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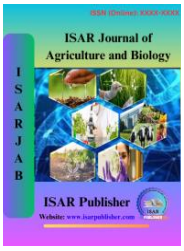

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Physiological factors affecting chicken ovarian function and the potential mitigation strategies - A critical review

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Contents

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Abstract: The poultry industry has performed a leading role worldwide, and reproductive efficiency is an important economic factor in poultry production. However, various physiological factors adversely affect the ovarian function of laying hens, such as environmental, hormonal, genetic, disease, and immune factors. Environmental stress impairs hen's health by reducing feed intake, body weight, egg production and follicle development rate. Nutritional toxicity, excessive nutrient absorption, and obesity are serious issues in poultry production. Extensive research has linked overfeeding to chicken ovarian dysfunction, including oviduct inflammation, prolapse, erratic oviposition, and defective egg syndrome. Various poultry diseases such as Newcastle disease, fowl pox, and coccidiosis cause huge production losses. The Newcastle disease causes the highest percentage of mortality in both domestic and wild birds, resulting in substantial economic losses. Hence, managing drinking water sanitation, chicken body weight, flock uniformity, and reproductive function (follicular growth and maturation) can decrease the risk of stress-associated metabolic diseases. To increase the sustainability of the egg industry, the current review paper's objective is to explore the physiological aspects that have a detrimental impact on chicken ovarian function and their potential mitigation techniques.

Keywords: Ovarian function, Chicken, physiological factor, production loss, mitigation strategy.

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INTRODUCTION

The poultry industry has been leading worldwide (Nawab et al., 2018). Among other countries, China is the top producer of chickens, with a population of 5.14 billion chickens on the mainland(Yuhuan & Fu, 2019). Chicken eggs provide rich protein sources among farm animals, and chicken meat is classified as economically healthier food than red meat, etc. (Nawab et al., 2020). In poultry farming, reproductive efficiency is a crucial economic trait. Precision nutrition improves growth, production, and fertility rates. Fertility depends on species, age, health status, nutritional, and environmental factors (Assersohn, Brekke, & Hemmings, 2021) (Assersohn, Brekke, & Hemmings, 2021) (Assersohn, Brekke, & Hemmings, 2021) (Assersohn, Brekke, & Hemmings, 2021) (Assersohn, Brekke, & Hemmings, 2021) (Assersohn, Brekke, & Hemmings, 2021) (Assersohn, Brekke, & Hemmings, 2021) (Assersohn, Brekke, & Hemmings, 2021). Laying rate is associated with the poultry industry, indicating the reproduction efficiency of hens. So, poultry feed must contain vitamins and minerals to get the best consequence (Pal, 2017). In 2018-2019, the Food and Agriculture Organization reported that the number of laying hens was 7.891 billion globally and 3.12 billion in China (Yuhuan & Fu, 2019) (Yuhuan & Fu, 2019) (Yuhuan & Fu, 2019) (Yuhuan & Fu, 2019) (Yuhuan & Fu, 2019) (Yuhuan & Fu, 2019) (Yuhuan & Fu, 2019) (Yuhuan & Fu, 2019).

There are some significant parameters in poultry production, such as feed intake, growth rate, hen's age, body weight, eggshell weight, egg quality, shell strength, bone health, and laying rate (Azmal et al., 2019; Du et al., 2020). All the above parameters are essential for egg-laying performance. The productivity of the hens depends on the number of developed ovarian follicles for ovulation. A study observed that goose egg production is associated with developed ovarian follicles. Notably, some growth differentiation factors play important roles in the follicular development of hens. GDF-9 (Growth differentiation factor *9)* controls the reproductive traits of various species, including poultry. The *GDF-9* gene controls the follicular growth and ovulation process of hens. Thus, a study examined that *GDF-9* uniquely improves the ovarian function of laying hens. Numerous studies revealed that egg production traits could be enhanced by improving the growth and development of a hen's ovarian follicles, like the genotype of the Chinese chicken breed (degu) (Zhang et al., 2012), the genotype of the Nigerian chicken breed, and the genotype of the Egyptian chicken breed .

However, various essential factors adversely affect the ovarian function of laying hens, such as hormonal, disease, immune, genetic, and environmental factors (diet, stress, pollution, etc.). As the world population is increasing, we may need to consider and overcome the above physiological challenges to avoid food scarcity over the coming years. Thus, there is an urgent need to enhance the reproductive capabilities of hens to fulfill the growing global demand. Therefore, this review aims to explore the physiological factors that negatively affect the ovarian function of laying hens and their potential strategies for mitigating risks to address the above challenges faced by the Poultry markets worldwide.

CHICKEN OVARIAN PHYSIOLOGY

In poultry farming, reproductive efficiency is an important economic consideration (Stephens & Johnson, 2020). The reproductive system of a hen is made up of two parts: the ovary and the oviduct (Fig 1).[1] Mostly, animals have two active ovaries, but in all avian species, including poultry, the left ovary and the oviduct are functional, whereas the right ovary and the oviduct are regressed during development. Thousands of ova in the ovary can develop into the yolk and finally into an egg, while the ovum doesn't develop to the point of ovulation (Bain, Nys, & Dunn, 2016). When an egg matures, it leaves the ovary and enters the fallopian tube. This is known as ovulation. Ovulation occurs every 24-26 hours, so a hen lays an egg later each day. [2] Clutch size varies depending on species and breed. The clutch is the total number of eggs laid by a bird during each nesting attempt, and its size is ordinarily large in commercial layers; however, the principle is usually the same in all poultry species. After ovulation, the ovum reaches the oviduct, and the second important component of the chicken reproductive system is the oviduct. The infundibulum, magnum, isthmus, uterus, and vagina are the five components of the fully mature oviduct, which is 25–27 inches in length (Stephens & Johnson, 2020).

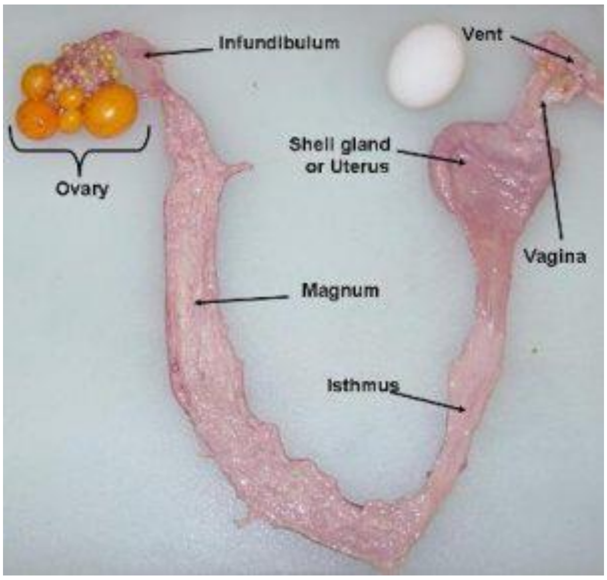

Fig. 1: *Various parts of the hen's reproductive system.*

The infundibulum, which is 3-4 inches long, is the initial section of the oviduct. When a mature follicle ruptures, it releases an ovum that is transported into the infundibulum. In the infundibulum, the ovum (egg yolk) remains for 15 to 17 minutes. Fertilization occurs in the infundibulum. The magnum is the second and the longest portion of the oviduct (13 inches long). The ovum remains for roughly 3 hours, during which time the thick albumen (egg white) is added around the yolk (Bharti, 2013). The isthmus, which is 4 inches long, is the third part of the oviduct. This section includes the addition of the inner and outer shell membranes. Here, the developing egg stays for roughly 75 minutes (Bharti, 2013). The

[1] The reproductive system of a hen is made up of two parts: the ovary and the oviduct (Fig 1)

[2] Ovulation occurs every 24-26 hours, so a hen lays an egg later each day.

subsequent component of the oviduct is the shell gland or uterus. The egg stays for about 20 hours, and the shell gland is 4-5 inches long. Additionally, the shell is formed on the egg in the shell gland. The main component of the shell is calcium carbonate.[3] The chemical compound calcium carbonate (CaCO3) is made up of three primary elements: carbon, oxygen, and calcium. It is a common mineral that may be found in rocks all over the world (most notably as limestone), and it is the principal ingredient in the shells of many marine animals, snails, coal balls, pearls, and eggshells. Different polymorphs of CaCO3 exist, and each has a unique stability that depends on a variety of factors. The hens mobilize calcium from their bones to provide 47% calcium for the egg's shell, and the remainder is supplied by diet. The vagina makes up the final portion of the oviduct. Its length is approximately 4-5 inches. It does not contribute to egg formation, but it aids in egg laying. Before oviposition, the cuticle (bloom) on the egg is formed in this section (Bharti, 2013)

HORMONAL MECHANISM CHICKEN OVARIES

The ovary is the primary reproductive organ in poultry birds, and it produces an ovum (Mfoundou et al., 2021). The hypothalamus is a very small organ that regulates the hen's ovarian function (Fig 2). The key role of the hypothalamus is to connect the endocrine (hormonal) system to the neurological system through the pituitary gland. The hypothalamus is linked to the adenohypophysis by a specialized network of blood vessels. The adenohypophysis receives chemical messages from the hypothalamus, and subsequently, the adenohypophysis produces two gonadotrophin hormones, namely luteinizing hormone (LH) and follicle-stimulating hormone (FSH). L.H. is a pituitary hormone involved in daily egg production and sexual development (Munoz et al., 2012). L.H. receptor is present in theca cells, interstitial cells, luteal cells, and granulosa cells (Munoz et al., 2012). L.H. interacts with receptors on ovarian follicles and promotes the growth and maturation of the follicles. A surge in L.H. triggers ovulation, and the ovarian follicle produces progesterone hormone after ovulation. L.H. stimulates the theca cells in the ovary to produce sex hormones such as estradiol.[4] Estrogen (Estradiol) helps in the growth of the egg follicles in the hen's ovaries (Fig 3)

The ovarian axis, which encompasses the hormones released in the chicken ovary, has a crucial impact on the performance of layer hens via complex regulatory systems.

FSH and LH have a complex interaction in order to control the production of eggs in chickens. FSH promotes the formation and development of ovarian follicles by stimulating the proliferation of granulosa cells and the generation of estrogen. These processes are crucial for preparing the reproductive tract for ovulation. LH initiates ovulation by releasing a fully developed egg from the follicle. Additionally, LH promotes the development of the corpus luteum, which produces progesterone that is essential for sustaining the reproductive cycle. The coordinated effects of FSH during the first stages of follicular development and LH in inducing ovulation guarantee the consistent generation of eggs. Research has shown that FSH has a role in preserving the weights of the ovaries and oviducts, as well as triggering ovulations (Prastiya, Madyawati, Sari, & Nugroho, 2022).

On the other hand, LH increases the creation of progesterone in granulosa cells, highlighting its crucial function in the process of ovulation. Estrogen promotes photostimulation, which boosts the neuroendocrine processes responsible for the release of FSH and LH, hence affecting the reproductive cycles related to egg formation (Barros, Barros, Sartor, Raimundo, & Rossi, 2020). Inhibin A, which is released by preovulatory follicles, has a regulatory function in controlling levels of FSH. This indicates the presence of a feedback mechanism that is crucial for maintaining constant egg production. Elevated levels of FSH are linked to a higher frequency of egg-laying, while appropriate levels of LH are required for ovulation. Studies have also demonstrated that insulin-like growth factor I (IGF-I) collaborates with FSH and LH to boost the production of progesterone and the growth of granulosa cells. This effect is particularly pronounced when animals are subjected to limited food intake. By reducing the occurrence of multiple ovulations and accelerating the maturation of follicles, this mechanism enhances egg production (Uyanga et al., 2022). Activin, inhibin, and follistatin play important regulatory functions by interacting with gonadotropins to control follicular development (Lovell, Gladwell, Groome, & Knight, 2003). IGF-I amplifies the impacts of FSH and LH, leading to an increase in progesterone synthesis, multiplication of granulosa cells, and a decrease in apoptosis. Activin, inhibin, and follistatin exert control of follicle growth by modifying the activity of gonadotropins.

The levels of inhibin and activin fluctuate during the ovulation cycle, which affects the levels of follicle-stimulating hormone (FSH) and the recruitment of follicles. This ensures a well-balanced hormonal environment for the most efficient egg production (Qin et al., 2013).

[3] The main component of the shell is calcium carbonate

[4] L.H. stimulates the theca cells in the ovary to produce sex hormones such as estradiol.

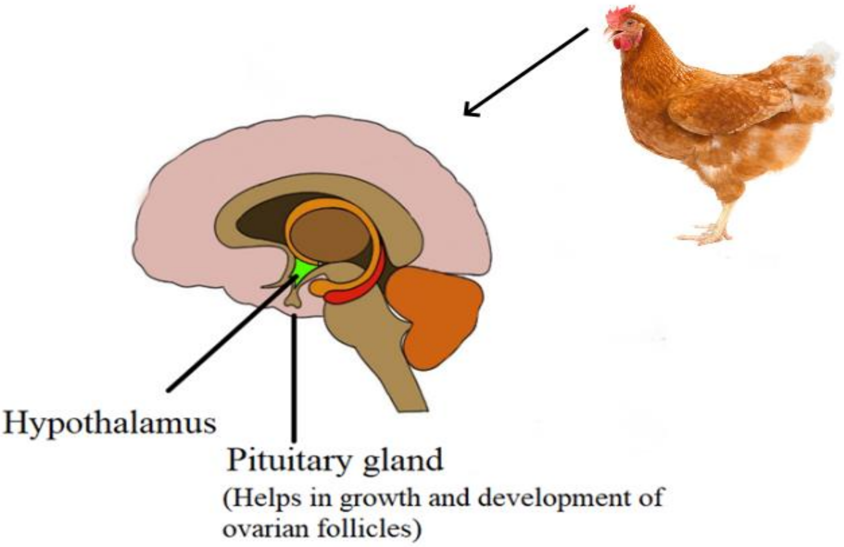

Fig.2: *The role of the pituitary gland in ovarian function*

Fig. 3: Development of follicles in the hen ovary. F5–F1 (yellow preovulatory follicles), SWF (small white follicle), SYF (small yellow follicle).

Estrogen is responsible for oviduct development and decreases prolactin production (Munoz et al., 2012)[5]. Additionally, estrogen is involved in regulating calcium metabolism, which is essential for the production of medullary bone and eggshell. In magnum, estrogen stimulates the production of egg components like ovalbumin, conalbumin, ovomucoid, or lysozyme, and vitellogenin is produced in the liver. Theca interna cells of the ovaries produce androgens, which are the precursors of estrogen (Franks & Hardy, 2018). Another function of androgens is the development of secondary sex characters and the ovarian follicle. Additionally, the other hormone is progesterone (P4), produced by the most prominent follicles' granulosa cells. It has been observed that the synthesis of progesterone (P4) is increased during follicular growth (Rivas, Nieto, & Kamiyoshi, 2016). The second hormone, follicle stimulating hormone (FSH), is important for hen's fertility and reproduction. FSH stimulates the ovarian follicles to mature the eggs for ovulation (Stamatiades & Kaiser, 2018). Ovarian follicle dominance is a process in which one or more follicles are selected for further development. It has been examined that the dominant follicle secretes estradiol and inhibin, which in turn, suppress the secretion of FSH (Stamatiades & Kaiser, 2018). It has observed that the concentration of FSH and L.H. was maximum at ovulation.

Table 1: Classification of the Chicken ovarian follicle.

Abbreviation	**Classification**	**Color**	**Minimum diameter (mm)**	**Maximum diameter (mm)**	**Follicles number/ovary at maturity**	**Reference**
LYF	Large yellow follicles	Yellow	10		7-9	(Hrabia, 2021)
SYF	Small yellow follicles	Yellow	5	10	5-15	
LWF	Large white follicles	White	2-5	5	5-15	
SWF	Small white follicles	White		1	> 1000-12000	

PHYSIOLOGICAL FACTORS AFFECTING CHICKEN'S OVARIAN FUNCTIONS

Nutritional factors

Nutrition plays a vital role in a hen's reproductive system[6]. Nutrition has a significant effect on chicken ovarian function by improving the development of follicular growth (Scaramuzzi, Brown, & Dupont, 2010). It is essential to understand the process of ovarian follicle development (folliculogenesis). It is a nutritionally sensitive process in poultry birds. So, there is a link between nutrition and folliculogenesis. Nutritional association with folliculogenesis is believed to be mediated by various physiological pathways. Various studies exposed that the impact of short-term nutritional supplements on folliculogenesis is mediated through glucose, insulin, IGF-1, and leptin, all of which have a direct effect on the ovarian follicle **(**Fig 4). Insulin stimulates glucose uptake by the majority of hen cells, including follicular cells. The insulin-glucose metabolic

[5] Estrogen is responsible for oviduct development and decreases prolactin production (Munoz et al., 2012)
[6] Nutrition plays a vital role in a hen's reproductive system.

pathway promotes folliculogenesis by increasing ovulation rate and follicle number (gonadotrophin-responsive) (Downing, Joss, Connell, & Scaramuzzi, 1995)[7]. Additionally, IGF-1 (insulin-like growth factor) is largely produced in the liver to enhance estradiol synthesis by ovarian follicles, hence raising L.H. receptor expression(Kishi, Kitahara, Imai, Nakao, & Suwa, 2018). Thus, insulin is a key regulator of adipose function, and leptin is secreted by adipose tissue (Lecker et al., 2012).

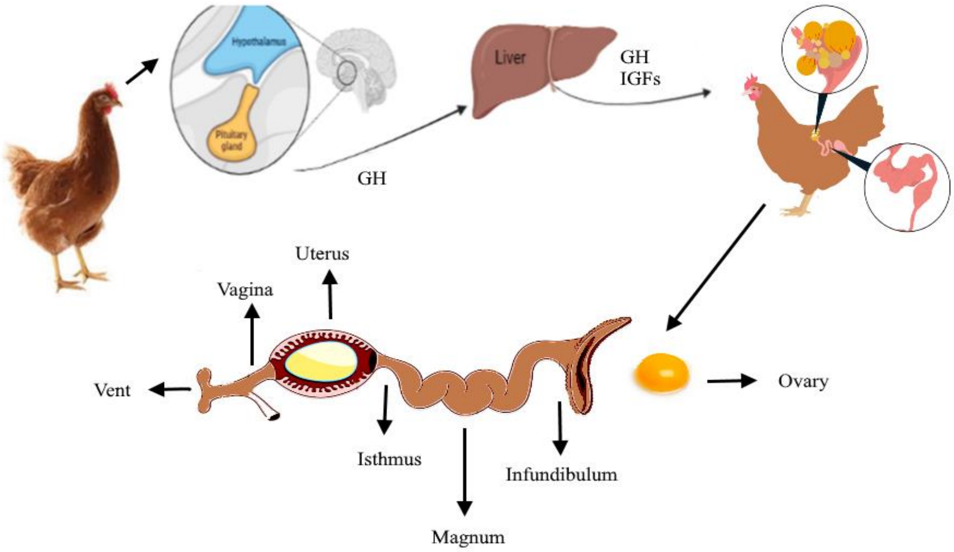

Fig. 4: Ovarian *physiology is primarily affected by GH and IGF. In granulosa and theca cells, both substances alter metabolizing enzymes, promoting steroidogenesis. The effects of GH/IGF on steroidogenesis may also be mediated by changes in gonadotropic receptors, and this may occur synergistically with gonadotropins.*

Leptin regulates folliculogenesis by inhibiting L.H. and FSH secretion. On the other side, the significant constraints in poultry production are poor feeding management, such as overfeeding or underfeeding, poor nutrition, overweight or underweight and poor health. Nutrient toxicity, excessive nutrient uptake, and obesity are major concerns in poultry farming[8]. A study reported that overfeeding causes hepatic steatosis, obesity and systemic inflammation (Wei et al., 2019). So, overfeeding induces ovarian dysfunction like oviduct inflammation and prolapse in broiler breeder hens which in turn, negatively affect egg production performance.

Fig. 5: *Prolapse of Oviduct in Poultry*

A high protein and lipid diet can cause a metabolic challenge in the hen's body during the laying period. Another study revealed that overfed broiler breeder hens produced EODES (erratic oviposition and defective egg syndrome) caused by the development of too many egg follicles (Eitan & Soller, 2009). This condition results in egg peritonitis (Gebremichael, 2017) which is also known as yolk stroke, abdominal sepsis,

[7] The insulin-glucose metabolic pathway promotes folliculogenesis by increasing ovulation rate and follicle number (gonadotrophin-responsive) (Downing et al., 1995)

[8] Nutrient toxicity, excessive nutrient uptake, and obesity are major concerns in poultry farming (Brière, Brillard, Panheleux, & Froment, 2011)

septicemia, and egg yolk peritonitis (Gebremichael, 2017). Peritonitis is defined as the inflammation of the peritoneum due to a bacterial infection (Demark-Wahnefried et al., 2008). It occurs when egg yolk doesn't go to the oviduct or into the abdominal cavity. A report described that egg yolk formation requires significant changes in the lipid metabolism in the laying hens. Moreover, lipogenesis is affected by hormonal and dietary factors, and overfed broiler breeder hens caused ovarian abnormalities and follicular atresia due to lipotoxicity which in turn, declined hen's production.

A study stated that a high carbohydrate diet greatly promotes lipogenesis in hen livers, resulting in hepatic steatosis (Bain et al., 2016). Hepatic steatosis arises due to an imbalance between the protein and energy ratio and generates obese hens, negatively affecting egg production[9].Furthermore, fatty liver hemorrhagic syndrome is a metabolic condition that affects laying hens. That generally happens throughout the summer. It causes large fat deposits in the liver, as well as hemorrhages and sudden death in layers. It is different from hepatic steatosis and lethal to poultry birds, resulting in a decrease in egg production.

Fig. 6: *Fatty Liver Disease in hens*

An issue with lipid metabolism called "fatty liver disease" is a prevalent reason for backyard and industrial laying hen deaths. The liver becomes hemorrhagic and unstable, and there is an excessive buildup of fat deposits in the abdominal cavity and liver. The equivalent "animal model" for NAFLD research is therefore hens. Because a chicken's lymphatic system is undeveloped, the liver is the first organ to come into contact with dietary lipids (i.e., adipose tissue). Here, lipid production and metabolism take place. This is different from mammals, who primarily produce fatty acids in adipose tissue rather than the liver. The liver of the chicken has a high level of lipogenesis, which is especially prevalent in ovulating females. Oestrogens significantly increase hepatic lipogenesis to support vitellogenesis.

Endocrine factors

The ovaries are the most important parts of the chicken reproductive system, which produces mature ovum. Ovarian function is controlled by gonadotropic hormones secreted from the hypothalamus, which activates the anterior pituitary gland to produce L.H., FSH, and prolactin

[9] Hepatic steatosis arises due to an imbalance between the protein and energy ratio and generates obese hens, negatively affecting egg production

(PRL).[10] The basic principle of the chicken ovaries' hormonal mechanism is simple. FSH initiates follicular growth and development, and L.H. is involved in the corpus luteum (CL) function. Moreover, L.H. is also responsible for inducing ovulation. The proper functioning of the chicken endocrine system is vital for follicular development. Hypothalamic neurotransmitters are influenced by photoperiod and affect seasonal reproductive physiology (Ross, Helfer, Russell, Darras, & Morgan, 2011). Photoreceptors in the quail's brain detect light stimuli and transfer them to the endocrine system (pars tubercles), which secretes thyroid stimulating hormone (TSH). TSH controls the release of GnRH from the anterior pituitary gland. TSH stimulates gonadal development by activating the type 2 and 3 deiodinase (dio2 and dio3) switching systems (Kang, Pierzchala-Koziec, Smulders, Ohkubo, & Well-Being, 2023; Ono et al., 2008). However, hormonal disorders can adversely affect male and female reproductive efficiency. A study in avian has reported that the hypothalamic-pituitary-gonadal (HPG) axis is rapidly 'switched off' by altering the photoperiod, and significantly reduced the growth of gonads (Sasanami, 2017). A similar study revealed that medio basal hypothalamic lesions in *Coturnix japonica* (Japanese quail) inhibited the response of photoperiod and gonadal activity.

In hens, there are two types of infundibulum: membranous and muscular[11]. Both enclose the entire ovary. The muscular infundibulum is coated with ciliated cells and serves as a pathway for the yolk inside the oviduct, while the membrane infundibulum covers the ovarian cluster. The egg stays in the infundibulum for just 15 to 30 minutes before moving down into the magnum, where albumen is laid down all around it. Therefore, any potential ovum fertilization also takes place at the infundibulum. The magnum, the biggest section of the oviduct, produces the egg-white proteins that encircle the yolk. While the ciliated epithelial cells assist in egg transport, the glandular epithelial cells of the magnum synthesize the various egg-white proteins, store them and only secrete them for 2-3 hours when the egg is present in it.

The egg white, which is high in protein, serves as the embryo's primary food supply while it is developing. Additionally, it contains a few antibacterial proteins that guard the embryo against harmful microorganisms. The weight of the egg and the hatchling are determined by the albumen, which makes up more than 60% of the entire egg. The egg descends later and spends the next one to two hours in the isthmus, which connects the shell gland and the magnum. The egg albumen is surrounded by the outer and inner eggshell membranes (ESM) in the isthmus. The fibrous networks that make up the eggshell membranes maintain the jelly egg white in place and serve as the site where eggshell mineralization first begins. The egg moves within the shell gland after being encased by the ESM, where it remains for roughly 18 to 22 hours, during which time calcite crystals are deposited to create the eggshell on the ESM. Since the eggshell contains 95% calcium by composition, it serves as the growing embryo's primary calcium source. The structure of the eggshell prevents external microorganisms from entering the egg while allowing air to circulate the egg to allow the inchoate embryo to breathe. The egg is kept in the vagina for a short period when the eggshell has fully mineralized. Some birds finish the pigmentation of their eggs in the vagina before laying them.

On the other hand, it is unclear how endocrine disorders affect wild birds. Endocrine disorders like cystic ovaries, hypothyroidism, and cystic hyperplasia are clinical issues in captive species (Akbarian, Golian, Sheikh Ahmadi, & Moravej, 2011; Crosta, Gerlach, Bürkle, & Timossi, 2003). Numerous studies showed that hormonal disorders negatively influence the egg production performance of captives. A study found that domestic fowl given LH 8.5 hours immediately after ovulation caused follicular atresia (degeneration) of the next ovarian follicle within the hierarchical follicles. The goal of the study was to find out how recombinant activating A and inhibin affected granulosa cells from varied-sized follicles. These elements were also believed to have autocrine and paracrine effects on the formation of ovarian follicles in addition to their known endocrine roles. Small yellow follicles (SYF; 6-12 mm) and large pre-ovulatory follicles (F1, F3, and F4) were taken from chickens in their first year of lay, respectively. With access to food and water, these hens were kept on a 14:10 lighting cycle.

Inhibin/Activing -B-subunit mRNA expression was generally low in granulosa cells from all follicle sizes, including SYF, according to the study's findings[12]. However, inhibin/activating -B-subunit expression was considerably upregulated in granulosa cells from all follicle sizes after activating a treatment at a dose of 50 ng/ml compared to the control treatment. A smaller dose of 10 ng/ml did not, however, show this impact. The research also revealed that granulosa cells had low levels of follicle-stimulating hormone receptor (FSHR) expression.

[10] Ovarian function is controlled by gonadotropic hormones secreted from the hypothalamus, which activates the anterior pituitary gland to produce L.H., FSH, and prolactin (PRL).

[11] In hens, there are two types of infundibulum's: membranous and muscular

[12] Inhibin/Activing -B-subunit mRNA expression was generally low in granulosa cells from all follicle sizes, including SYF, according to the study's findings

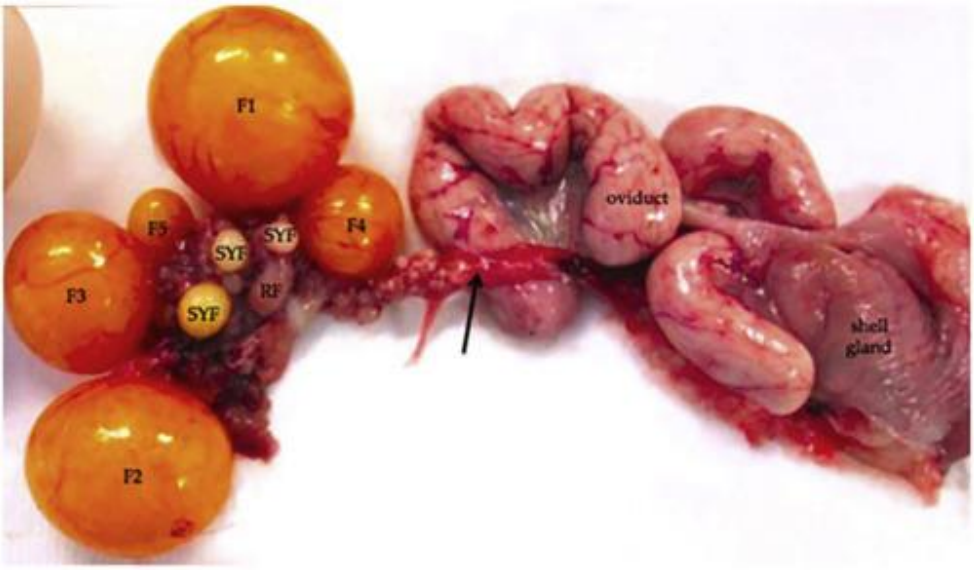

Fig. 8: *Follicle Development*

Inhibin/activating -B-subunit and FSHR expression in granulosa cells across different follicle sizes was shown to be positively affected by activating A at a concentration of 50 ng/ml. This shows that activin A may have a regulatory role in regulating ovarian follicle growth. The study's findings are unique because they shed light on activating A's effects on granulosa cells from different-sized follicles. They tie those effects to previously noted localization patterns of activin A and inhibin A inside the avian follicles. Similarly, the administration of synthetic GnRH in pigeons (*Columba Livia)* reduced the concentrations of L.H. and suppressed egg production (Grčević, Kralik, Kralik, Galović, & Pavić, 2016). The role of inhibin is vital in improving or reducing cell proliferation and is involved in folliculogenesis and hormonal secretion. Primarily, inhibin is produced by luteal cells, theca cells, and granulosa cells in the ovary. A study examined that inhibin, a treatment in laying hens, increased granulosa cells' proliferation.

In contrast, follicle atresia was observed in chickens during downregulating the expression of α -inhibin subunit (Cui et al., 2020). On the other side, injections of FSH in Australian zebra finches (*Taeniopygia gut Tata)* decreased egg production due to negative feedback on FSH secretion. However, it is thought that treatment timing is vital for FSH because its function varies with follicular size during normal conditions(Sasanami, 2017). Anti-Mullerian (AMH) hormone is a naturally occurring hormone in the hen's body that indicates reproductive fertility. It plays a significant role in developing ovarian follicles (Gruijters, Visser, Durlinger, & Themmen, 2016). However, the results of a study examined those higher levels of AMH caused restricted fertility in hens.

Disease and immune factors

There are some diseases of ovaries, such as neoplasia, cystic hyperplasia, salpingitis, ruptured oviducts, and ectopic ovulation, which decrease the profitability of the poultry industry (Keymer, 1980). Egg yolk coelomates are a common reproductive disease in laying hens. It causes inflammation of the hen's ovaries (Keymer, 1980). Poultry diseases like avian influenza (A.I.), avian hepatitis (A.H.), and infectious bronchitis (I.B.) cause inflammation of the oviduct, which, in turn, prevents the capturing of ova after ovulation. The highly pathogenic H5N1 strain of AI remains a significant problem, leading to significant interruptions in output and requiring expensive control measures such as culling and movement restrictions (Khan et al., 2021). Newcastle disease, known for its rapid spread, has a significant influence on the respiratory and neurological health of chickens, resulting in decreased production and higher death rates (European Food Safety Authority et al., 2023). Both disorders have a negative impact on the health of birds and also on the financial viability of the poultry business. This is particularly apparent in poor countries where there are fewer strict measures in place to prevent the spread of diseases (Rehman et al., 2022).

The above pathogens can induce oviduct injury, which can lead to bacterial infection (egg peritonitis) due to the presence of egg yolk in the coelomic cavity(Nawab et al., 2018). Various diseases cause a huge percentage of mortality in poultry birds, such as Newcastle disease (57.3%), fowl pox (31.6%), and coccidiosis (9.4%) (Nawab et al., 2018)[13]. Newcastle disease (N.D.) causes the highest percentage of mortality (death) in both domestic and wild birds. Secondly, chicken fowl pox, coccidiosis, and salmonellosis are associated with higher mortalities. The diseases mentioned above negatively affect the hens' follicular growth, ovarian function, and egg performance. The domestic laying hen spontaneously develops ovarian cancers (O.C.) with high prevalence. The incidence of O.C. increases with age; 24% occurs when ovarian cancer occurs at two years, and 30 to 35% occurs at 3.5 years of age (Johnson, Stephens, & Giles, 2015). O.C. is an age-associated disease caused by ovulatory events over time due to DNA damage.

Genetic and dietary variables are essential in determining poultry susceptibility to diseases and immune response. Avian species with certain genetic profiles may exhibit greater resistance to illnesses, whereas a well-balanced diet promotes a strong immune system, hence decreasing susceptibility to infections (Rehman et al., 2022). Environmental stresses, such as high temperatures, worsen these vulnerabilities, negatively

[13] Various diseases cause a huge percentage of mortality in poultry birds, such as Newcastle disease (57.3%), fowl pox (31.6%), and coccidiosis (9.4%) (Nawab et al., 2018)

affecting reproductive health and increasing the likelihood of illnesses. To counteract these repercussions, it is crucial to effectively control environmental conditions and implement targeted genetic and dietary treatments (Adlhoch et al., 2023).

Fig. 9: Breeder Hens Suffer from Egg Peritonitis

The mucosal immune system serves as the initial line of defense against pathogens like viruses, fungi, and bacteria in the hen's reproductive tract. Toll-like receptors (TLRs) activate the immune system and disease resistance by recognizing pathogen-associated molecular patterns (PAMPs)—[14]Ovarian cells from several species, such as chicken, bovine, and murine, show TLRS expression. An innate immunological response is started by TLRs in the chicken ovary. TLRs identify pathogens and produce antimicrobial peptides, pro-inflammatory cytokines, and chemokines (Sasanami, 2017; Yoshimura, 2015).

The innate immune response also includes natural killer cells (NKC), macrophages, and avian-defensins (antimicrobial peptides) (Sasanami, 2017). During bacterial infection, TLR affects steroidogenesis, which controls ovarian follicle growth. Salmonella infection is associated with food-borne diseases. A study has reported that poultry eggs and egg by-products are associated with >75% *Salmonella (S. enteritis)* outbreaks. Thereby, Salmonella-contaminated eggs are serious threat to human health. Furthermore, it is essential to understand the process of immunological response in the ovary of laying hens.

Adaptive immunity involves specific immune cells in the follicles, such as macrophages and B and T cells (Sasanami, 2017). MHC (major histocompatibility complex) proteins serve an important role in antigen presentation, T cell activation, and adaptive immunological mechanisms. Immunocompetent cells grow in the oviduct during sexual organ maturation but decrease considerably with age (Yoshimura, 2004). Ovarian autoimmunity causes infertility and premature ovarian failure in humans. However, the mechanisms of chicken ovarian autoimmunity are still unclear. However, it is supposed that antibodies that selectively target ovarian cells cause a decrease in egg production with increasing hen's age. During sexual maturation, the population of immune cells in the hen's ovarian follicles grows but decreases with aging, indicating that disease resistance is reduced in older hens, which can adversely affect egg production (Barua, Yoshimura, & Tamura, 1998). A study has revealed that immunity declines in aged hens due to increasing infectious agents in the ovary, which affect the hen's ovarian functions (folliculogenesis) (Sasanami, 2017) (Barua et al., 1998; Yoshimura, 2004). The findings of a study observed that obesity is associated with thyroid diseases, and autoimmune thyroiditis declines fertility in obese chickens.

Environmental stress and pollution factors

Reproduction efficiency is a critical aspect of poultry farming success (Ibtisham et al., 2017). Environmental conditions like diet, pollution, temperature, pH, and ion concentration all have an impact on the productive and reproductive abilities of chickens. Environmental stress reduces GnRH-induced FSH and L.H. secretion in poultry birds and causes infertility. Climatic change reduces the size of follicles, estradiol concentrations, and the expression of L.H. receptors (Kala, Shaikh, & Nivsarkar, 2017), which delays the process of ovulation. High temperature suppresses the hen's reproductive performance by decreasing the growth of follicular development[15]. Indeed, heat stress disturbs the balance of pro-oxidants and antioxidants, producing ROS (reactive oxidative species) in the poultry body and causing ovulatory dysfunction. A study exposed that antioxidant levels, heat shock proteins (HSP), and fatty acid composition were suppressed under hot climatic conditions, reducing the egg yolk maturation process. Moreover, heat stress decreases feed intake and causes nutrient deficiencies, reducing the production of laying hens.

Thermal stress and high stocking densities have a major negative impact on reproductive efficiency in chickens, creating considerable difficulties for farm management approaches. Elevated ambient temperatures cause thermal stress, which compromises the vital physiological

[14] Toll-like receptors (TLRs) activate the immune system and disease resistance by recognizing pathogen-associated molecular patterns (PAMPs).

[15] High temperature suppresses the hen's reproductive performance by decreasing the growth of follicular development

and hormonal balance necessary for reproduction. Elevated temperatures may induce heat stress, which has a negative impact on the hypothalamic-pituitary-gonadal axis, a crucial component for reproductive function. When birds experience heat stress, they consume less food, which leads to nutritional deficits that worsen their reproductive health. Oxidative stress caused by this stressor results in harm to reproductive organs, decreased sperm quality in males, and lower egg production in females (Rostagno, 2020; Wankar, Rindhe, Doijad, & Production, 2021).

Increased stocking densities worsen these problems by increasing competition for resources such as feed and water, leading to elevated stress levels. The presence of excessive numbers of individuals in close proximity enables the fast spread of diseases, leading to a decline in the general well-being and efficiency of the group. High stocking densities may induce stress, leading to aggressive behaviors, including feather pecking and cannibalism. These behaviors can result in injuries and further decrease reproductive success (Costa et al., 2021).

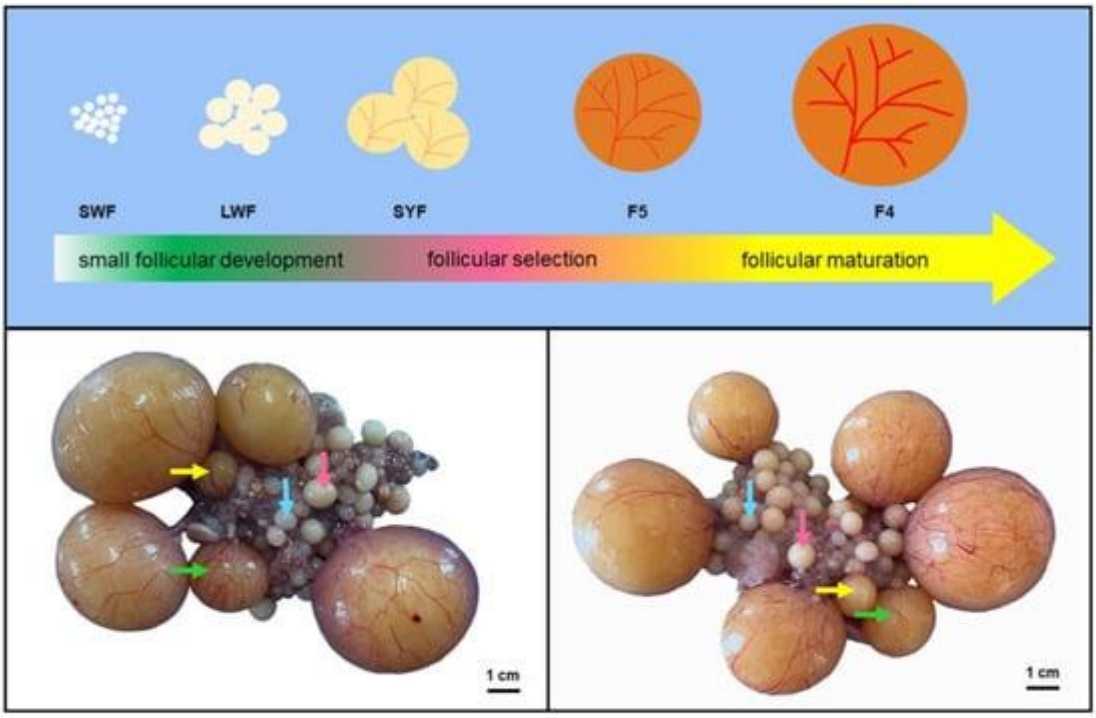

Fig. 10: *Follicular development and ovarian follicle sampling in Yangzhou geese are depicted graphically.*

Elevated ambient temperatures result in heat stress, causing disturbances in homeostasis and metabolic processes. Chickens experiencing heat stress demonstrate a drop in their consumption of food, resulting in a loss in body weight, slower development rates, and a decline in egg production. Heat stress also hampers reproductive functioning, diminishing egg quality and decreasing hatchability. In addition, heat stress may trigger oxidative stress, leading to tissue damage and compromising the general health of birds (Rostagno, 2020).

A study reported that hens who feel distressed above 30°C observed that laying hens exposed to 34°C high temperature had reduced egg production by 28.8% during two weeks of the experiment[16]. Elevating temperature is a big challenge for the poultry sector, which results in greater mortality and welfare problems, particularly during transportation (Vecerek, Voslarova, Conte, Vecerkova, & Bedanova, 2016). A similar study revealed that higher-weight chickens caused higher mortality during transportation. In another study, laying hens experienced a 12-day heat stress period during which their feed intake decreased by 28.58 grams per bird per day, and their egg production dropped by 28.8%. According to a study's findings, high temperature reduced egg weight by 3.24 %, eggshell thickness by 1.2 %, and eggshell weight by 9.93 %.

Various factors affect the hen's reproduction, but environmental pollution significantly affects chicken ovarian function (Ottinger et al., 2002). Over 90,000 toxic chemicals are released into the environment, adversely affecting human and animal health. Endocrine-disrupting compounds (EDCs) cause reproductive abnormalities in developing embryos. A study has reported that a low concentration of EDCs exposed to the environment negatively affected reproductive organs in poultry birds. The findings of a similar study revealed that seabirds exposed to a minute quantity of crude oil had depressed egg yolk formation, while American kestrels (*Falco sparverius*) exposed to flame-retardant additives had reduced reproductive performance (Fernie, Shutt, Letcher, Ritchie, & Bird, 2009). In addition, an estrogen-polluted environment produces reproductive abnormalities in female birds (Fry, 1995). Toxic metals also act as EDCs and disturb the bird's reproductive efficiency. A study has confirmed that Japanese quail exposed to cadmium rare earth elements significantly reduced egg production. In contrast, the results of another study indicated that lead adversely affected the ovaries of chickens, pheasants and Japanese quail (He, Wang, Li, & Zhao, 2020) which reduced the size of ovaries and delayed egg production. Additionally, zebra

[16] A study reported that hens feel distressed above 30°C (Nardone, Ronchi, Lacetera, Ranieri, & Bernabucci, 2010). (Deng, Dong, Tong, & Zhang, 2012) observed that laying hens exposed to 34°C high temperature had reduced egg production by 28.8% during 2 weeks of the experiment

finches exposed to low mercury concentrations significantly reduced reproductive organs.

At an altitude of 650 meters above sea level and between the latitudes of 11°N and 12′N and the longitudes of 7°E and 8′E, the Northern Guinea Savannah zone of Nigeria sees three distinct meteorological seasons: Hermitian (November to February), hot and dry (March to May), and rainy (June to October). The average annual maximum and lowest temperatures are respectively 31.8 3.2 °C and 18.0 3.7 °C, with a relative humidity of 71.1 9.7%. The rainy season has an average rainfall of 148 68.4 mm (69.2-231.9 mm). Understanding the effects of these climatic factors on chicken production is essential for efficient management.

In tropical regions like Nigeria's Northern Guinea Savannah zone, heat stress is a significant problem while raising chickens. Heat stress can be very severe when ambient temperatures and relative humidity are high, especially during the hot, dry season. Extensive management methods are prevalent in tropical areas, leaving chickens exposed to temperature changes, in contrast to temperate zones where controlled indoor conditions reduce heat stress.[17] Different facets of poultry production are significantly impacted by heat stress.

Heat stress lowers feed intake, which impacts hen days and egg quality in terms of egg production. High temperatures alter the pulsatile gonadotrophin-releasing hormone generator frequency, impairing ovarian and follicle-stimulating hormone release and affecting reproductive processes. Thus, egg quality, size, albumen consistency, and eggshell quality are affected.

Male fertility is similarly impacted by heat stress. The quantity and quality of semen are affected by elevated temperatures, which also affect sperm motility and fertilizing ability. Sperm structure and function are harmed by heat stress-induced lipid peroxidation of cell membranes. Male fertility dramatically declines, and male infertility contributes more to overall reproductive failures when combined with females subjected to identical conditions.

The mechanisms behind heat-induced infertility are disruption of the connection between sperm and uterine epithelial cells, capacitation, the acrosome response, and zonal vesicle binding. Lipid peroxidation occurs when reactive oxygen species produced by thermal stress attack polyunsaturated fatty acids in sperm cell membranes. This impairs sperm viability and functionality and destroys cell membranes.

MITIGATION STRATEGIES TO OVERCOME CHALLENGES AFFECTING CHICKEN OVARIAN.

A high protein and lipid diet causes a metabolic challenge in the hen's body during the egg-laying period. A study revealed that overfed broiler breeder hens produced erratic oviposition and defective egg syndrome (EODES) caused by the development of too many eggs. This condition results in egg peritonitis. Hence, managing chicken body weight, flock uniformity, reproductive performance (follicular growth and maturation), and drinking water sanitation can decrease the risk of EODES (Gebremichael, 2017). Thus, it is recommended to avoid over-feeding and supplemental lighting in the young cage layers, and a high-quality diet, as well as adequate room for exercise, should be provided to layers. It has been proposed that ammonia concentration, dry and dusty environmental conditions, and overcrowding should be reduced in poultry farming to improve the hen's production performance. Therefore, adequate ventilation, fresh drinking water, and moderate feeding are the best preventive strategies (Bassiony, Aluko, & Radosevich, 2020; Keller et al., 2013). A metabolic disease that affects laying hens is called fatty liver hemorrhagic syndrome (FLHS).[18] It is caused by the deposition of too much fat in the liver, which results in hemorrhages and rapid death in layers (Choi et al., 2012). Thus, FLHS can be avoided by consuming enough fat (< 3.5%) and energy levels (CP > 17.5%) in the poultry diet, which may reduce the liver metabolic burden. To avoid tissue rancidity, poultry diets should contain sufficient amounts of antioxidants such as vitamin E (50–100 kg) and selenium (0.3 ppm). To metabolize liver fat and heal affected hens, lipotropic feed additives, including chlorine (500 mg/kg), methionine (0.1%), and vitamin B12, should also be supplemented. Calcium insufficiency is a result of FLHS. So, it can be prevented by providing vitamin D and large calcium particles in the layer ratio.

Various dietary strategies overcome the adverse effects of high temperatures. So, it is recommended that freshwater, nutrients, electrolytes, vitamins, and minerals should be provided during hot environmental conditions. The data from a study observed that drinking fresh water can reduce the symptoms of heat stress(Teeter & Belay, 1996). Therefore, it is suggested that adding electrolytes (Na, Cl, K, and $NaHCO_3$) may increase the capacity of layers and broiler hens to withstand heat, and these strategies are successful in poultry production[19]. For example, supplementing vitamins A, C, and E in poultry diets improves egg production, hatchability, and fertility, as well as reduces egg breakage and mortality in hot environments. As a result, it has been discovered that vitamin supplementation is required to decrease the negative effects of heat stress.

A study found that supplementing stressed chickens with vitamin A at 9,000 IU/kg enhanced their feed intake, laying rate, and immunity when compared to the control group (3,000 IU/kg) examined that Niacin (vitamin B3) supplementation prevents various metabolic diseases in animals, including poultry (Panda et al., 2017), and helps in proper metabolism, digestion, and blood circulation. Vit B2 (Riboflavin) reduces lipid peroxidation and improves the level of antioxidants in poultry birds. A study (Rajabi & Torki, 2021) observed that vitamin C and zinc supplementation at a dose of 240 mg/kg diet improved the egg quality of laying hens under cold stress conditions (13 to 15◦C). A USA study exposed those hens fed vitamin E supplementation at a dose of 65 I.U. /kg diet had increased the egg quality, egg mass, and egg yolk formation under hot climatic conditions. A similar study found that probiotic treatment reduced the negative effects of high temperatures on laying hen intestinal health and egg performance (Deng et al., 2012).

[17] Extensive management methods are prevalent in tropical areas, leaving chickens exposed to temperature changes, in contrast to temperate zones where controlled indoor conditions reduce heat stress.

[18] A metabolic disease that affects laying hens is called fatty liver hemorrhagic syndrome (FLHS).

[19] Therefore, it is suggested that adding electrolytes (Na, Cl, K, and $NaHCO_3$) may increase the capacity of layers and broiler hens to withstand heat, and these strategies are successful in poultry production.

As a result, various environmental circumstances and nutritional techniques are recommended to mitigate the negative consequences of environmental stress. For example, several housing systems such as cage systems, perforated plastic floor-rearing systems, and deep litter-rearing techniques should be adopted to prevent the adverse effects of heat stress on poultry production and ovarian function. The installation cost of a cage system is high, so a deep litter-rearing system should be preferred for rearing broilers and laying hens in developing countries due to low pathogenic infections and better immunity (Ghanima et al., 2020); (Farghly et al., 2018). In poultry housing, the high temperature needs to be kept under control to minimize its negative effects on hens[20]. Moreover, ventilation technologies can minimize the effect of heat stress (Pawar et al., 2016). Hence, adequate ventilation and cooling systems should be applied in hot climates to maintain the environmental temperature in a comfort zone. Ventilation equipment should be appropriately implemented and kept up with frequently. In an emergency, extra ventilation fans and generators must be accessible (Nawab et al., 2018).

In the last 40 years, genetic selection has increased broiler growth rate and feed efficiency while lowering heat tolerance compared to broiler chicks that develop slowly. It has been found that laying hen's egg quality and production are adversely affected by high temperatures (Barrett et al., 2019). Hence, genetic improvement projects are assisting in improving egg quality and laying hen productivity (Radwan, 2020). Previous studies indicated that quantitative trait locus (QTL) could help scientists select heat-tolerant chicken breeds to improve ovarian function, immunity, and growth performances. A study found that QTL can improve the egg albumen quality of laying hens , and the Integrin beta-5 (ITGB5) gene improved the ovarian function of ducks (Longyan Shan-ma breed). A transcriptomic study showed that the High-temperature requirement factor A3 (HtrA3) gene is involved in the duck's ovarian development (black Muscovy breed) (Singh, Endo, & Nie, 2011)[21]. Moreover, the gene for transforming growth factor (TGF) 2 is essential for controlling duck ovary germ cells. The nerve growth factor receptor (NGFR) gene is involved in the growth, development, and function of female duck's reproductive organs (Black and White Muscovy).

Hyperfunction disorders can be suppressed by using radiation therapy, surgery, and drugs that can decrease hormone production. In the poultry industry, pollutants such as nitrogen, phosphorus, ammonia, and methane cause air, soil, surface, and groundwater pollution. So, pollutants should be minimized by modernizing poultry farms. Poultry manure contains many nutrients, such as potassium, phosphorus, and nitrogen. It is also a good source of zinc, manganese, and copper, which are valuable organic fertilizers that improve soil quality (Ayers, 2020). Hence, manure as a fertilizer can reduce environmental pollution (air, surface, and groundwater). Poultry farmers can't use expensive technology, so affordable technologies should be used to minimize the effect of poultry pollutants on the environment.

[20] In poultry housing, the high temperature needs to be kept under control to minimize its negative effects on hens

[21] A transcriptomic study showed that the High-temperature requirement factor A3 (HtrA3) gene is involved in the duck's ovarian development (black Muscovy breed) (Singh et al., 2011)

CONCLUSION

In the layer industry, reproductive efficiency is a critical economic aspect. However, various important physiological factors (diet, stress, disease, and pollution, etc.) adversely affect the ovarian function of laying hens. For example, heat stress costs the poultry business $128 to $165 million in economic losses each year, and both disease and environmental stress reduce feed intake, growth rate, egg quality, and reproductive health of laying hens. Hence, managing chicken health status, flock uniformity, reproductive performance, and drinking water sanitation can decrease the risk of stress-associated metabolic diseases. Therefore, adequate ventilation, fresh drinking water, and feed are the best preventive strategies to overcome the harmful effects of environmental stress. Various nutritional strategies should be used to alleviate the detrimental effects of high temperatures[22]. Therefore, it is strongly recommended that the above mitigation strategies can be used commercially to improve the ovarian function of laying hens in hot areas of the world.

FUTURE RECOMMENDATION

i. Examining the mechanisms regulating follicular recruitment and maintenance is necessary because it is a major challenge in avian reproductive studies.
ii. The CD9 gene has fertility effects in avian species. More knowledge is needed on CD9's involvement in bird sperm-egg fusion. So, the impact of the CD9 gene in laying hens should be explored.
iii. The anti-millenarian hormone (AMH) is involved in ovarian follicular development, and its higher level causes fertility restriction in hens. Therefore, it is important to examine how the anti-millenarian hormone affects avian female fertility.
iv. Exposure to endocrine-disrupting substances (EDCs) has various effects on bird species. Thus, it is important to investigate how EDCs affect laying hen fertility, which will include long-term monitoring, the development of analytical methodologies, and laboratory investigations.

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