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Gut Health and Immunity in Improving Poultry Production

Naga Raja Kumari Kallam and Veerasamy Sejian

Abstract

A healthy gastro intestinal system is important for poultry to achieve its maximum production potential. This paper aims gut health and immunity to improve production in the poultry sector. Genetics, Nutrition and Bio security are the factors influencing the production. Gut consisting of various pH and micro biota throughout is an advantageous feature to prevent infections. Various components like Goblet cells, paneth cells, endocrine cells and absorptive enterocytes, tight junctions, GALT and Mucus play a major role in gut health. Balanced diet with optimum carbohydrates, proteins, amino acids, minerals, vitamins, enzymes, organic acids and good management practices are important for improving production. Alteration in supplementation essential amino acids, Zn, Vit E, Se ... viz. are needed according to changes in environment and production state of the bird to develop good immunity. Stress free environment with fine hormonal balance are imperative for maximum output. Exploration of genes involved in resistant to food borne pathogens and research towards bio markers for gut health is the need of the hour. It can be concluded that good gut health and immunity play a key role in production. These can be achieved by maintaining birds with optimum nutrients and stress free environment.

Keywords: gut health, immunity, micro biota, poultry, production

1. Introduction

The emerging global agrarian crisis associated with the growing human population has signified the role of livestock sector in catering their nutritional demands. Among the livestock species, poultry sector has emerged as the fastest growing enterprise over the years with their significant contribution to the total animal protein production as well as consumption [1, 2]. Accompanying this growth, the poultry industry is faced with an enormous challenge to maintain the health and well-being of the birds.

1.1 Global significance of poultry production

Remarks of [3] indicate predicted human population by 2050 is 2097 millions means expecting addition of 877 million to the existing population of 1220 millions.

As of now the available eggs are 58no's, and meat is of 2.2 kg/capita/annum [4]. As per [4] report growth rate of poultry industry is 7.52% and 8.51% in broiler and layer respectively to cater the needs of animal protein demand. Conversely, the projected growth and production output was mainly depends on availability of quality feed ingredients, over and above the emerging and reemerging diseases.

The growth and development of poultry industry is crucial in sustaining the supply of safe, nutritious and good quality protein sources to balance the diet composition of humans. Productive performance of poultry had influenced by the host factors like: genetic background (bird species, type of bird, breed and sex), gut development and maturation (immune system, gut morphology and micro biota acquisition) and stress (environmental factors, type/form of feed, poor management, health interventions, litter management, nutrition). Gut health is a major concern and more complex with more than 640 different species of microbiota, over 20 hormones which digest and absorb the majority of the nutrients accounts 20% of energy utilisation [5]. It infers that factors fatal to gut certainly influences the nutrient intake as well as compromised output.

A healthy gastro intestinal tract (GIT) will be able to efficiently carry out activities viz. protection against insults (infectious and non-infectious), transport of ingested feed and digesta through the entire track, digestion, absorption process, hosting microbiota and excretion of undigested feed. Whereas, it may not be possible with a compromised GIT due to various deviations. Factors like nutrients/feed; microbiota and environment/stress will influence the functionality, integrity and health of gut.

1.2 Factors to be considered for good gut health

1. Environment factors: improper ventilation and temperature causes poor development and functioning of intestinal epithelium both in catabolism and absorption.
2. Bio security: poor management and improper bio security leads to the domination of pathogenic bacteria in the gut.
3. Nutrition: sudden change in feed, feed composition will affect the balance of gut microbes. Mycotoxins in the feed also damage the gut tissues.
4. Challenging situations like vaccination and disease out breaks.
5. Early Nutrition/brooding: making the feed available immediately after the hatch fastens the development of gut. Sub optimal management impairs the gut development and immune system.

Here in this chapter is an insight into the role of gut health and integrity, through their roles, in modulating bird's ability to be resilient towards the infections on immunity and production.

2. Importance of gut health

The immune and non-immune cells in the gut interact and help to provide intestinal protection, tolerance and homeostasis. In general, these components work in coordination with each other to maintain homeostasis as well as to prevent diseases, in turn maximise the utilisation of acquisition of dietary nutrients and further leads to improvement in production.

2.1 Gut health

Gut health influences nutrient assimilation, intestinal barrier and integrity, immune response and efficiency, inflammatory balance, susceptibility to enteric

pathogens. The livestock/poultry utilises several non –specific ways to maintain their health status. Lower pH of the gut and cilia in the respiratory tract is one among the additional barriers in this scenario to counter the pathogenic challenges.

2.2 Components of gut and functions

Gut consists of a single layer of epithelial cells and the underlying lamina propria, along with the immune cells and muscularis layers (**Figure 1**). Epithelial cells are in the top most place covered with mucin, include goblet cells, Paneth cells, entero endocrine cells.

2.2.1 Goblet cells and mucin

Mucous layers covering the epithelia secreted by Goblet cells, and act as a protective barrier, defending the underlying epithelium from damage and infection by pathogenic bacteria and acts as a substrate and fixing medium for communal bacteria [6]. Improper coverage of epithelial by mucous harbours more invasive to pathogenic microbes [7, 8]. Proper nutrition is important for good mucus production and gut immunity to prevent colonisation of infectious microbes.

2.2.2 Paneth cells

It plays an important immune defence role in the intestine, particularly relating to production of host defence peptides (HDPs), repair of intestinal epithelium especially during damage/inflammation. Paneth cells are majorly located in small intestine crypts. Along with goblets cells, entero ednocrines these will form tight junction. Tight junctions are nothing but multiprotein complexes, form a continuous intercellular barrier between epithelial cells and regular para cellular

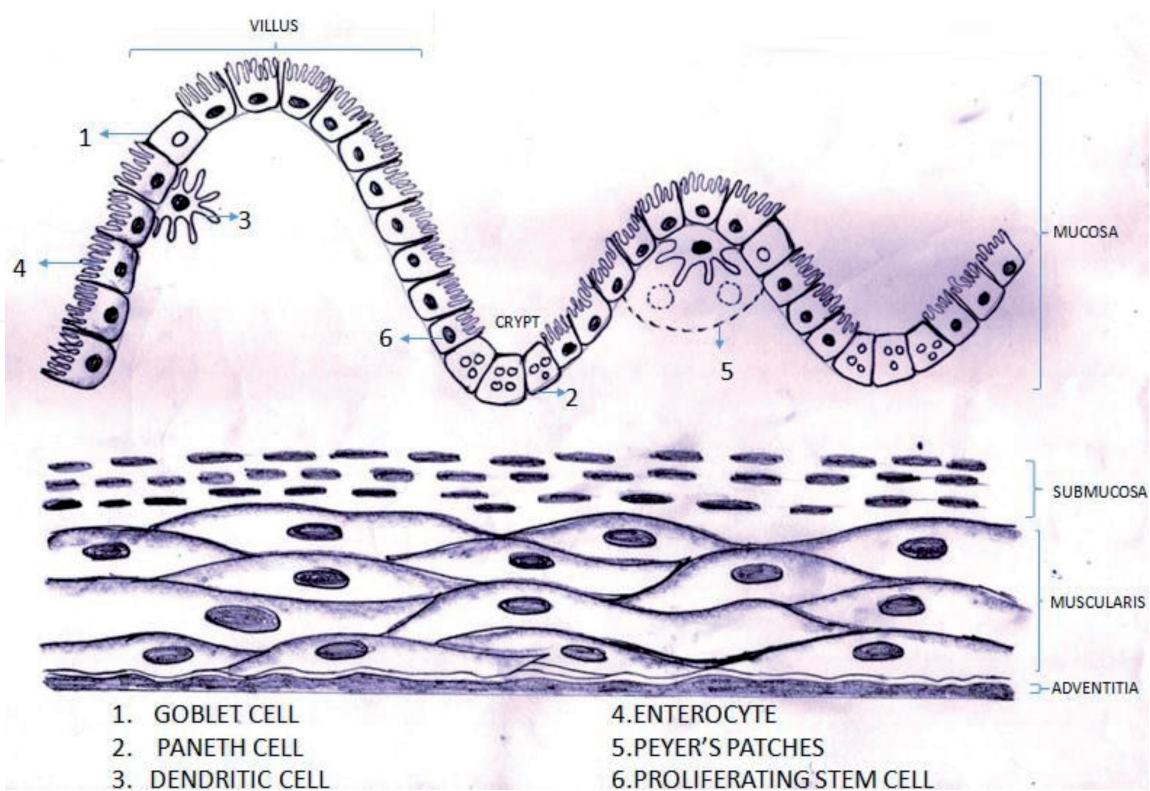


Figure 1.
Cross section of small intestine.

permeability. More number of Paneth cells are presents at small intestine crypts i.e. Crypts of Lienerkuhn. These consist of ER, Golgi network and large granules produce HDPs viz. α -defensins/cryptdins, secretory phospholipase A₂ and lysozyme.

Antimicrobial peptides or immune modulators released from the Paneth cells protect the host from enteric pathogens. The glycosidase secreted from the paneth cells named Lysozyme, which hydrolyses peptidoglycan and is one of the major components of the bacterial cell wall. Lysozyme also observed in gastric and small intestinal secretions, as well as in the granules of macrophages and neutrophils and the G₂-type, which is identified in the small intestine, liver, and kidney [9]. In the gastrointestinal tract, lysozyme C is expressed in the gastric and pyloric glands, duodenal Brunner's glands, and in the Paneth cells.

2.2.3 Enteroendocrine cells

Even though they are less in number, compared to other intestinal epithelial cell population (about 1%). In response to chemical/mechanical stimuli these cells secretes a variety of hormones viz. GLP-1, GLP-2, PYY, CCK and serotonin. These play a very important role in birds while regulating hormone secretion, gastrointestinal enzymatic activity, and feeding behaviour.

2.2.4 Lamina propria

Lamina propria is a loose connective tissue. Consist of dendritic cells, macrophages, heterophills, natural killer cells immune cells like T and B cells and intra epithelial lymphocytes.

2.2.5 Microbiota

Microbiota forms a protective layer by attaching to the epithelial walls of enterocyte and minimise the options for the colonisation of pathogenic bacteria by competitive exclusion. Microbiota plays an important role in production of Short chain fatty acids, organic acids, vitamins (B group and K), bacteriocins (Antimicrobial property), lower triglycerides finally induce non pathogenic responses which give both nutrition and immunity to the bird [10, 11]. Incontrast some of the pathogenic bacteria like Salmonella and camphylobacter which may circulated to humans while consumption may act as a pool for antibiotic resistance and transmission which is having more public health concern [12].

The chicken gut microbiota (**Figure 2**) includes hundreds of bacterial species dominated at the phylum level by Firmicutes (*Lactobacillus*, *Clostridium*, *Ruminococcus*, *Turicibacter*), Bacteroidetes (*Flavibacterium*, *Fusobacterium*), Proteobacteria (*Enterobacter*) and Actinobacteria(*Bifidobacterium*). The microbial communities differ throughout the chickens GIT with particular microbial profiles have been detected in crop, gizzard, ileum, cecum and colon of chickens.

Functional output of microbiota includes production of SCFAs [13–15] added metabolic potential and competitive exclusion of pathogens by decreasing the pH. Lactic acid bacteria (LAB) favour renewal and barrier function of the gastrointestinal epithelium by SCFAs production [16].

Fatty acids produced from microbiota plays an important role. Among the SCFAs acetate is produced more followed by propionate and butyrate. Even though less amount of butyric acid is produced it acts as a source of energy for colonic epithelia and helps in maintaining homeostasis at colonocytes and further helps in good morphometry. Functions like enterocyte growth and proliferation, mucin production, intestinal blood flow, intestinal immune response are influenced by the SCFAs.

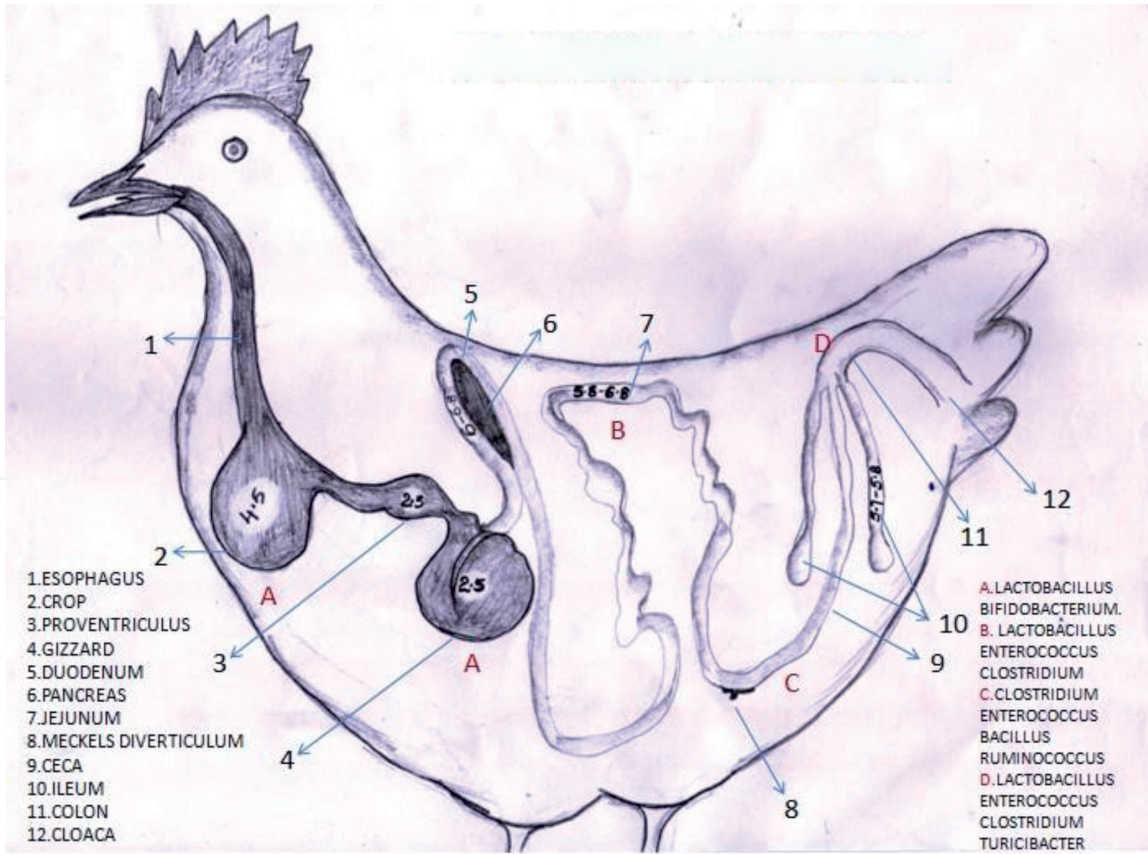


Figure 2.
Microbiota in gut of fowl.

An imbalanced microbes in the gut is termed as Dysbiosis, this imbalance is majorly due to stress, change in nutrition and infections which alters immune system. It causes a sequential reaction in the GIT, including reduced intestinal barrier function (e.g., thinning of intestinal wall) and poor nutrient digestibility, and therefore, increasing the risk of bacterial translocation and inflammatory responses [17]. The severity of dysbiosis varies depending on situation but it is generally characterised by loose and foamy caecal droppings. Post-mortem examination of affected birds reveals thinning of the gut wall along with gassy and watery gut contents.

Proper bacterial balance i.e. at least 85% of total bacteria should be good bacteria is vital for the host, and the impact on gut health often comes from microbial imbalance in the gut of chicken [18].

In micobiota phylum Bacteroidetes (i.e., *Bacteroides fragilis*) associated with production of IL-17 producing T cells [19]. Lactobacillus group of commensal bacteria stimulate intestinal immune system and increase the resistance to diseases, as part of that brings about release a low molecular weight peptides [20].

2.3 Activities in gut

Anti microbial peptides (AMPs) and Ig A are secreted in the gut by the epithelial cells [12]. Mucus layer protects the epithelium and acts as a first line of defence against infection. Small intestine goblet cells in chicks starts functioning in the late embryonic and post hatch period and can be observed by 17th day of incubation. At that time the produced mucin is of acidic in nature. Whereas, until day 7 after post hatch the same goblet cells produce both acidic and neutral mucin. Later age onwards expansion of goblet cell number towards ileal axis get initiated [19].

3. Factors influencing gut health

3.1 Nutrients in relation to gut development & Health

In diet certain nutrients play a crucial role in metabolism, absorption as well as participate in maintain gut health and homeostasis. In diet ingredient quantity, quality, form, type, processing method, additive types..etc. play a dynamic role in maintain gut microbiota and integrity [20]. Some of the reports regarding application of nutrients more than recommendation and its impact on gut health was presented in **Table 1**.

3.1.1 Carbohydrates

Production of molecules involved in defecation mechanism like monocytes and heterophils, Ig, nitric oxide, lysozyme, communication molecules (eicosanoids, cytokines, and clonal proliferation of antigen-driven lymphocytes) are depending on availability of energy, amino acids, enzyme co factors etc. [20].

Energy from carbohydrate source is the best choice since immunological stress is known to impair triglyceride clearance from the blood, thus decreasing fat utilisation. Ingredients of plant origin contain considerable amounts of fibre (non-starch polysaccharides, NSP, plus lignin), with the majority being insoluble which has various roles in improving gut health, enhancing nutrient digestion and modulating the behaviour of animals. It is postulated that monogastric animals have a 'fibre requirement' because their gut development requires physical stimulation by hard, solid particles of feed [34].

3.1.2 Proteins and amino acids

Using dietary protein intake as an example, at elevated temperatures, digestion and absorption are altered, favouring protein catabolism, and subsequently a reduction in protein synthesis and deposition [35]. Kumari et al., [36] reported that low protein diets (17 vs. 15.58 & 13.4%) for layers supplemented with ideal amino acid lysine @ 0.70% at high temperature (32°C) from 25 to 36 weeks of age is essential for better performance on par with 17% protein in diet. However, Temim et al. [37] reported that high protein diets (28 and 33%) improved the performance when compared to low protein diets (20%) in broiler chicks. Burkholder et al. [38] noticed that stress conditions either due to high temperatures or due to fasting for more than 24 hrs, changes in microbial population and increased attachment or colonisation of pathogenic bacteria like salmonella.

Role of some amino acids (Glutamine, Arginine, Threonine and Cysteine) on the integrity, growth, and development of the intestinal epithelium, gene expression, cell signalling, antioxidative responses, and their associated immune functions have been investigated by [39–42].

Digestion and absorption are influenced by gut health and villi length especially infections which damages the epithelia during such situation supplementation of amino acids favours the production of SCFAs which improves the immunity [43, 44].

3.1.3 Minerals

Research findings inferred that the role of trace minerals in maintaining the intestinal health supports anti oxidant system, balancing micro biota and repair. Shanon and Hill [45] reported importance of copper in growth and mechanism of gut, high concentration of Zn prevents proliferation of pathogenic (cystotridum and E.coli) bacteria.

Strain/type application	Biological activity	Reference
Probiotics		
<i>L.reuteri</i> , <i>L.gallinarum</i> , <i>L.brevis</i> , <i>L.salivarius</i>	Lactobacillus and bifido bacter population is increased and E.coli counts are decreased in caeca.	Mookiah et al. [21]
<i>L. acidophilus</i>	Induced T-helper-1 cytokines in caecal tonsil cells	Brisbin et al. [22]
<i>L. salivarius</i>	Induced anti-inflammatory responses (interleukin [IL]-10 and transforming growth factor [TGF]-b) in caecal tonsil cells	
<i>L.plantarum</i> , <i>L.bulgaricus</i> , <i>L.acidophilus</i> , <i>L.rhamnosus</i> , <i>B.bifidum</i> , <i>S.thermophilus</i> , <i>E. faecium</i> , <i>A. oryzae</i> and <i>C. pintolopessi</i>	Increased antibody titre against Newcastle disease (ND). Increased the geometric means haemagglutination inhibition (HI) titres of birds	Khan et al. [23]
<i>Saccharomyces boulardii</i>	Increase in intestinal villus height and crypt depth in the jejunum and ileum and goblet cell number.	Naga Raja Kumari and Susmita [24]
Prebiotics		
FOS	Provided nutrients for the growth of beneficial bacteria in the gut	Alloui et al. [25]
Inulin	Increased bifidobacterium counts and decreased <i>E. coli</i> counts in caecal contents	Nabizadeh [26]
GOS	Increased Bifidobacterium spp. and decreased Campylobacter spp. in the faecal samples	Baffoni et al., [27]
IMO	Increased the caecal populations of lactobacilli and bifidobacteria and decreased the caecal <i>E. coli</i>	Mookiah et al. [21]
Fibregum and Raftifeed-IPE	Increased serum concentration of IgA and IgM, and enhanced systemic immune capacity in chickens	Vidanarachchi et al. [28]
Prebiotic-based MOS and b-glucan	Increased the relative weight of spleen, decreased the heterophil-to-lymphocyte ratio and increased antibody titres against <i>S. enteritidis</i>	Sadeghi et al. [29]
Symbiotics		
Commercial synbiotics (BiominiMo)	Increased the LAB population and reduced <i>E. coli</i> and total coliform populations in the intestine	Amerah et al. [30]
Bifidobacterium-based symbiotic product	Reduced <i>C. jejuni</i> concentration in poultry faeces	Baffoni et al., [27]

Strain/type application	Biological activity	Reference
Synbiotic 11 Lactobacillus strains plus IMO	Increased the caecal populations of lactobacilli and bifidobacteria and decreased the caecal E. coli	Mookiah et al. [21]
Exo genous enzymes		
Carbohydrase	Increased the proportion of lactic and organic acids, reduced ammonia production, and increased VFA concentration through hydrolysis fragmentation of NSP and supporting growth of beneficial bacteria.	Adeola and Cowieson [31]
Xylanase	Minimise the counts of Salmonella	Amerah et al. [30]
Exogenous enzymes	change in the gut microbial populations increased immunity	Bedford and Cowieson [32]
Xylanase	Reduced crypt depth of jejunum	Yang et al. [33]

Table 1.
Results of some of the works in application of additives in poultry diets.

Whereas, Baxter et al. [46] inferred that chelated minerals and EAA at optimum concentration in diet has great influence on gut health especially during heat stress.

Zn in the form of ZnO protects the intestinal cell from E.Coli infestation, inhibits adhesion and internalisation of bacteria, prevents the commotion of barrier integrity, and modulates cytokine gene expression [47].

Several elements in diet have been shown to have a negative effect on the immunological response in the bird when they are deficient in the diet. Several studies revealed that adequate levels of Zn supplementation (between 50 and 70 mg/kg) in poultry diet have been shown to minimise the impact of oxidative damage in the intestine of broilers under stress [48, 49]. Zinc is especially important in wound healing, thymic function and proliferation of lymphocytes. Growth depression usually observed due to catabolic response during nutritional stress induced immune stimulation.

3.1.4 Vitamins

Vitamin E appears to be an immune system “booster” and by inhibiting the synthesis of prostaglandins [50].

Vitamin A deficiency [51, 52] and excess [52, 53] have been shown to depress immune responses in chicks. Most research suggests that vitamin A deficiency is associated with reduced cellular immune responses whereas; vitamin A excess impairs antibody responses.

To reduce stress in the form of vaccination/handling/environment boosting the diet with B vitamins, fat-soluble vitamins (A, D, and E), and electrolytes in drinking water are helpful in antibody production and also to reduce mortality from the stress [54].

3.1.5 Probiotics

Feed microbials are used to colonies in the intestine with microbes of desirable attributes that can promote competitive exclusion and/or promote beneficial gut barrier and immune function. Choice of in feed eubiotic additives in diets have positive influence on intestinal microila community and to improve the birds immune system [55–57].

Commonly used probiotics species at poultry industry are LAB, i.e., *Lactobacillus bulgaricus*, *L.acidophilus*, *L.casei*, *L.helveticus*, *L.lactis*, *L.salivarius*, *L.plantarum*, *Streptococcus thermophilus*, *Enterococcus faecium*, *E. faecalis*, *Bifidobacterium spp.*, [55, 58].

3.1.6 Prebiotics

Prebiotics are non digestible feed ingredients acts as a substrates for microbes, can helps in shaping the gut microbiome and, in turn, developing the immune capabilities [57, 59]. Prebiotics provide nutrients for endogenous favourable bacteria like bifido acteris and LAB and improves host microbiota balance [57]. Oligosaccharides (inulin, fructooligosaccharides (FOS), mannanoligosaccharides (MOS), galactooligosaccharides (GOS), soya-oligosaccharides (SOS), xylo-oligosaccharides (XOS)) pyrodextrins, isomaltooligosaccharides (IMO) and lactulose..etc. [25, 59, 60] are commonly used prebiotic in poultry.

3.1.7 Synbiotics

A combination of probiotic(s) and prebiotic(s), which attempts in providing favourable microorganism(s) along with a nutrient source.

3.1.8 Exogenous enzymes

Alter the availability of nutrients from the substrates and increase the digesta viscosity. Poultry rations are mainly based on ingredients of palnt origin with more phytate phosphorus, to make use of P from the source phytase enzyme are normally used, apart from this proteases, NSPases are very common [61]. Various exogenous enzymes including b-glucanase, xylanase, amylase, a-galactosidase, protease, lipase, phytase, etc. have been supplemented in poultry diets for decades [31, 32].

3.1.9 Phytobiotics

Phytobiotics are the compounds (terpenoids, phenolics, glycosides and alkaloids etc.) derived from the plants, which posses antimicrobial and some functional properties [59, 62]. Some of the phytobitics enhance the growth of useful bacteria like LAB in gut, improves immunity, protects intestinal cells by altering the membrane permeability [63, 64].

3.1.10 Organic acids

Butyric acid, Lactic, acetic, tannic, fumaric, propionic, caprylic acids, etc. comes under this category, which had antimicrobial properties, enhance gut structure and alter pathogen gene expression and enhance the performance of birds [65, 66].

3.1.11 Polyunsaturated fatty acids

Fish oil and corn oil are the main source of n-3 fatty acids and n-6 fatty acids, respectively in poultry diets and improves the body's function and immunity [56].

3.1.12 Mycotoxin mitigation

This limits intestinal damage and suppression of immune responses for application in the gut health arena.

3.2 Immune system in relation to gut health

Genetically superior birds are in immunologically stress full condition which creating pressure in the producers due to ban of antibiotic growth promoters. This creates tremendous pressure on immune system of the birds by various vaccination schedules.

Feed deprivation at early stage of life delays the development of mucosallayers and process of mucin synthesis in chicks [67].

3.2.1 Position of lymphoid tissues associated with mucosa and spread in different organs: mainly GALT

(Gut associated Lymphoid Tissue): Meckels diverticulum, Payers patches (Intestinal wall), Oesophagus –proventriculus junction, caecal tonsils. Additionally, gallbladder, liver, pancreas, kidney and oviduct are also having some role in protection and immune competence in birds [67].

Gut is the key immunocological organ comprises of myeloid and lymphoid cells [68] with its associated structures it forms a site for production of many immune cell types that needed for initiate and mediate immunity.

Immune system in gut depends on microbiota and maturation of the system eliciting by antigen-specific responses mainly influenced by dendritic cells [69]. The non invasive microbes initiates the production of IgA, which controls the host commensal interaction by both impacting commensal gene expression in the lumen and preventing adhesion of commensal bacteria to the epithelial surfaces [70].

3.2.2 Interrelationship between nutrition and immunity

Poultry encounter numerous stressors during their lives. Alterations in feed intake, poor FCR, varied nutrient metabolism, suppressed immune system are the consequences due to stress [71]. To overcome stress birds defence system prioritise the nutrient utilisation during challenge period [72].

Birds immune system get affected by nutrition in several ways [73] like.

- a. Development of lymphoid tissues.
- b. Mucus Secretion by goblet cells.
- c. Production of immunologically active substances.
- d. Cellular proliferation and activation
- e. Intracellular killing of pathogens.

4. Stress

Another important factor influences the suppression of immunity as well as production is stress [48]. It may be due to environment (other than comfort zone), diet, vaccination- and medication, microflora imbalance, as well as a result of pathogen or parasitic load [74]. Disruption of gut function may occur and imbalance between production and elimination of ROS is a common phenomenon during stress [48]. Excess ROS in intestine causes destruction of PUFA in the cell membrane and leads to production of peroxides (malondialdehyde) which ruin the intestinal integrity [40]. A compromised epithelium creates a good opportunity for opportunistic pathogens, in addition to this dietary deficiencies in certain nutrients can increase the stress-induced susceptibility of poultry to oxidative stress [48, 49, 75, 76]. The outcome of this is an economic loss to the producer. Improper management makes the poultry exposure to disease causing agents, stress, and Meagre immunity, birds prone to less production or even death [76]. Increased feed efficiency and gut integrity was noticed [77] during in vitro experiments by addition of *Lactobacillus* species which produced bacteriocin Reuterin that might inhibit the growth of *Salmonella*, *Shigella*, *Clostridium* and *Listeria*.

5. Endocrine regulation of gut health in poultry

Intestinal microbiota structure and function plays a crucial role in health and production of poultry. The micro biota modulates the intestinal homeostasis, integrity and are essential for good out put [78].

Two types of signals produced by the gastrointestinal tract which influence the feeding behaviour and feed intake, which were in turn influenced by ghrelin, CCK, GLP-1, GLP-2 and PYY and these are released from the intestines and transmit satiety signals to the brain after food intake, resulting in the suppression of appetite [78].

6. Genes that govern gut health and immunity

Genes present in the body will regulate all the activities in the body including gut, but in gut, genes do not have any role without the microbiota [78]. It is considered that microbiota will regulate the activity of genes in the gut. The microbiota present in the gut mainly defines the gut condition whether it is in good condition or not [79].

The main target of Nutrients to alter the activity of genes and results in more activation of good genes and suppresses the activity of bad ones. Through nutrigenomics careful selection of nutrients for fine-tuning genes and DNA present in every cell and every tissue of an animal is possible stated in the review [80]. In **Table 2** results of some the researches were presented regarding influence of nutrients on gene expression.

Jiang et al. [86] reported variations in expression pattern of hepatic genes apolipoprotein A-I (ApoA-I) and apolipoprotein B (Apo B) with varying amount of nicotinic acid in feed indicates the lipid metabolism. Addition of prebiotics like mannan oligosaccharides (MOS) to broiler diets increases the expression of mucin, and down-regulates selected genes involved in cell turnover and proliferation [78]. Delay in feeding immediately after hatch alters the hepatic gene expression [87]. Nutrigenomics provides a way to identify precisely which nutrient or nutrient combinations that is optimal to elicit maximum benefits [79].

	Gene expression	Reference
Immunomodulators like Corticosterone, ascorbic acid and 1,3–1,6 β-glucans.	Cytokine gene expression (ILreceptors 4 and 15) in spleen-1β, IL-2,toll-like.	Kumar et al. [81]
MOS	Expression of 77 protein synthesis gene, including superoxide dismutase 1, lumican, β 2-microglobulin, apolipoprotein A-1, fibronectin 1 etc.	Xiao et al. [82]
High and low nutrients (HN and LN)	The gene expressions of Rheb, TOR, S6K1 and 4E-BP1 in muscle were the highest in the WYFC fed with LN diets.	Wang et al. [83]
Lead	Down regulation of all sugar, peptide and amino acid transporters. Up regulation of stress related genes.	Ebrahimi et al. [84]
Low protein (13.46% CP and 0.65% lysine at 66% threonine) diets at peak production in layers	Up regulation of MUC2 expression	Kumari et al. [85]

Table 2.
Gene expression related to nutrition in chicken.

Nutrigenomics is an emerging science which would reveals the diseases induced by nutrient availability or alteration in diets [88]. For sustainable poultry production there is an emerging need to trace the relationship between economic traits and dietary regimen [57].

Among the different diseases occurring in poultry, those caused by the genus *Salmonella* is the most common, causing serious economic losses to the poultry industry in terms of mortality, reduced growth and loss of egg production [89].

Some of the works [29] inferred that MHC-B haplotypes reactions were different towards genetic resistance against salmonellosis. Resistance to salmonella was linked to ILs, IFN γ , TLRs, iNO and apoptosis genes, and expression of IL-2, IL-6, IL-8 and IFN γ genes was higher, microsatellite analysis inferred [90] that MHC-1class was linked to colonisation to salmonella. Ocak et al. [91] noticed salmonella at genus level by PCR-RV, and ST at serovar level.

7. Bio markers

Determination of biomarkers to know the intestinal health is important breakthrough. Inflammation is the first sign of infection or injury to the system [92].

Baxter et al., [46] reported serum citrulline and IFN- \tilde{E} , cloacal IgA, are the potential biomarkers to identify the inflammation in intestine due to dysbacteriosis, and impaired gut permeability.

Alterations in gene expression of claudin-1 and occludin indicate mitochondrial respiration and ATP production variations which indicate the state of intestinal permeability at tight junctions and cellular energy status [89].

Whereas oxidative stress is measured [93] by superoxide dismutase enzyme activity Thiobarbituric acid reactive substances produces during peroxidation and damage of the cells, break down of nitrite and nitrate produces nitricoxide which can be noted by griess assay to identify the concentration of nitric oxide in the cell [74].Pathogens like coccidian directly damages the epithelial cells and loss of villous epithelia, results in decreased absorption [94]. Simple techniques like measuring the villi length, crypt depth and ratio are helpful standards to know the gut health. Villus height at duodenum, jejunum and ileum are 1400,900 and 700 mm and crypt

depth of 190,170,160 mm with villus height to crypt depth ratio were 8, 6 and 5 were reported by Verdal et al. [95] in broilers at 23 days of age.

8. Conclusion

The gut represents a continuously evolving ecosystem where a dynamic interaction between host immune, neuroendocrine and entero-endocrine cells. The gut micro biota of the birds has influence on normal physiological development and homeostasis. Ban on AGPs make the evaluation of precision feeding as well as availability of various additives, probiotics, nutraceutical...etc. are forcing the nutritionist to formulate the least cost rations for better production. Change in dietary regimen to boost immune system, minimise stress, good management and bio security practices are needed. Identification of genes/bio markers that regulates health and immune system is essential. Relationship among economic traits, dietary regimen and gene expression are the gaps. This review reveals that nutrition, immunity and stress are factors that influences the gut integrity in birds and production output.

9. Future research

- Introduction of new technologies that unveil the underlying transcriptional and other molecular mechanisms for disease resistance in chicken.
- Technologies that aid in identification of disease resistant genes include next generation sequencing, microarray analysis, RNA sequencing and high density SNP genotyping.
- Exploring of genes related to degradation and digestion of complex NSP for better utilisation of alternative feedstuffs to incorporate in large-scale industrial production.
- Development of biomarkers of gut health is for understanding the pathophysiological events which influence the intestinal barrier, its functionality and the ecology of the GIT microbiota.
- Quantification of *Enterobacteriaceae* using Q-PCR or other means may be of use to measure dysbiosis in poultry.

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