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# A comprehensive report on poultry intestinal microbiota

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**Abstract**
Productive performance of poultry depends on a complex interaction between host factors, environmental factors and gut microbiota. Gut microbiota residing in the gastrointestinal tract of chickens plays an important role in gut homeostasis and affects the animal's health & physiology. The composition of gut microbiota depends on several factors. Alteration in the microbial community can be detrimental to host on one hand but on another hand can be utilized profitably, so it should be monitored carefully. Though it is difficult to evaluate entire microbial community but newer techniques like targeted amplicon sequencing and metagenomics make it possible up to a large extent. In future, these techniques along with other biomarkers can be used to find out the peculiar gut microbial signature concerning particular factor or diseased condition. The present review is about the structure, alteration pattern and evaluation of gut microbiota.

**Keywords:** Gut microbiota, poultry, dysbiosis and gut health

## 1. Introduction
The growth of the global human population is increasing day by day and estimated to be 9.7 billion by 2050 [1]. To feed such a huge population with quality food is a big challenge. Current agricultural production is already in peak and there is shrinkage/reduction of cultivable land day by day. So there is increase pressure on the livestock population to increase productivity in a profitable manner. Poultry represents one of the most efficient ways to convert food into biomass. It gains 3.48 kg body weight on the consumption of 6.37 kg of feed in just 49 days [2]. Feed consist of 70% of the total production cost of poultry [3]. The present breed has been evolved as a result of years of intensive genetic selection done by geneticists in such a way to reduce feed conversion ratio at a minimum level. So in order to increase daily weight gain, there is very high feed intake which puts pressure on the gastrointestinal tract even in the absence of pathogenic organisms [4]. The microbial population residing in the gastrointestinal tract of chickens is essential for the gut homeostasis, host metabolism and affect the animal's health & physiology. They play an important role in the digestion of food, toxin neutralization, influence organ development, endocrine activity, pathogen control, interact with the gut-associated immune system and cause immune stimulation [5, 6, 7]. The microbiota is defined as the microbial community, including commensal, symbiotic and pathogenic microorganisms, which usually colonize an area of human and animal organisms, and are around two times more plentiful than somatic and germinal cells of the host [8].

## 2. Normal microbiota of poultry gastrointestinal tract
Gut flora, or gut microbiota, or gastrointestinal microbiota, is the complex community of microorganisms that resides in the digestive tracts of poultry and other animals. The total number of bacteria in the gastrointestinal tract is higher than the number of eukaryotic cells of the host body [9]. As food moves from anterior to posterior part of gastrointestinal tract different group of microbial communities residing start digesting the food. Broadly chicken GIT divided into three category *viz* anterior part, small intestine and large intestine. The microbiota in different part of gastrointestinal tract serves different function and the community composition also vary to a large extant so it is studied as separate ecosystem [10]. Though these entire segments contain different diversified microbiota but they influence the microbial community of each other [11]. The microbial colonization and the type of microbiota present in specific segment depend on gastrointestinal microenvironment e.g. type of nutrient

availability, pH, redox potential and antimicrobial secreted from the host etc. Age dependent variation in type of microbial colony has also been detected [12]. At the time of hatch poultry gastrointestinal tract is free of microbiota but immediately after hatching within hours the establishment of microbiota has been documented which reaches $10^8$-$10^{10}$ cells/gm on day first and $10^{11}$ cells/gm on day third in ileum and caecum and become stable afterward [5]. The type of energy metabolism also depends on redox potential of particular segment of GIT. That is why the composition of small intestine and large intestine differ significantly. The bacterial population in upper GIT is mainly fermentative type. Though they do not require oxygen but presence of oxygen is not detrimental to these. So crop and small intestine is mainly inhabited by lactic acid bacilli comprising of 95% population of this segment. Some oxygen may present in small intestine which is responsible for presence of facultative anaerobe e.g. *Salmonella enterica* and *Escherichia coli*. In contrast to crop and small intestine which are mainly inhabited by *Lactobacillus* spp., *Streptococcus* spp. and *Enterococcus* spp. [13.14]. The chicken caecum predominantly contain order Clostridiales [15] and two important families Ruminococcaceae and Lachnospiraceae, which differ in their digestive ability. Ruminococcaceae are able to degrade cellulose and complex polysaccharides while Lachnospiraceae bacteria are more important in digestion of less complex polysaccharides and starch [16]. Small amount of bacteria belong to families Bifidobacteriaceae which are capable of digesting simple carbohydrates and play role in lipid and cholesterol metabolism are also present. [17]. Microbial density in crop is approximately $10^9$ per gram reduced to $10^8$ per gram in stomach due to action of gastric juices and it again increases in intestine and ranges between $10^9$ to $10^{11}$ per gram, highest in caecum $10^{11}$per gram. Wei *et al* documented presence of 13 phyla consist of 117 genera and 915 species of microbiota in chicken gastrointestinal tract [18]. Out of these 13 phyla majority (90%) of which comprised of only three genera. These belongs to Firmicutes (70%), Bacteroidetes (12.3%) and Proteobacteria (9.3%). In their study they also found that both chicken and turkey GIT microflora is predominated by Clostridium, Ruminococcus, Lactobacillus, and Bacteroides. There is difference in luminal microbiota and the mucosal microbiota. Composition and distribution of the microbiota also depends on pH, transit time and diet. Luo *et al* observed low level of C. perfringens in poultry with diets containing soya oil than fats of animal origin [19]. In natural situation initial colonization occurs through pores present in shell at the time of hatch [20]. Now a days in modern poultry farms the chicks do not come in contact with the adult birds. They acquire the microflora from the environment when they come in contact with the litter material. This have also been proved by Oakley *et al.* 2013 who found approximately 50 bacterial genera common in the litter, faecal material and the poultry carcass [21]. After hatching gut is primarily colonized with Enterobacteriaceae on very first day and later on Firmicutes approximately from 7 days of age [22].

## 3. The role of chicken gastrointestinal microbiota

Nutrient exchange and host defense are two important function of gut microbiota. It helps in digestion and absorption of nutrients. The animals inhabiting the gut microbiota are considered as supra-organisms [23] as they are capable of degrading undigestible complex feed and more efficient in utilizing the feed for generating the energy. Like other animals poultry also lack carbohydrate esterase, glycoside hydrolase, and polysaccharide lyase enzymes which are necessary to facilitate the process of digestion. The microbiota present in gut is populated according to the substrate available there. Small intestine which is rich in mono- & di-saccharides and amino acids, have Proteobacteria and Lactobacillales while large intestine which is rich in host-derived mucin, cellular debris, complex carbohydrates, plant foods, which are indigestible by the host have Bacteroides and Clostridiales. Rinttilä and Apajalahti, found positive correlation between caecal *Lachnospiraceae* spp. and feed conversion ratio [24]. The poultry feed contain many of the readily available nutrients which are mainly utilized by microbes present in anterior part of GIT and as food passes to posterior part the concentration of these decreases and mainly indigestible complex part remains which mainly comprise of resistant protein and starch [25]. Gut bacteria utilize complex carbohydrate and polysaccharides and produce simplified products which are further used as substrate for fermentation by another microorganism. They also produce short chain fatty acids (SCFA) which is very beneficial for gut health [7]. Cecal microbiota utilize uric acid for recycling the nitrogen [26]. Gut microbiota produce short chain fatty acids (Acetate, propionate and butyrate) which are bacteriostatic, stimulate fluid and electrolyte uptake, primary energy source of colonic epithelia and upregulate plasma glucagon like peptide GLP-2. Diao et al summarized that SCFA are important for improving gut morphology, reduce apoptosis and maintain intestinal barrier function [27]. Second important function is exclusion of pathogen. Term competitive exclusion has been used by Nurmi and Rantala when he found reduced salmonella colonization in the birds which are exposed orally with intestinal content of salmonellae-free birds [28]. Normal microflora produce certain chemicals like lactic acid, ethanol and reuterin etc which is detrimental to coliforms, salmonella and other pathogenic organisms [29] Undefined mixture of microbiota have been proved to be more effective inoculum than the defined mixture, so poultry litter obtained from the healthy flocks is an better alternative to populate microbiota of newly hatched chicks. Introduction of beneficial microflora used successfully to treat recurrent *C. difficile* and other gartrointestinal infections in human beings [30]. Microbiota mainly produces short chain fatty acid which increases absorptive surface area of gastrointestinal tract for absorption of nutrients [31] and also reduces the colonic pH which in turn reduces bile catabolism [32]. Microbiota present in gut produces vitamin B and vitamin K [33]. In addition to nutrient absorption gut also plays important role in pathogen defense by secreting mucous, immunoglobulin A, antimicrobial peptides and also act as tight junctions between gastrointestinal epithelial cells. Interaction between microbiota and GIT epithelial cells leads to increased goblet cells [34] and mucous production which flushes out the pathogenic organisms. The microbiota also stimulates lymphocytic proliferation in chicken [35]. Bacteroides fragilis suppress Tregs and induces anti-inflammatory cytokine production [36]. There is positive correlation between diversity of gut microbiota and T cell receptor [37]. Lactobacilli produce low-molecular weight peptides and wide variety of short chain fatty acids (SCFAs) which leads to immune activation and inhibits the growth of pathogenic bacteria by reducing the gastrointestinal pH, producing bacteriocins and modifying the receptors for attachment [38, 24]. The gut microbiota is also known to modulate the production of anti microbial proteins

from intestinal epithelial cells [39], B cell response and IgA production [40]. Both these are important to kill the pathogenic microorganism. Anti microbial proteins induce production of defensins (C-type lectins, angiopoietin 4, ribonucleases and S100 proteins) while IgA modulates expression of proteins on helper T cell associated with programmed cell death [41].

**4. Undesired effects of gut microflora**

While the intestinal microbiota promotes promote gut health of the host, they also utilize energy, compete with the host for nutrients within the gastrointestinal tract and thus reduces the feed conversion ratio and production. The gut microbiota may sometimes cause excessive stimulation of immune system, breakdown of bile, enzymatic digestion of mucus and produce few harmful protein catobolites [42]. They may secrete antinutritional and toxic compounds; induce a continuous inflammatory response and turnover of epithelial cells in the gastrointestinal tract on the expense of bird performance [43].

**5. Alteration of gut microbial community**

In order to increase body weight there is heavy feed consumption which puts pressure and stress to gastrointestinal tract of poultry. This may cause damage to GIT mainly by three ways i.e. dysbiosis, inflammation, and leakage of the mucosal barrier [44]. Alteration in gut microbial population is known as dysbiosis. Though there is no defined pattern of these GIT microbial compositions but it can be estimated and correlated upto some extent with gut health [45]. Intestinal barrier permeability allows the passive diffusion of molecules across the intestinal epithelium. This barrier permeability may allow some potential harmful molecules, but these molecules are taken out by ATP dependent efflux pump which are present on plasma membrane called ATP-binding cassette transporters or multi-drug resistance (MDR) pumps [46]. GIT barrier permeability also depends on intercellular tight junction which may be loosen by inflammatory cytokines [47] and dysbiosis [48]. Dysbiosis and associated GIT disorders are increasing day by day and now culminating as major non-communicable inflammatory disease of twenty first century in case of human beings [49]. There is increased use of therapeutic antibiotic specially in case of necrotic enteritis and gastrointestinal disturbances after the ban on antimicrobial growth promoters (AGP)[50]. Chicken gut microbiota also contain several potential pathogenic bacterial population; upto $10^7$ CFU per gram in most of the birds as well as human beings [51]. These are mainly comprise of *Campylobacter*, *Escherichia coli*, *Salmonella* and *Clostridium perfringens.* The susceptibility depends on many factors including age of bird, immune status, stress and strain of pathogen etc. *Campylobacter* is non pathogenic to poultry [52]. There is two important difference in E.cili infection as compared to mammals. First, unlike mammals infection in poultry is mostly through respiratory route and second there is also no clear virulence genes in avian pathogenic E. coli (APEC)[53]. Most of the microflora is acquired by the chicks are from litter material which may some times have serious implication as it may contain some of the pathogenic organism [54] so this management practice must be closely monitored. Alteration in gut microbiota can be caused by several factors in feed which have positive and negative impact on chicken health. One of the most important is use of antibiotics as growth promoter. In addition to effect on gut microbiota the antibiotics are also detrimental for consumers. The antibiotic remains as residue in meat and other products e.g. macrolids, penicillin, chloramphenicol and aminoglycosides are frequently detected [55]. There is increase in Firmicutes/Bacteroidetes ratio due to antibiotic supplementation. Danzeisen *et al.* observed reduction of Lactobacillus and increase in Coliforms in the caecum with the use of virginiamycin and tylosin [56]. High protein and low carbohydrate can stimulate growth of proinflammatory and potentially pathogenic microbiota. Feeding excessive protein may cause some undigested leftover which are fermented in hindgut to produce amines, phenols, indoles, thiolsand branched chain fatty acids. Though biogenic amines are beneficial and important for gut development but when these are produced in large amount leads to gizzard erosion and other harmful effect [57]. Gut inflammation leads to generation of free radical which reacts with luminal sulfur to form tetrathionate. This tetrathionate act as electron acceptor for energy production and growth advantage for S. Typhimurium over normal microflora [58]. Similarly alteration of food can be used to aid some GIT disease management e.g. reducing sulphur containing amino acid (milk, eggs, cheese) in feed reduces hydrogen sulphide production which inturn help to prevent ulcerative colitis [59].

**6. Evaluation of gut microbiota and gut health**

Evaluation of gut microbiota is very difficult task. Previous knowledge of gut microbiota was limited to cultivable microorgamisms. The gut microflora is very diverse and less than 20% can be identified by culture on media [42]. The requirement of anaerobic environment, interlinked microbial community in terms of metabolites is the major difficulty to grow these on culture media [60]. Fecal microbiota cannot be directly extrapolated because fecal and cecal microbiota are qualitatively similar but quantitative different within the different bacterial groups [61]. Older techniques like denaturing gradient gel electrophoresis, terminal restriction fragment length polymorphism, single-strand conformation polymorphism, temperature gradient gel electrophoresis, temporal temperature gradient gel electrophoresis and automated ribosomal intergenic spacer analysis are cheap but low sensitive and semiquantitative [62]. Sequencing of 16S ribosomal RNA bacterial gene from fecal samples will give conformity about the identification of bacterial population but do not tells about the community strucure so to know about community composition seqencing of entire DNA present in sample is employed known as targeted amplicon sequencing. The microbial community residing in gut are also related and interdependent on metabolites they produce and share, so there is need to study metabolomics in future. For this Shotgun metagenomic sequencing may be employed. In addition to molecular techniques gastrointestinal markers can also be used to estimate gut health. Crypt depth, villus height and the villus/crypt ratio are commonly used at the level of duodenum, the jejunum or the ileum as a standard test to monitor gut health in poultry. Epithelial oxygenation in GIT have been used as biomarker by several scientists showing both reduction and increase in oxygenation of mucosal epithelium [63, 64]. Upregulation (interleukin 8, IL- 1, transforming growth factor-β4) and down regulation (fatty acid-binding protein 2, occludin and mucin 2) of cytokines have been noted in case of inflammatory oxidative stress [44]. Enteroendocrine cell density is influenced by prebiotics [65]. Upregulation of gut microbiota derived metabolite sensing receptors on host gastrointestinal epithelial cells have been observed in laboratory animals [66]. FoxP3-positive regulatory T-lymphocytes mainly concentrated in lamina propria

decreases in inflammatory intestinal disease in humans [67] and this can be adopted as marker in poulty and other animals. Increased production of D-lactate (amicrobial metabolite) produced by gut microbiota which increases in serum as a result of increased GIT permeability in poultry. Enzymes diaminoxidase, an intestinal specific protein found to be increased as a result of damage to GIT cells [68]. There is increase in concentration on alkaline phospahate noticed in dysbiosis [69]. Though Acute phase proteins show marked increase and specific pattern in many animals in response to inflammation but it has not been found an specific biomarker of gut health [70]. Healthy Intestinal epithelium do not permit lipopolysaccharide to cross the GIT barrier it is generally detoxified after internalization so its presence in the serum can be of diagnostic significance [71]. Although there is alteration in bacterial population in ill health but science there is no specific signature of bacterial community [72] so it is difficult to correlate with particular disease. Scientist are working in the direction and in some cases like Crohn's diseasein human they found loss of Firmicutes [73] while increase is seen with prebiotics [65]. In case of dysbiosis some specific proteins are secreted by the host cells among these few are stable and used as biomarker of hut health e.g. Calprotectin, aneutrophilic protein is frequently detected in infectious bowel disease of human beings [74]. Concentration of terminal microbial metabolites and gases present in faeces can be used as use useful biomarker of gut health. The gastro intestinal microbiota is known to convert complex carbohydrate protein and fiber to simpler one. These are absorbed upto some extent and there quantification can be extrapolated with gut health. Though not used in poultry but faecal Zink can be used as useful biomarker of GIT epithelium damage [75].

## 7. Future research prospects related to gut microflora

To manipulate the gut microflora in useful manner, we must have to enrich ourself by the knowledge of diversity and interrelation between microbiota by employing newer techniques like metagenomics and metabolomics etc. Most of the studies currently available are based on the effect of different feeding strategies and pathogenic organisms on gut microbiota but there is paucity of sufficient data to come at common conclusion. There is also lack of standard protocol. Currently we are having ample data regarding poultry genetics, health hazards (necrotic enteritis, metabolic and skeletal disturbences), gut motility, feed & feed suppliments (minerals, vitamin, prebiotic, probiotic and enzymes), managemental factors etc. but to improve chicken health and to get better performance futuristic approach must include newer technologies like omics (metagenome shotgun sequencing, metaproteomics and transecryptomics etc.) for genetic selection, microbiota host interaction and designing new supplementation [7].

## 8. Conclusion

Gut microbiota is the complex community of microorganisms that resides in the digestive tracts of poultry and other animals. It plays important role in gut homeostasis, digestion, detoxification, influence organ development, endocrine activity, pathogen control, interact with the gut-associated immune system and causes immune stimulation. Structure of microbial community is influenced by many factors. Alteration may adversely affect health and production. Deep knowledge of microbial signature concerning to health and particular diseased condition may help researchers to manipulate the complex microbial community in profitable manner in future.

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