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Assessment of a Nutritional Rehabilitation Model in Two Modern Broilers and Their Jungle Fowl Ancestor

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Abstract

Inclusion of rye in poultry diets induces a nutritional deficit that leads to increased bacterial translocation, intestinal viscosity, and decreased bone mineralization. However, the effect of diet on developmental stage or genetic strain is unclear. Therefore, the objective of this chapter is to evaluate the effects of a well-established rye model diet during either the early or the late phase of development on performance, bone mineralization, and morphometric analysis. Furthermore, intestinal integrity evaluated by liver bacterial translocation, leakage of FITC-d, and gene expression of tight junctions across three diverse genetic backgrounds Modern 2015 (Cobb 500) broiler chicken, 1995 Cobb broiler chicken, and the Giant Jungle Fowl are also discussed.

Keywords: nutritional rehabilitation, chicken lines, compensatory growth, bone mineralization, morphometric analysis, intestinal integrity

1. Introduction

Multiple metrics of growth are utilized when determining a child's nutritional status [1]. Both height and weight relative to age are essential benchmarks when monitoring growth because these growth metrics exhibit similar trends across human development [1]. Stunting is defined as low height/length for a child's age and is often reflected in poor linear growth [1, 2], while wasting is low weight for length/height [1]. It should be noted that before the age of 2, a child's height is measured as length. The World Health Organization (WHO) defines stunting as two or more standard deviations (SD) below the standard height for children at that particular age, often referred to as Z score. The typical growth pattern for stunted

children is a sharp decline in height/length from birth until 24 months or until the child reaches 1.5–2 SD below the median and then plateaued till 59 months [1]. Globally, stunting, underweight or wasting are major contributors to morbidity and mortality in children [2]. A report from 2000 indicated that stunting has decreased by 14% globally since the 1980s; however, the reduction in stunting was unevenly distributed [3]. A projected trend for 2020 expects a decrease in the rate of stunting in Asia from 100 million to 68 million, while the number of stunted children in Africa is expected to increase from 60 million to 64 million as population increases [2, 3] .Globally, 26% of children under the age of 5 have a–Z score, two standard deviations below the average, indicating stunting [4]. Childhood stunting increases the risk of mortality from an infectious disease and reduces cognitive ability and lowers adult learning [4]. Undernutrition in infants 6 months of age or younger is often attributed to low birth weights and breastfeeding patterns [1]. The most vulnerable time for childhood stunting is from conception until 24 months [3]. During the first 2 years of life, children are more vulnerable to the long-term effects of stunting, like cognition, executive function, and school attainment [5]. Stunting that occurs after this time is less correlated with the long-term effects of stunting [5]. Therefore, the first 2 years of life is the time when interventions are more effective [1]. Therefore, it is evident that prenatal and early life interventions are required to ensure proper growth.

It has been estimated that 43% (250 million) of children under the age 5 subjected to poverty and stunting will not reach their development potential [5, 6]. There is a growing body of evidence that documents that healthy children tend to become healthy and wealthy adults [7, 8], and there is a positive correlation between higher birth weights and social, economic, and cognitive outcomes [7]. For example, anthropometric markers such as birth weight and child height are related to future schooling, employment, earnings, family formation, and health [9]. Low- to middle-income countries have a higher risk of children not reaching their developmental potential due to poverty and stunting [5]. Exposure to poverty early in life affects the individual's health and well-being as an adult which can lead to 19.8% lower income than those individuals not exposed to stunting [5]. Low socioeconomic status in early childhood has been associated with smaller hippocampal gray matter, which has been associated with low cognition, academic, and behavioral performance [10]. Early life stressors have long-term effects that reach into adulthood where there are low task-related activation of brain regions supporting language, cognition, memory, and emotional reactivity [11, 12]. Interventions to annihilate poverty have been shown to improve wage earning, intelligence, better health biomarkers, reduction violence, depression, and social inhibition [5]. The negative effects of early childhood stunting can also be attenuated when the child receives nurturing care [5]. Positive home environments had longer effects on cognition where children were more susceptible to their environment for up to 63 months [5]. Romanian children placed in foster care had a better cortisol response than those children who remained in an institution. The cortisol response may be the link between cognition and early childhood stressors [5]. Poverty often leads to exposure to multiple physical and psychological stressors, which can affect the child's physiological response as well as inhibit self-regulation and stress management [5]. For the first 2 years of life, macronutrient supplementation for the increase in intellectual development is required [5]. Nutrients promote healthy brain development [5].Therefore, it is evident that reducing the incidence of stunting

can have positive long-term effects on the health and the economy and may be able to break the cycle of poverty. The purpose of this chapter is to evaluate the etiology of stunting and present chickens as a viable model to study stunting in children.

2. Etiology of stunting

The top five predictors of childhood stunting in India were maternal stature and weight, maternal education, household incomes, and diversity in the diet [13]. Macro and micronutrient deficiencies also play a role in stunting. Semba et al. [14] found that stunted children in rural Malawi have a low circulating level of nine essential amino acids and lower levels of sphingomyelins. In addition, certain phosphatidylcholines were in lower concentrations in the serum suggesting that stunted children may also be deficient in choline [14]. Phosphatidylcholine and sphingomyelin play a major role in chondrogenesis, which can determine linear growth in bones [14]. This study suggests that the inefficiency of micronutrient and lipid supplementation in stunting may be due to the deficiency in essential amino acids [14]. There is also a direct relationship between systemic inflammation, growth hormone (GH) signaling, and linear growth [15]. Blocking tumor necrosis factors-alpha, via antibodies, reverses the GH signaling suggesting an interaction between GH and inflammation [16]. Systemic inflammation has been linked with higher levels of GH, and lower levels of IGF-1 and IGF binding protein-3 (IGFBP-3) systemically in the liver and lower linear growth [15]. The higher systemic levels of inflammation are likely caused by the recurrent infections in children subjected to poverty [15]. HsCRP (high-sensitivity C-reactive protein) has been utilized as a biomarker of mild inflammation during viral or bacterial infections [15]. Higher levels of serum hsCRP was correlated with higher systemic and hepatic GH and lower level of IGF-1 and IGFBP-3 [15]. Higher GH and lower IGFBP-3 were associated with short stature and states of undernutrition. This data suggests that both diet and environmental pathogen exposure can have direct effects on growth in children.

A longitudinal study was conducted on Malawian twins from age 0 to 3 in rural communities to evaluate the effect of genetics on child malnutrition [17]. Between sets of twin pairs, there was a high rate of discordance in the effect of severe and moderate malnutrition [17]. In addition, nutrition alone was not an effective treatment for stunting, as feeding interventions only improved growth by 30%, suggesting that stunting is a multifactorial disease [4]. Disease is another factor to consider when determining the etiology of stunting. Infections can affect nutrient absorption, which can lead to undernutrition and stunting. However, it should be noted that there is not a strong correlation between growth, diarrhea, and disease [4]. It has been theorized that unsanitary living environments lead to asymptomatic but chronic intestinal injury which results in immune stimulation and poor growth [4]. An effective intervention in reducing the incidence of stunting focuses on three core issues: water, sanitation and hygiene (WASH). Another factor that contributes to stunting is environmental enteropathy dysfunction (EED) [4, 18]. EED is a subclinical disease of the small intestine characterized by villous atrophy, crypt elongation, infiltration CD8+ T-cells in the lamina propria and increases intestinal permeability associated with intestinal inflammation [4, 18]. Also, there is

an inverse relationship between enteric inflammation and linear growth and vaccine efficacy [18]. EED is prevalent in low-income countries with poor sanitation and high environmental loads of enteropathogenic bacteria and is often associated with the pathogenesis of malnutrition [18]. The effects of EED are cyclic further proliferating growth faltering. The cycle starts with damage to the intestinal morphology causing a loss of barrier function, which triggers hyperstimulation of the immune system [4, 18]. This perpetuates the loss of barrier function and a reduction in absorptive function and secretion of digestive enzymes causing poor digestion and malabsorption [4, 18]. The etiology of EED is unclear but the continuous exposure to pathogenic bacteria and their enterotoxins causes villous atrophy that correlates with crypt hyperplasia [4]. This causes villous blunting which reduces absorption capacity and fewer secretions. Also, the high intestinal pathogenic load causes hyperstimulation of enteric T-cells which contribute to the crypt hyperplasia [4]. Therefore, both the host's immune system and the pathogenic bacteria are causing mucosal damage. The hyperstimulation of the cell-mediated immune response is thought to occur due to the high concentration of fecal microorganisms but may also be caused by severe nutritional deficiency, HIV, or mycotoxin exposure [4]. Certain pathogens and/or endotoxins can disrupt the intestinal barrier via tight junctions or by activating pro-inflammatory immune mediators. Chronic pathogen exposure causes chronic immune activation. Intravenous infusion of endotoxin administered to healthy humans increases gut permeability [19]. There is a correlation between intestinal permeability and stunted growth, where 55% of linear growth faltering occurred while Gambian infants had impaired intestinal permeability [20]. It is believed that there are three primary reasons for growth impairment during EED. First, the hyperstimulation of the immune response it metabolically expresses [20]. Second, proinflammatory cytokines can act to reduce growth-related hormones impeding growth [20]. Lastly, proinflammatory cytokines can attenuate bone remodeling causing more permanent stunting [20]. Regardless if the child had diarrhea, pathogenic bacteria was found in the stool of children with EED under the age of 60 months in both sub-Saharan Africa and South Asia [21]. Suggesting that there is subclinical inflammation caused by EED is a major contribution to stunting [21]. Malabsorption may also play a role if the severity of EED causes a high abundance of nutrient loss in the stool [21]. It is evident that regardless of etiology of EED, the disease is dependent on the environment. In areas where the incidence of EED is high, newborns do not have the intestinal histopathology associated with EED and when individuals removed environment, individuals were able to restore normal intestinal morphology and barrier function [22]. However, it should be noted that recovery of this disorder is relatively slow and individuals who presumably had the condition longer take longer to recover [4]. Bangladeshi children living in environmentally clean households had less severe EED and higher HAZ than children from contaminated households [23].

There are limited efficacious treatments for EED; antibiotics have been shown to have modest improvements in growth [18, 24]. Improving micronutrient status via supplementation did not affect linear growth [18]. Energy dense, micronutrient-fortified ready-to-use therapeutic food can accelerate short-term weight gain affecting metabolism by switching from fatty acid oxidation to amino acid oxidation, which increases fat deposition and weight gain [18]. There is a lack of information on the optimal time and duration of the nutritional intervention [18].

It is evident that stunting and malnutrition are multifactorial issues and that the microbiota plays a role in the mediating nutrition and pathogenesis of disease. It has been suggested

that in order to determine microbiota into equation, there needs to be a benchmark set to determine significant changes [18]. Microbiota for age Z is currently being defined as the degree of deviation of an unhealthy individual microbiota age from a reference cohort of a chronological age matching a child with normal growth. This data revealed that Bangladeshi and Malawian children had "immature" gut microbiota, which is similar to the bacterial profile of a younger child [25, 26]. They hypothesized that microbiota maturation is functionally linked to the growth rate of the host [25, 26]. Breast milk contains a lactose core and linked glucose, galactose, N-Acetyl galactosamine, fructose, and/or sialic acid residues [18]. These carbohydrate sources have prebiotic actions to promote colonization of bifidobacterial taxa. Bifidobacterium has multiple benefits to the host including improved vaccine response, enhanced gut barrier, and protection from enteric infection [18]. Gnotobiotic mice that were colonized with bacteria isolated from stunted infants in Malawi were supplemented with sialylated bovine milk oligosaccharide (BMO) or fructo-oligosaccharides and given a micro and macronutrients deficient diets [18]. They found that mice on the BMO diet had growth increase that was dependent on the microbiota [18]. Therefore, it is evident that microbiota play a key role in modulating growth and EED.

Animal agriculture has shown that low levels of antibiotics can reduce the number of pathogenic bacteria [4]. It is evident from animal trials that growth and intestinal morphology can be improved when the animals are placed in an environment with a low bacterial load and environmental immunogens. Research conducted in Bangladesh found that household with lower levels of parasites and less severe EED had better growth than those less hygienic environments [23]. This suggests that improved household sanitation and hygiene in areas with high parasitic loads can improve the severity of EED. However, in highly contaminated areas with little access to clean water, it was found that handwashing was not able to reduce the levels of subclinical mucosal damage and immune stimulation [27]. Infants' exploratory behaviors can lead to increased ingestion of pathogenic bacteria [28, 29]. Therefore, it is evident that still much is unknown about EED.

3. Compensatory gain

Compensatory growth, also known as catch-up growth or compensatory gain, is an accelerated growth of an organism following a period of slowed development, particularly because of nutrient deprivation. Growth may be measured with respect to weight, length, or height in humans [30, 31]. In some instances, body weights of animals under feed restriction will catch-up to control animals with ad libitum feed intake [32, 33]. In fact, high compensatory growth rates in feed restriction animals result in overcompensation due to excessive fat deposition and animals recover their normal weight without additional time [34, 35]. Nevertheless, when the nutrient restriction is severe, the growth period must be extended to reach the normal weight, but if the nutrient restriction is severe enough, permanent stunted growth may occur [36]. Compensatory growth has been reported in metazoans, plants, fungi, and even prokaryotes [35, 37–39]. Although the exact biological mechanisms for compensatory growth are poorly understood, it is clear that in some animals the endocrine system is involved [38]. During the first stages of starvation, there is a reduction of

basal metabolism [40]. The intestinal tract is the first organ to be reduced in both weight and activity [41, 42]. Then, as feeding is normalized, dietary protein and energy support intestinal growth, followed by muscular tissue and at the end adipose tissue [43]. Some of the factors that affect compensatory growth include composition of the restricted diet; severity of undernutrition; duration of the period of undernutrition; age; genotype; and gender among others [40, 44–46]. An epidemiological study determined that 56% of childhood mortality (aged 6–59 months) was attributed to malnutrition potentiating effects, and 83% of these was attributed to mild-to-moderate as opposed to severe malnutrition [36]. The present and other studies propose that malnutrition plays a major role in child mortality and suggest that strategies involving only the treatment of the severely malnourished are not enough to reduce the negative impacts of malnutrition [25, 47, 48]. Furthermore, malnutrition remains the major focus of nutritional intervention efforts, especially because dietary deprivation during early life can also have adverse effects on brain anatomy, physiology, biochemistry, and may even lead to permanent brain damage [49]. When diarrhea was followed by diarrhea-free periods, children exhibited compensatory gain and were put back on the growth trajectory [4].

4. Chickens as a model for research in humans

Using appropriate animal models is essential when studying human health [50]. Chicken has been an important experimental model in biology for more than 2000 years having led to many central discoveries [51–53] . However, with the latest advances in genetics and nutrition technologies, chicken has attained a superb model organism status [53, 54]. Hence, chickens are the system of choice for many vertebrate biologists, especially in the field of human sciences, who are interested in gene function [51, 55], as well as nutrition [53]. Typically, pigs are used as a model to study human nutrition because rodents have vastly different nutrient requirements and nutrient-nutrient interaction, and they are coprophagic and utilize different feeding strategies [56]. Roura et al. [56] reported that the mechanism of intestinal permeability and intestinal immunity system are well conserved across species; however, pigs often make an excellent model for humans due to their similarity in gastrointestinal anatomy. Although chickens have a shorter intestinal tract when compared to humans [57], there are many reasons as to why chicken are an appropriate model to study human nutrition. The first being the liver is the primary site of lipogenesis in both chicks and humans [58]. Also, both neonatal chicks and humans are able to efficiently utilize sucrose as an energy source. [59]. In both chickens and humans, iron is primarily absorbed in the duodenum [57]. Although the pig is the model organism for conducting human nutritional research, it appears that poultry have a more severe reaction to rye-based diets. It has been hypothesized that pigs are able to digest non-starch polysaccharides (NSP) better than poultry due to the high volume of the large intestine allowing for more fermentation and longer transit time of the digesta [60]. It also should be noted that chicks are able to double their starting body weight in 3 days, where it takes pigs 20 days and in children 5–6 months [50]. Therefore, from a practical standpoint, more trials can be completed in a shorter amount of time.

5. Chicken and rye

Starch and non-starch polysaccharides (NSPs) are primary carbohydrate sources in plants [61]. Cellulose arabinoxylans and β-glucans are the primary NSPs and require microbial digestion to be utilized by monogastric animals [61]. Arabinoxylans are the primary components of the thin lignified cell wall of the endosperm [62], and insoluble arabinose and endogenous enzymes do not efficiently degrade xylose residues. NSPs can be further classified by their water solubility, which is dependent on the chemical structure of these sugars [61]. The greater the solubility of the polysaccharide, the more viscous the digesta which reduces its nutrient availability. Rye is a cheap raw feed material to produce as it is tolerant to low temperature and drought, irregular soil pH, and requires less chemical treatments [61]. However, on a dry-matter basis, rye grain contains 9.7% soluble NSPs likely in the form of arabinoxylans. Hybrid rye variants have been bred to reduce the amount of anti-nutritional factors allowing rye to be added to poultry diets at a higher inclusion rate [61].

Soluble NSPs have beneficial effects on human health by lowering blood sugar levels, facilitating regular bowel movements, and reducing risk of heart disease and other metabolic syndromes [63]. Wild avian species consuming NSPs as whole grains prolong digestion time in the crop and allow for more microbial digestion, eliminating some of the anti-nutritional factors [61]. In modern agricultural animals, diets containing excessive amounts of NSPs negatively affect health and perpetuate a state of disease [61]. It is evident from the literature that broiler chickens consuming diets high in NSPs have increased ileal viscosity which leads to less interaction of endogenous enzymes and nutrients and reduces nutrient digestion [61]. Lower digestibility results in less energy available for growth, which reduces body weight (BW) and increases feed consumption that increases production costs [61]. It has also been reported that chickens consuming diets high in NSPs have increased feed intake in an attempt to maintain nutrient intake which increases the transit rate and increases intestinal viscosity even further [64]. Broilers consuming wheat-based diets had significantly higher gut viscosity, reducing AME and depressing growth and feed conversion efficiency [65]. Broilers and turkey poults consuming rye as the primary carbohydrate source had increased digesta viscosity, increased intestinal permeability, reduction in bone strength and mineralization, and changes in microbial composition [66–68]. The anti-nutritive effects of rye were attenuated when the diet was supplemented with bacillus-based direct-fed microbial [68]. Inclusion of 5% and 10% rye from d14 to d28 decreased performance and litter quality and increased gene expression of cellular growth and differentiation in cell survival processes [69]. Rye also upregulated complement and coagulation signaling pathway which is characteristically upregulated to eliminate infections [69]. Laying hens fed a diet containing rye, had a reduction in egg production, feed conversion efficiency, and eggshell cleanliness. The anti-nutritive effects of rye in laying hens could be improved when the diet was supplemented with a NSP degrading enzyme complex [70]. The higher digesta viscosity of soluble NSP diets also increases litter moisture, which can increase the incidence of footpad dermatitis [61].

There is a negative correlation between the digestibility of fat and dietary fiber inclusion [62]. The increased digesta viscosity associated with high NSP diets reduces fat digestibility by

interfering with emulsification and subsequent absorption [71]. The reduction in fat absorption of chicks consuming diets high in NSP also puts chicks at risk for fat-soluble vitamin deficiencies. It has been previously observed that hepatic vitamin E levels were significantly lower in rye-fed birds [72]. Higher viscosity also increases gastric passage rate, which can increase the possibility of pathogen proliferation. Higher potential pathogenic load within the lumen of the intestinal tract can increase risk of bacterial translocation stimulating the inflammatory response that increases intestinal leakage, and leads to higher amounts of bacterial translocation [61]. Rye-fed chicks also had a higher abundance of coliforms in the small intestine [68]. The higher abundance of coliforms in high NSP diets was also observed in an in vitro system [73]. Adding silage, rye, and chicken manure to a biogas reactor led to a high abundance of *Clostridia*, which plays a vital role in the digestion of polysaccharides and oligosaccharides [73]. There have been varied observations on the effect of soluble fibers on microbial population [61]. Diets containing 10% rye decreased population of commensal bacteria like *Lactobacillus* [69]. Certain populations of commensal bacteria can utilize resistant starches, NSPs, oligosaccharides, or proteins to produce short chain fatty acids (SCFA) which can be used as an energy source by the animal [61]. Particular types of SCFA are able to cross the lipid membrane of prokaryotes where they dissociate in the cytoplasmic, destroying the bacterial cells [61]. SCFA also reduce the luminal pH, which can limit pathogen proliferation [61]. Soluble fiber has also been reported to prevent the adherence of certain pathogenic bacteria to epithelial cells [74]. Mathlouthi et al. reported that wheat and barley consumption increases bacteria in the caeca—both commensal (*Lactobacillus* strains) and pathogenic (*E. coli*) [75]. Non-ruminant enzymes are unable to degrade arabinoxylans which enter the colon relatively intact where they stimulate growth of residing bacteria such as *Bacteroides*, *Bifidobacterium*, *Clostridium*, *Lactobacillus*, and *Eubacterium* [76]. Chickens consuming wheat/rye diets resulted in a higher abundance of mucosa associated bacteria especially enterobacteria and enterococci [77]. This indicates that the higher digesta viscosity associated with a rye-based diet results in an increase in the bacterial activity in the small intestine [77]. Also, NSPs containing diets that were not supplemented with enzymes had significantly more ileal volatile fatty acids, which indicates higher bacterial fermentation [78]. Furthermore, preliminary microbiome analysis from our laboratory found drastic differences in cecal microbiome profiles between chicks consuming rye and corn-based diets (**Figure 1**). Rye-fed chicks had a higher abundance of beneficial bacteria like *Lactobacillus and Bifidobacteria* but also a higher abundance of potentially pathogenic bacteria like *Clostridium* and *Proteus*, indicating dysbacteriosis. Corn-fed chicks had a higher abundance of SCFA-producing bacteria like *Faecalibacterium*, *Dorea*, *Oscillospira,* and *Blautia*, which maybe more representative of a "healthy" microbiota. Soluble NSPs have been reported to improve the development of the intestinal mucosa by increasing villus height and crypt depth in broilers consuming a diet containing 10% rye [69]. Insoluble fibers have also shown to improve intestinal morphology by increasing absorptive surface area [79]. Broilers fed a barley-based diet had changes in intestinal morphology compared to those birds fed corn-soy where there were shorter and thicker and atrophied villi and increased goblet cell size [80].

High-NSP diets supplemented with enzymes have shorter passage time by decreasing digesta viscosity [72]. Supplementation with starch degrading enzymes can ameliorate some of these negative side effects while again there was no observed effect of antibiotics supplementation on performance parameters [65]. The addition of a multicarbohydrase enzyme
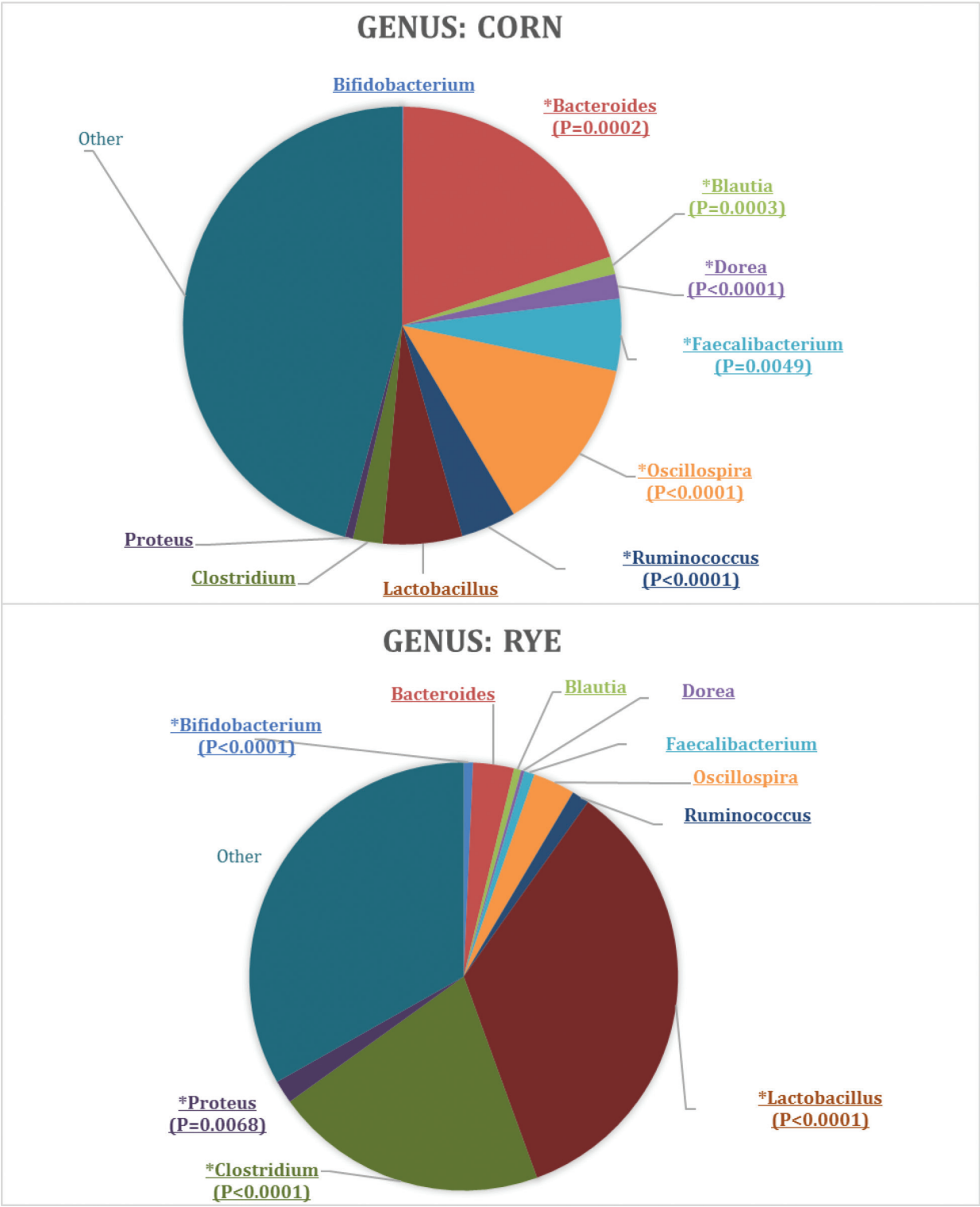
Figure 1. Cecal microbiome of 10-day-old broiler chicks consuming rye- or corn-based diets at the genus level. Data are expressed as relative abundance (%). *indicates significant differences in genera between chicks fed a corn- and rye-based diet.

complex containing both xyalanses and arabinofuranosidases improves digestibility of diets containing various amounts of different NSPs [62]. The higher apparent metabolizable energy of diets was attributed to the starch crude protein and crude fiber but the NSPs did not

increase energy availability [62]. The proposed mechanism of action of this enzyme complex is that the carbohydrases allow for improved endogenous enzyme and substrate interaction, allowing for improved digestibility [62]. Similar improvements in broiler performance were observed when the cereal grain was soaked in water where there was a decreased digest viscosity, increased growth parameters, increased villus height and reduced muscularis thickness and crypt depth proliferation, and increased volatile fatty acids (VFA) concentration in the ceca [81]. Pettersson et al. also found that steam-pelleting diets containing barley, wheat, and rye had increased digestibility in broiler chickens [82]. Young chicks are less tolerant to high-NSP diets because the higher digesta viscosity limits peristalsis which prevents the maintenance of digesta flow rate [64]. The inability of nutrients to move through the intestine rapidly prevents the absorption of nutrients to meet energy requirements for maintenance [64]. Antibiotics growth promoters are thought to improve performance via modulation

Figure 2. Visually comparing fecal viscosity and body weight of rye- and corn-fed jungle fowl and modern broilers. (A) Jungle fowl consuming a corn-based diet had feces with relatively normal consistency (red arrow) and a relatively clean vent. (B) Jungle fowl consuming a rye-based diet had feces pasted to the vent and diarrhea like consistency (red arrow). (C) Modern broilers consuming a rye-based diet had diarrhea pasted to the vent. (D) Illustrates the overall appearance and the size difference between modern broiler chicks fed a corn-based diet (red arrow) and a chick fed a rye-based diet (green arrow).

of the intestinal microbiome [83]. Previous research has suggested that antibiotics supplemented with rye-based diets attenuated some of these effects by eliminating the ability of the microbiota to ferment soluble NSP [84]. However, Choct and Annison did not observe any improvement in digestion and growth when antibiotics were added to the feed, which may be due to the antibiotic used in this study [78].

Figure 3. Litter quality and behavior observation of chickens consuming a rye- or corn-based diets (a) modern broiler maintained on a rye-based diet for 20 days of age had higher litter moisture and tended to huddle (red arrow). (B) Modern broiler maintained on a rye-based diet from 0 to 10 days of age and then the diet was switched to a corn-based diet from 10 to 20 days of age had a reduction in litter moisture. (C) Modern broiler maintained on a corn-based diet for 20 days of age and appear to have similar litter moisture to those chicks consuming rye in the first phase of the experiment. (D) Jungle fowl maintained on a rye-based diet exhibited diarrhea (seen in **Figure 1**); however, litter moisture did not appear to be affected by the diet.

The aim of future studies is to evaluate a nutritional rehabilitation in chickens to determine if it is an appropriate model to study interventions in childhood malnutrition. To the best of our knowledge, there is limited information on whether nutrition alone can facilitate intestinal recovery after the consumption of a rye-based diet in chickens. The model utilized rye and corn to evoke early- or late-phase malnutrition in three different genetic lines of chickens. To study early phase malnutrition, chicks were fed rye for the first 10 days and then switched to a corn-based diet. To study late phase malnutrition, chicks were fed a corn-based diet for the first 10 days and then switched to rye-based diet. The two control groups were maintained on a rye- or corn-based diet throughout the experiment. Preliminary results from our laboratory had comparable results to what has been reported in rye-fed chicks. **Figure 2** illustrates that rye fed Jungle fowl (B) and modern broilers (C) had feces pasted to their vents while the corn-fed birds had more normal fecal viscosity (A). As mentioned earlier, this is likely due to the higher digesta viscosity caused by diets containing high amounts of NSPs. **Figure 2(D)** also illustrates the drastic difference in body weight between modern broilers which were fed a corn-based diet (red arrow) and those fed a rye-based diet (green arrow). Litter quality was another qualitative observation made when chicks were fed high NSP diets. **Figure 3A** illustrates that modern broilers maintained on a rye base had higher litter moisture. Broilers in the early phase malnutrition group (**Figure 3B**) appeared to have comparable litter moisture with those broilers maintained on the control corn-fed diet (**Figure 3C**). This indicates that the modern broilers in the early phase malnutrition groups were able to reduce digesta viscosity which reduced litter moisture. Although the Jungle fowl had pasted feces (**Figure 2**), consumption of a rye-based

Figure 4. Histology of the ileum in modern broilers on a corn- or rye-based diet program. The histology of the ileum of chicks maintained on different combinations of rye- and corn-based diet. (A) Modern broiler maintained on a corn-based diet from hatch to 20 days of age. (B) Modern broiler maintained on a rye-based diet from 0 to 10 days of age and then the diet was switched to a corn-based diet from 10 to 20 days of age. (C) Modern broiler maintained on a rye-based diet from hatch to 20 days of age. (D) Modern broiler maintained on a corn-based diet from 0 to 10 days of age and then the diet was switched to a rye-based diet from 10 to 20 days of age.

diet appeared to have little effect on litter moisture (**Figure 3D**). There was observable difference in body weight, litter moisture, and pasted feces in the modern broilers; however, there are no obvious differences in histology of ileum consumption in the various diets (**Figure 4**).

6. Conclusion

Almost half the children under the age of 5 are living in impoverished conditions, putting them at greater risk of becoming stunted. The short-term effects of childhood stunting increase risk of mortality from an infectious disease and has long-term effects like reduced cognitive ability and lower adult learning [4]. It is evident from case studies that the incidence of stunting can be reduced when people have access to primary health care and education, increased sanitation, improved wealth distribution, and access to food [85, 86]. However, treatment opportunities tend to be time sensitive and most effective in reducing long-term effects of stunting if implemented within the first 2 years of life. Multiple factors contribute to the etiology of stunting, making it difficult to find a treatment. There has been limited treatment success by improving diet alone, and high environmental load of enteropathogenic bacteria can affect nutritional state and growth [4]. The histopathology of EED includes villous atrophy, crypt elongation, increased intestinal permeability, and intestinal inflammation [4, 18] which can be observed in stunted patients. Also, there is an inverse relationship between enteric inflammation and linear growth and vaccine efficacy [18]. However, treating EED with antibiotics has had limited success in improving growth [18, 24]. There is a lack of information on the optimal time and duration of the nutritional intervention [18]. Therefore, to determine effective ways to treat stunting, a viable animal model is essential. Avian species are a common animal model for human research especially in the field of gene function, nutrition, immunology, and developmental biology. The physiological response of poultry to a rye-based diet is like what is observed in patients with EED. The inclusion of rye in poultry diets has been fraught with problems, principally related to the production of sticky droppings, malabsorption syndrome, poor growth performance, increased intestinal permeability, and intestinal bacterial overgrowth [66, 67, 87–89]. The similarities between poultry consuming a rye-based diet and patients with EED and stunted children suggest that chickens would make a viable stunting model to determine potential interventions and treatments.

Conflict of interest

There was no conflict of interest.

Author details

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