier females⁵⁶.

Spastic Paresis: This syndrome is generally found in the Belgian Blue, Simmental, Chianina etc of the beef breeds. The affected gene and type of defect is not known yet⁵⁷.

Major clinical findings are hyperextension of the hock with increase in tibio-tarsal angle. Severely affected legs might permanently held in extension and typical pendulum movement is observed.

Skin Tissue

Hypotrichosis (Hairlessness): Hairlessness occurs in some breeds of beef cattle. It expresses itself as complete or partial loss of hair. The affected gene is PMEL 17 (BTA5) encoding the premelanosome protein. Encoded protein enriched in melanosomes (melanin producing organelles in melanocytes). The defect is due to putative causative mutation: 3 bp deletion c.54delCTT in exon 1.

Calves are often born with no hair but with age it will grow like a short curly coat of hair. Calf generally having black diluted charcoal or chocolate coloured coat⁵⁸. Affected animals are prone to environmental stress (cold and wet) and skin infections are more prevalent. A recessive gene causes hairlessness⁵⁹.

Muscle Function Disorders

Congenital Pseudomyotonia: This defect is normally found in dual purpose breed Chianina. Now it is used for beef purpose. The defect is due to the missense mutation in c.491G>A in exon 6 (p.Arg164His).

Clinically exercise will generate muscle contracture which prevents animals from performing muscular activities⁶⁰. The clinical signs were characterized by an exercise induced muscle contraction that prohibited animals from performing muscular activities of greater intensity than a simple walk. When animal motivated to move faster, the muscles immediately became stiff and froze up temporarily inducing a gait. The stiffness disappeared as soon as exercise ceased⁶¹.

Crooked Tail Syndrome: It is the disease of beef cattle like Belgian Blue. The mainly affected gene is MRC2, encoding Endo180 protein. This defect is of two types i) Allele homogeneity in which deletion of c.2904-2905delAG (complete absence of transcripts) and ii) Allele heterogeneity in which point mutation c.1906T>C in exon 13 (p.Cys636Arg) are observed⁶².

The main clinical symptoms are retardation of growth, increased muscular development; tail deviation, stocky head, short straight limbs etc are observed. Along with that scoliosis and spastic paresis are found⁶³.

Strategies for Controlling Genetic Diseases: The best control of genetic diseases is to prevent animals that carry these genes by culling.

The bulls for natural service and Semen for A.I. should be screened for undesirable genes.

The purchase of bull or semen should be preferred from reputable breeders who maintain detailed pedigrees.

Modern genetic tools allow early diagnosis of disease and contribute significantly to improved animal disease control. Identification of undesirable genes by DNA testing and their elimination in a rapid and efficient manner to prevent further propagation in future generation and to avoid future economic losses.

Whenever there is birth of phenotypically abnormal calf, examine all symptoms and possible causes before concluding the problem is inherited or environmental. If problem is inherited the animal should be send for cytogenetic and molecular screening.

If the cause is genetic, inform the breed association/ society and give them a full report of the findings. Some progressive breed associations which are working to reduce the frequency of genetic abnormalities within their breed can take benefit of it for betterment of the breed. Treatment is usually unsuccessful; however symptomatic treatment can be given for relief up to certain limit.

Development of DNA based tests for all the genetic diseases will aid to identify the diseased animals very early in life, so as to prevent further propagation of undesirable alleles in future generations. Cytogenetic and Molecular genetic testing of every elite male and female carriers is must to prevent dissemination of undesirable, recessive lethal alleles of various genetic diseases.

A rigorous control systems and evidence-based program should be set up for accurate recording of carrier animals in the herd, which will ultimately lead to the prevention of recessive genetic diseases that appeared in cattle populations as part of selective breeding practices. Those will ensure that the appearance of recessive autosomal genetic disorders in cattle remains a manageable health problem for the foreseeable future.

Conclusion

The genetic disease causes the heavy losses because of poor animal performance; structural unsoundness reduces the production and reproductive potential of the animal. If genetic disease remains undetected, then it will get propagated from generation to generation continuously which will increase the occurrence of the undesirable genes in the breeding population affecting negatively on per animal productivity. Most of genetic diseases are recessive and rare still they affects economics of animal breeders and farmers in long run. Hence it is necessity to have awareness about the genetic diseases of cattle. In the last decade BLAD and Citrullinemia has become a disease of economic importance in the dairy industry and development of DNA tests for detecting them is helping us to check effectively the spread of undesirable genes of that disease in breeding population of dairy and beef cattle breeds.

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