Explor Anim Med Res.
Vol. 13, Issue 2, 2023
DOI: 10.52635/eamr/13.2.146-157

ISSN 2277-470X (Print), ISSN 2319-247X (Online)
Website: www.animalmedicalresearch.org

Review Article

GENETIC VARIATION IN HOST IMMUNE RESPONSE TO MAJOR INFECTIOUS DISEASES IN BOVINES AND ITS APPLICATION IN ANIMAL BREEDING : A REVIEW

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Received 02 December 2022, revised 24 August 2023

ABSTRACT: Livestock infectious diseases pose a significant threat to animal health and welfare on a worldwide scale, and efficient management of these diseases is essential for maintaining agronomic health, securing national and international food supply, and reducing rural poverty in developing nations. It is challenging to eliminate the negative effects of disease effectively, economically, and permanently in livestock because of the shortcomings and constraints of current non-selection disease management approaches (*e.g.*, vaccination, treatment, eradication strategy, and genome editing). Due to these shortcomings and restrictions, breeders are more interested and committed to addressing livestock health issues by selecting animals with favorable health traits. Selecting animals with specific health traits (such as disease tolerance, disease resistance, and immune response) can help to improve the health of livestock. Variability in host immune responses to infection plays a major role in host genetic variation in disease resistance. An approach can be employed as a strategy to fight infections by finding animals that are relatively immune or tolerant to diseases and revealing the inherent genetic variations in immune response at the molecular level. The accelerated and expanding understanding of genes and genomes in livestock, such as the evaluation of a broad number of DNA markers in phenotypic registered populations, could be used to identify and classify candidate genes responsible for variation in the immune response against major infectious diseases which would undoubtedly improve animal selection processes. Advancements in marker research could influence the selection programs if incorporated with the herd's genetic variant details as well as production traits. In this review, we have highlighted the genetic variation observed in host immune response to infectious diseases in bovines and its use in animal breeding for disease resistance.

Keywords: : Disease resistance, Susceptibility, Genetic variation, Animal breeding, SNPs.

INTRODUCTION

The national economy and socio-economic growth of a country growth largely depend on the livestock sector. With a total contribution of 6.17% of the total GVA of India (at current prices) and 30.87% of the GVA of the Agriculture and Allied sector [1], the livestock industry plays a significant role in the country's economy. It also contributes to household income, nutrition security, and employment in rural areas, especially for landless, small, and marginal farmers. India has the world's biggest livestock reserves and ranks first in livestock number (535.78 million) as per the latest (20th) livestock census.

However, the prevalence of various infectious diseases that result in significant economic losses through morbidity and mortality limits the productivity of the livestock and farmer's profit. Diseases have a significant impact on livestock performance as infected animals perform poorly, have higher medical expenses, and are more likely to die. Infectious diseases continue to limit livestock production and productivity despite government attempts to provide veterinary services

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through a network of physical and human infrastructure. The disease is one of the most significant biological factors that affect livestock productivity across a wide range of nations It occurs if there is a sufficient relationship between the host, pathogen, and environmental conditions (Fig. 1).

For several factors, infectious diseases are extremely important to livestock breeders as they impose a high cost on livestock production, with nearly all of them susceptible to disease [2]. Overall disease costs were reported to be up to 20% of revenue in developed countries and as high as 35-50% of revenue in the livestock industry in developing countries relying on direct costs of single diseases [3]. In India, a study conducted at IVRI [4] revealed that total losses due to mastitis per lactation in nondescript (ND) cows, crossbred (CB) cows, and buffalo were 868.34, 1,314.10, and 1,272.36 rupees, respectively. Total losses due to hemorrhagic septicaemia per animal in ND cows, CB cows, and buffaloes were 2,355.78, 3,228.52, and 4,262.57 rupees, respectively. Total losses due to surra per animal in ND cow, CB cow, and buffalo were INR 3,328.18, INR 6,193, and INR 9,872.33, respectively. Another study [5] reported that brucellosis infection in livestock results in economic losses of around Rs 9212 crores. The cost of treatment of infectious diseases increased for the development of resistance against the used drugs in bacteria [6, 7], parasites [8], fungi [9] and others. Investment of inadequate funds for the development of newer drugs [10] and the development of quick resistance to the drugs [11] are accelerating the problems.

The actual costs for disease, on the other hand, are complicated, including direct, indirect, and intangible costs that differ based on presumptions as to who is infected by the disease and the disease management steps [12]. Disease, for instance, can spread between organisms, and many of the other animal diseases, including bovine tuberculosis, are zoonotic concerns to human wellness, and pathogens in one species may serve as reservoirs for infections in another [13]. Endemic infectious diseases present specific problems because they are diseases for whom conventional disease prevention methods have failed due to their endemic status. Tick, nematode, and blood protozoa infestations, for example, are of global importance with widespread acaricide, anthelmintic or anti-protozoal drug resistance, correspondingly [2, 13].

Therefore, breeders and farmers are being challenged to choose livestock that is more disease-resistant and tolerant, as well as have higher healthcare levels. As a result, complementary and alternative controlling approaches are needed and one such strategy is breeding for enhanced infection or disease resistance in the host. However, as heterogeneity exists in host immune responses to infections, disease resistance between hosts is frequently genetically variable [14].

Comprehensive knowledge of the disease mechanism behind the observed symptoms of a disease is essential to initiate treatment or medication. Thus, there is a need to establish a sustainable system that offers a persuasive incentive for breeding to choose for disease resistance, such as anthelmintic resistance to nematode parasite problems, which is now prevalent in many countries with significant sheep industries (Fig. 1) [15]. A functional pipeline for the discovery of potential genome editing targets for disease resistance candidate genes or markers.

GENETIC VARIATION LINKED WITH MAJOR INFECTIOUS DISEASES IN BOVINES

Disease can be characterised as the negative effects of infection [13], whereas resistance is described as the host's ability to assert some control over the pathogen's life cycle [16]. The above broad description includes a variety of forms of a more resistant host species if possible (*e.g.*, less prone to getting infected, decreased pathogen multiplication as getting infected, reduction in shedding or spread of infection) and it also recognises that resistance is always relative rather than absolute. Tolerance can be characterised as the overall impact of a given degree of infection on the performance of an animal [16]. Resilience, a related term, can be described as an animal's productivity in the face of infection, whereas resistance means that the host has a negative impact on the pathogen's fitness [13].

With-in and between breed genetic variation in infectious disease resistance, such as bovine tuberculosis, brucellosis, paratuberculosis, mastitis, and FMD, has been well recorded and these evidences can be divided into three categories: variations between breeds or strains, associations with particular genes or genetic regions, and the presence of significant heritabilities [17]. Most of the research has focused on the first two areas. Major endemic diseases for which vaccination and other control techniques have failed to eradicate the disease have received a lot of attention. In developing countries, genetic disease resistance is especially important because indigenous

breeds are more resistant to local diseases than exotic breeds raised in a similar environment. Disease resistance is also a genetic trait due to within-breed variation, allowing for the selection of animals with improved disease resistance. Susceptibility to Bovine Tuberculosis (BTB), Somatic Cell Count (SCC), and MAP infection is estimated to be 0.18, 0.11, and 0.16 respectively [18], illustrating genetic variation for vulnerability to different infections in dairy cattle. When compared to Bos indicus cattle, the prevalence of bovine tuberculosis (bTB) and the intensity of its pathology were stated to be higher in Bos taurus and crossbreds [19]. Nellore breed's macrophages were found to be more effective than Holstein macrophages in controlling Brucella abortus intracellular survival [20]. Tick-borne tropical theileriosis resistance has been reported to be higher in Sahiwal cattle than in Holstein dairy cattle [21].

In Irish herds, the heritability of susceptibility to *M. bovis* PPD (purified protein derivative) was reported to be 0.2769, though, in British herds, the heritability of bTB susceptibility was estimated to be 0.18 [18]. Genes found in the ovine MHC class I and II regions are strong candidates for resistance because of their important role in antigen presentation to T cells and their relation to nematode resistance [22]. These promising results suggest that genetics may play a role in a broader risk management approach. Genes that code for protein playing a very special role in immune responses may be used to find resistant superior genotypes for the development of new resistant animal populations [23, 24]. Different genes/SNPs/ markers related to resistance/susceptibility to major infectious diseases in bovines have been listed in Table 1.

Brucellosis

Brucellosis is a serious bacterial zoonosis that affects animals and humans all over the world. Since Bruce's discovery in 1888, the disease has remained a global concern [25]. Brucellosis is caused by a group of gram-negative facultative intracellular bacteria of genus Brucella that causes abortion during the third trimester of pregnancy, which results in impaired fertility and decreased milk output in cows leading to significant economic losses and poses a significant zoonotic risk [26].

The (GT)13 microsatellite allele at the 3'UTR of the SLC11A1 gene was reported to have a stronger association with natural brucellosis resistance in cattle [27], while polymorphisms at the 3'UTR of the SLC11A1 gene were also found to have a stronger correlation with resistance/susceptibility to brucellosis in buffalo [28]. A study [29] used GenBank accession number AC149748 and already published findings [30] to identify novel genetic variants in exons of the SLC11A1 gene. Study using an in vitro macrophage challenge research, [31] demonstrated that the (GT) 13 allele inhibited Brucella intracellular replication. Genetic variants in other regions of the SLC11A1 gene, however, may be used as a marker [32]. Research [33, 34], on the other hand, found no connection between 3'UTR genetic variants and resistance to bovine brucellosis. Besides, TM4 is also known to aid in the localization of the NRAMP1 protein inside the phagosomal membrane [35].

According to a study [36], SNPs of the TLR gene, at the TLR4 (+10 C/T) locus, the frequency of the 'C' allele against the 'T' allele was considerably higher in brucellosis positive cattle, with an odds ratio of 4.73. Similarly, the TLR4 (+399 C/T) locus showed that in affected cattle, the frequency of the 'C' allele was slightly lower than that of the 'T' allele, with an odds ratio of 0.13. The findings also highlighted the significance of cytokines and accompanying receptors in imparting defence against brucellosis, indicating that these interactions need more functional characterization.

Bovine tuberculosis (bTB)

Bovine tuberculosis (a chronic bacterial disease) is caused by *M. bovis*, which is an obligate aerobic, facultative intracellular parasite, usually of macrophages that primarily involves the respiratory tract and is considered a zoonotic threat with considerable implications for public health. The disease has a negative impact on animal health and welfare, and it has put a significant financial strain on the dairy cattle industry worldwide due to the culling of infected animals, limits on animal movement, and the cost of control and eradication initiatives [10]. According to estimates, over 50 million cattle are infected with bovine tuberculosis (bTB) worldwide, which pushes livestock farmers through tremendous financial difficulty [37].

Genetic variation in susceptibility to bTB among cattle suggested that *Bos indicus* cattle are more robust than *Bos taurus* cattle [19]. Recent studies in Holstein cattle in the United Kingdom have also revealed substantial heritability to bTB susceptibility [18]. Studies have shown that polymorphisms in the SP110 nuclear body protein (SP110) gene are linked to tuberculosis [38]. bTB disease was mostly associated

with genetic variability in the bNRAMP1 gene [23]. Association of two single nucleotide polymorphisms (SNPs) and one microsatellite locus of the SLC11A1 gene with the occurrence of bovine tuberculosis manifestation (tuberculin reaction) in Indian cattle has been found, and, at rs109915208 locus, the genotypic and allelic frequencies varied significantly (p-value <0.05) in case-control animals where the odds ratios (OR) of the genotypes "CC" and "CT" and the alleles "C" and "T" were very high, suggesting that animals with the "CT" genotype and "T" allele were less susceptible to the tuberculin reaction than their contemporary genotype/allele [39]. Cattle with SNP g.11876(TG)1511903 had the lowest bTB incidents compared with cattle carrying SNP g.11876(TG)1311903 and SNP g.11876(TG)1611903 of the SLC11A1 gene [40].

In contrast to healthy controls, expression of candidate gene CXCR3 expression was significantly upregulated (5.22 fold) in PBMCs of *M. bovis* infected cattle [41]. In the case-control population, SNP loci rs210982793 and rs207807011 in the TLR9 gene were significantly correlated with susceptibility to bovine tuberculosis.

In cattle, the SNP locus rs55617172 in the TLR2 gene was found to be significantly ($p<0.01$) linked to susceptibility or resistance to tuberculosis [42]. A study was conducted using microarray analysis to identify TLR2, CD80, NFKB1, IL8, CXCL6, and ADORA3 as putative candidate genes based on differential gene expression in *Mycobacterium bovis* affected monocyte-derived macrophages of cattle, to determine the effect of four SNPs (G1793A, C1859A, A1980G, G1934A) in toll-like receptor 6 (TLR6) for a case-control analysis on bovine tuberculosis (bTB) resistance in Chinese Holstein cattle and found that genotypes AA or CA had a higher relative risk than genotype CC among bTB-infected and non-infected animals at the C1859A site, while genotypes GG or GA had a higher relative risk than genotype AA at the A1980G site [43]. T allele carriers, of -5C/T, G allele carriers of 613G/A, and carriers of TG haplotype from both SNPs in the CD14 gene in Chinese Holstein cows showed an increased BTB susceptibility, suggesting that -5C/T and 613G/A are possible causes for bTB in Chinese Holstein cattle, and could be used as candidate genetic markers in breeding cows with natural resistance to bTB [44]. According to the case-control study, the CARD15 gene variants E4 (-37)(C/T), 208(A/G), 1644(A/G), 1648(A/G), 1799(C/T), and E10 (+107)(A/G) were strongly linked to BTB susceptibility in Chinese Holstein cattle while The distribution of two haplotypes, TGGACA and CAGACA that showed significant differences between cases and controls could be used as genetic markers in marker-assisted breeding programs for breeding cows with high resistance to BTB [45].

Paratuberculosis

Mycobacterium avium subsp. Paratuberculosis (MAP) causes paratuberculosis, a chronic, progressive disease of ruminants' small intestine where the organism can live within macrophages. The primary symptom in cattle is severe malabsorption diarrhoea, which is accompanied by a decrease in milk output and body weight. In herds positive for MAP, the economic loss (due to decreased milk production, lower slaughter animal value, and premature death) has been estimated to be US $50 per cow [46]. The prevalence of paratuberculosis in herds varies by country, ranging from 0% to 71% of herds infected [47]. A Dutch study compared the heritability of paratuberculosis in vaccinated and unvaccinated cows, finding that the vaccinated cows had a heritability of 0.09, while the unvaccinated cows had a heritability of 0.10 [48]. SNP N23 of NRAMP1 (located in the BTA2 and containing 15 exons) was genetically linked with resistance to paratuberculosis infection [49].

A study investigated the occurrence of polymorphisms in the bovine CARD15 gene and their involvement with paratuberculosis infection in cattle, as well as an important correlation between infection level and the BoIFNGSNP12781 and SLC11A1-275-279-281 microsatellites [50]. Cattle with the CT and CC genotypes had 1.7 (95 % CI: 1.2, 2.8) times the likelihood of being MAP infected in contrast to cows with the TT genotype [51]. Using this genome-wide threshold [52], 22 SNPs on seven different chromosomes that were significantly linked to the disease trait were identified. SNPs in IL10RA have been linked to MAP infection in dairy cattle [53]. Four SNPs in IFNGR2, IL12RB1, IL12RB2, and IL23R are linked to the resource population's MAP infection status [54].

SNP (rs41945014) was shown to be strongly linked with MAP infection in cattle in a case-control association analysis carried out using 20 SNPs selected from the cattle QTL database based on their possible significance in mycobacterium susceptibility [55]. In *Mycobacterium avium* sub sp. Paratuberculosis infected cattle, differential expression of candidate genes of the Toll-like Receptors and Interleukins family, namely TLR2, IFN-γ, IL2, IL8, and TNF was identified [56].

Mastitis

Mastitis is an infectious condition that affects the mammary gland and causes inflammatory reactions as well as significant financial losses as milk production declines. Among the major infectious diseases posing a serious threat to Indian animal production systems, mastitis alone has a remarkably rising impact, where overall losses are estimated to be INR 71655.1 million including treatment costs, wasted milk, decreased milk production, and higher culling rates [57]. The multi etiology of mastitis is the main obstacle to controlling it.

Because of their role in mastitis, genes involved with mammary gland immune responses are possible genetic markers. Furthermore, genes involved with neutrophil activity may be used as genetic markers for mastitis, as neutrophil movement from the blood to the infection site is needed for most mastitis pathogens to be resolved [58].

Mastitis resistance appears to be a polygenic characteristic, based on somatic cell counts and mastitis genome scans [59]. However, genetic selection based on SNP chip technology looks to be a viable next

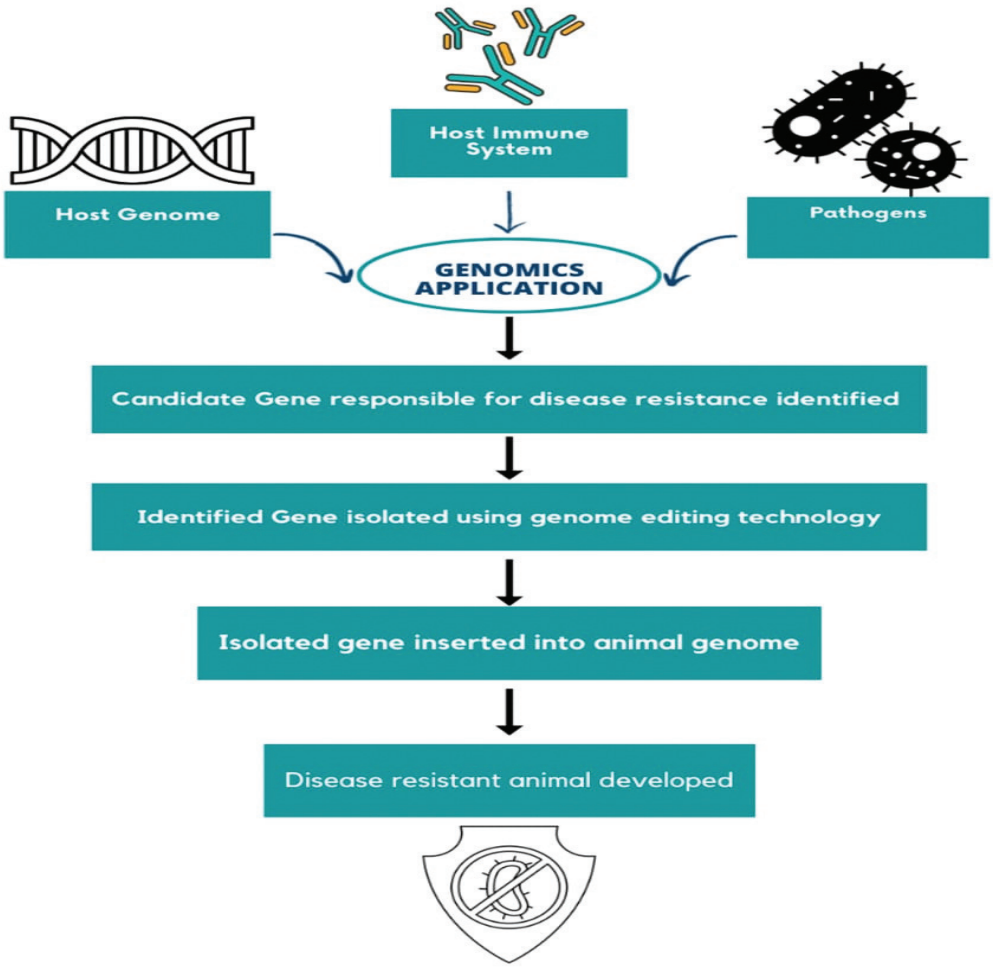

Fig. 1. A functional pipeline for the discovery of potential genome editing targets for disease resistance candidate genes/markers.

step, making precise predictions of mastitis resistance achievable [60]. Since the somatic cell count (SCC) has a higher heritability than mastitis (0.36 to 0.98) and a medium to high genetic correlation with mastitis (0.36 to 0.98), it is considered to be the best indicator trait for mastitis resistance [61, 62]. Although clinical mastitis has a low heritability and a negative association with production traits, selection for mastitis resistance is used in many countries [63, 64]. Using an *in vivo* infection model in uniparous dairy cows to see the effect of genetic selection for mastitis vulnerability under controlled conditions, substantial variations among the two genetically selected haplotype classes were identified [65]. Somatic cell count in sheep milk is invariably a heritable trait, with heritabilities often lying between 0.1 and 0.2 [66]. Evidence in goats indicates somatic cell heritabilities that could be higher than in sheep [67].

Table 1. Different genes/SNPs/Marker related to resistance/susceptibility to major infectious diseases in bovines.

Disease	Genetic loci	Species	Reference
Brucellosis			
NRAMP1/SLC11A1 gene	(GT)13 microsatellite allele at 3'UTR	Cattle	[27]
	3′ UTR, aa genotype	Buffalo	[28]
	3 UTR SSCP genotype	Cattle	[29]
	SLC11A1 (+1066 C/G)	Cattle	[36]
TLR1, TLR4 gene	TLR1 (+1446 C/A), TLR1 (+1380 G/A), TLR4 (+10 C/T), TLR4 (+399 C/T)	Cattle	[36]
Bovine tuberculosis (bTB)			
bNRAMP1/ SLC11A1gene	(rs109915208)	Cattle	[39]
	Alleles 211, 215 and 217	Cattle	[40]
TLR9 gene	(rs210982793 and rs207807011)	Cattle	[41]
TLR2 gene	(rs55617172)	Cattle	[42]
TLR6 gene	(C1859A, A1980G)	Cattle	[43]
CD14 gene	(5C/T, 613G/A)	Cattle	[44]
CARD15 gene	E4 (-37)(C/T), 208(A/G), 1644(A/G), 1648(A/G), 1799(C/T), and E10 (+107)(A/G)	Cattle	[45]
Para-tuberculosis			
TLR2 gene	1903 T/C SNP	Cattle	[48]
NRAMP1/ SLC11A1gene	(SNP N23)	Cattle	[49]
CARD15 gene,	SNP2197/C733R	Cattle	[50]
IL10RA (SNPs)	(984G > A, 1098C > T, 1269T > C and 1302A > G)	Cattle	[53]
IFNGR2, IL12RB1, IL12RB2, and IL23R		Cattle	[54]
Mastitis			
TLR4 gene	(+2021 C/T) locus	Cattle	[68]
	(+1656 C/T) and (+2021 C/T) loci	Cattle	[70]
	A-G SNP at nucleotide 4525 inside intron 1	Cattle	[73]
BRCA1 gene	(G22231T, T25025A, and C28300A)	Cattle	[71]
Markers DIK20, BM3 02, BM4505, CYP21 and BMS2684	-	Cattle	[76]
Markers BM1818 and BM1443	-	Cattle	[75]
Leptin gene	R4C and Sau3AI polymorphisms	Cattle	[77]
CXCR2 gene	SNP +777 genotype	Cattle	[74]
TLR-2, TNF-α, IL-8, IFN-γ and IL-10	-	Buffalo	[79]
MHC (BoLA)-DRB gene	DRB3.2*3 and *11	Cattle	[80]
Vitamin D-binding protein precursor (GC) and neuropeptide FF receptor 2 (NPFFR2)	(rs209323908)	Cattle	[81]
Foot and mouth disease			
BoLA-DRB3 gene	Allele Hae III A and Hae III C	Cattle	[86]
	0201, 0801 and 1501 alleles	Cattle	[89]
IFN-α/β	-	Swine	[87]
ITGB6 gene	SNP G29A mutation at 5’ UTR	Cattle	[88]

Mastitis was found to be substantially correlated with homozygous genotypes at the TLR4 (+2021 C/T) locus [68]. SNPs in cytokine genes (IFNG -639 T/C; IFNG +432 G/A; IFNGR1 +132 G/T; IFNGR1 +523 A/G) were found to have no major relations to somatic cell count and lactation timeliness [69]. In the Canadian Holstein population, polymorphisms in the TLR4 (+1656 C/T) and TLR4 (+2021 C/T) loci were linked to lactation persistency estimates and somatic cell ratings [70]. Using a combined genotype study of three SNPs in the bovine BRCA1 gene (G22231T, T25025A, and C28300A), the BBDDFF genotype was found to be associated with the highest SCS, indicating mastitis susceptibility [71]. The AACCEE genotype, on the other hand, was associated with the lowest SCS, which was beneficial for mastitis resistance. Using PCR-RFLP polymorphism in the BRCA1 SNPs, namely G22231T was identified. However, there was no substantial association with mastitis vulnerability in Vrindavani cattle [72]. A-G SNP at nucleotide 4525 inside intron 1 of the TLR4 gene, suggested that this variation could play a role in mastitis resistance in cattle [73]. The genotype CXCR2 SNP +777 was found to be significantly linked with the proportion of

Holstein cows with subclinical mastitis [74]. Depending on association with SCS [75], a major microsatellite marker allele influence on the risk of mastitis in Vrindavani crossbred cattle for markers BM1818 and BM1443 was discovered. For the markers, DIK20, BM3 02, BM4505, CYP21, and BMS2684 in crossbred cattle, significant marker alleles affecting the occurrence of mastitis based on the association with SCC were found [76].

The R4C and Sau3AI polymorphisms had a major impact on SCC ($p = 0.01$), with C and T as favourable alleles, respectively [77]. Selection for the R4C CC and Sau3AI TT animals can help reduce SCC in Jersey cattle, according to the findings. Buffalo and cattle sequences differ at positions 983, 1083, 1147, 1152, and 1221, with both SNPs being synonymous [78]. In PBMC of Crossbred, Murrah Buffalo and, Tharparkar Cattle, peptidoglycan and lipoteichoic acid triggered differential mRNA responses of immune-related TLR-2, TNF-α, IL-8, IFN-γ, and IL-10 genes were found [79]. The bovine MHC (BoLA)-DRB3.2*3 and *11 were linked with lower SCC, whereas alleles *22 and *23 were associated with higher SCC [80]. Studies have reported that the genes for the neuropeptide FF receptor 2 (NPFFR2) and vitamin D-binding protein precursor (GC) are promising candidates for affecting mastitis [81].

Foot and Mouth Disease

FMD is a highly infectious vesicular viral disease that affects domestic animals and even wild-toed ungulates. Fever, lameness, anorexia, and vesicles in and outside the mouth, teats and feet comprise the clinical features of FMD syndrome in ruminants. In India, FMDV serotypes O, A, and Asia-1 are all endemic, with more than 80% of FMD outbreaks accounted for O serotype [82]. As per the study, the annual total economic loss in India caused by FMD varies from INR 120,000 million to INR 140,000 million [83]. Many studies have established antigenic and genetic variants of FMDV in virus populations recovered from repeatedly infected cattle and buffalo through experiments [84] or natural field conditions [85]. Even though genetic variation within the host is normal during persistent infection, no consistent significant genetic changes linked to recurrent infection have been identified across studies.

A study using PCR-RFLP with the Hae III restriction enzyme revealed that allele Hae III A was linked to FMD susceptibility in Wanbei cattle, while Hae III C was linked to FMD resistance and may have a good protective effect against FMD [86]. In exon 2 of BoLA-DRB3, 89 amino acids were translated, with 13.70 % of nucleotides mutated, resulting in a 14.61 % amino acid shift, according to sequence analysis. It was discovered that Wanbei cattle could resist disease through mutations that resulted in changes in protein structure, allowing them to conduct cell control using various signalling channels in the long process of evolutionary adaptation. IFN-α/β is an appropriate candidate for promptly triggering FMDV resistance in animals [87]. The SNP G29A mutation in the 5'UTR of the ITGB6 gene (chromosome 2) was linked to zebu cattle resistance to FMD disease [88]. In crossbred cattle vaccinated for foot-and-mouth disease, DRB3 alleles 0201, 0801, and 1501 consistently ranked high for the defensive immune response while alleles 0701, 1103, and 1101 consistently ranked low for an uncontrolled immune response for all three serotypes of FMDV in cattle [89].

ROLE OF HOST GENETIC VARIATION IN ANIMAL BREEDING

One of the most significant biological factors that affect livestock productivity across a wide range of nations is disease. Animals are often selected for their excellent productivity to maximize the profits to the producer. Therefore, health characteristics are not given much consideration. Conversely, the prevalence of many infectious diseases, which pose great financial losses via morbidity and mortality, has impeded livestock production and farmer's incomes. A wider definition of breeding objectives includes enhanced functional characteristics like the health of the animal, feed intake and fertility, as well as higher productivity. Therefore, it is important to consider animals as an integral part of effective production processes while trying to set breeding objectives. Disease resistance should be perceived in breeding goals because it involves productivity constraints from monetary losses, the negative genetic correlation between productivity and disease, increasing customer demand for high-quality animal goods from healthy animals, improved antimicrobial drug resistance, biodiversity loss in native populations, and positive epidemiological reviews due to reduced disease transmission when the proportion of the resistant animal rise in the herd. Individual genetic variants for disease resistance do occur in animals, according to evidence. It has been observed that these changes are heritable and can be used to develop animals with higher disease resistance. The traditional methods for controlling disease include

immunization, treatment, isolating animals from pathogens, and eradication. Microorganisms frequently develop resistance to drugs and other substances, and some vaccinations are ineffective. A few of the numerous infectious diseases that affect livestock can be prevented by vaccines. Utilizing breeds or genotypes that are disease-resistant or tolerant and do not require expensive chemotherapy is therefore highly desired. The identification of genetic markers linked to disease resistance, especially resistance to major infectious diseases, is still being investigated. The strategy involves using Marker-Assisted Selection or genetic selection to choose animals free of the specific disease. Integrated research using quantitative and functional genomics, large-scale data collection (within and between breeds), and epidemiological prediction are modern techniques used by breeders to choose breeds for higher disease resistance.

CONCLUSION

Livestock is the main support system for any nation's dairy industry. The development of a dairy animal stock that is disease-resistant or immune-tolerant is currently underway. Efforts are in progress to develop a disease-resistant stock of dairy animals. The development of resistance to the synthetic drugs used in different healthcare purposes and demand for livestock products with lower levels of chemical residues and with the least effects on the environment has stimulated interest in disease control methods that are less reliant on chemotherapy. Interest in disease control strategies that rely less on chemotherapy has been sparked by drug resistance and consumer demands for products from livestock and the environment to have reduced amounts of chemical residues. There is a compelling rationale for incorporating genetic components into disease control techniques, especially considering the limitations placed on the viability of many other approaches. In terms of the diseases, breeds, and species investigated, research into the genetics of resistance and tolerance to livestock disease is quite limited. Breeds that became extinct before their disease-resistance traits were discovered will never again have access to genetic resources that could considerably enhance animal productivity and health.

ACKNOWLEDGEMENT

The author thanks all the reviewers for their expertise and assistance throughout all aspects of the manuscript writing.

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Cite this article as: Rani C, Chauhan A, Chauhan I, Vaishnav S, Ajay A, Saini T, Panda S, Gaur GK, Bhushan B. Genetic variation in host immune response to major infectious diseases in bovines and its application in animal breeding: a review. Explor Anim Med Res. 2023; 13(2), DOI: 10.52635/eamr/13.2.146-157.