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Chicken Infectious Anaemia Virus: A Mini-Review

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Abstract Chicken Infectious Anaemia Virus (CIAV), also known as Chicken Anaemia Agent (CAA) or CAV Chicken Anaemia Virus, is the smallest DNA virus classified in the genus *Gyrovirus* of the family Circoviridae. Since its first identification in 1979 by Yuasa and his colleagues, CIAV is a virus non-enveloped, stable and very resistant to the environment and disinfectants, it has a simple circular DNA chain. All CIAV strains are known until now belong to the same serotype, which means that there are no major antigenic differences, although there may be diversity in the genome of the virus. CIAV has caused great economic losses for the poultry industry, due to its serious immunosuppressive potential and ability to predispose to multiple secondary bacterial infections, subsequently playing a key role in the aetiology of several multifactorial diseases, immune suppression and the production of antibodies for chicken infectious anaemia in field challenge. Along with notable characteristics such as vertical/horizontal transmission, ubiquitous, contagiousness, resistance and propagated nature. The poultry industry needs the immunization of the breeding birds, in order to avoid the horizontal transmission of the virus and provide maternal antibody titers that give massive protection to the progeny. This review presents an updated comprehensive overview on CIAV.
Key words: Chickens, Chicken Infectious Anaemia Virus (CIAV), *Gyrovirus*, Immunosuppression.

فيروس أنيميا الدجاج المعدية: مـــــرجـــع مُـــصـــغّـــر

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الملخص فيروس أنيميا الدجاج المعدية (CIAV)، و المعروف أيضاً باسم العامل المسبب لأنيميا الدجاج (CAA) أو فيروس أنيميا الدجاج CAV، هو أصغر فيروس يحتوي حمض نووي منقوص الأكسجين د. ن. أ– DNA، مصنف ضمن جنس فيروس *جايروفيروس* (*الفيروس الملفوف*) *Gyrovirus* من عائلة الفيروسات الدائرية Circoviridae. منذ أول ما تعرف عليه في العام 1979م من قِبل يواشـــا Yuasa و زملائه، فيروس أنيميا الدجاج المعدية CIAV هو فيروس غير مغلف، ثابت و مقاوم جداً للبيئة والمطهرات، و له سلسلة د. ن. أ– DNA دائرية بسيطة. جميع سلالات فيروس أنيميا الدجاج المعدية المحددة حتى الآن تنتمي إلى نفس النمط المصلي، مما يعني أنه لا توجد اختلافات مستضدية كبيرة، على الرغم من وجود تنوع في جينوم الفيروس. يتسبب فيروس أنيميا الدجاج المعدية في خسائر اقتصادية كبيرة لصناعة الدواجن، تكمن خطورته بسبب إمكانية حدوث كبت مناعي وقدرته على تهيئة الطيور المصابة للاستعداد للعدوى البكتيرية الثانوية المتعددة، و من ثم يلعب دوراً رئيسياً في التسبب بالأمراض متعددة العوامل، الكبح المناعي و إنتاج الأجسام المضادة لفيروس أنيميا الدجاج المعدية في حالة التعرض الحقلي. إلى جانب الخصائص الملحوظة مثل الانتقال الرأسي/الأفقي، احتمال وجوده في في كل مكان و زمان مع سعة الانتشار ، السريان المعدي، و خاصية المقاومة و طبيعة التكاثر. تحتاج صناعة الدواجن إلى تحصين الأمات بمراحلها الجيلية المختلفة، و ذلك من أجل تفادي انتقال الفيروس بشكل أفقي و توفير كم معياري من الأجسام المضادة تعطي حماية هائلة للنسل. هذا المرجع يُقـــدم نظرة عامة محدّثة و شاملة عن ماهية فيروس أنيميا الدجاج المعدية.
الكلمات المفتاحية: دجاج، فيروس أنيميا الدجاج المعدية (CIAV)، *جايروفيروس*، كبت مناعي.

Background

CIAV was first described by Yuasa *et al.*, (1979) [1] in commercial chickens (both in broilers and layers); since then, the virus has been detected by isolation or serology in most countries, [2]. The first report of an CIAV isolation in the USA was by Rosenberger and Cloud in 1997, these authors makes a retrospective serological investigation and clinical evaluations that indicates that the virus has existed for at least 25 years in the USA [3].

Taxonomy and characteristics of CIAV

CIAV is the smallest DNA virus classified in the genus *Gyrovirus* of the family Circoviridae, of 25 nm, the aetiology behind CIAV, has gained great importance as an emerging poultry pathogen worldwide [4]. CIAV is 23.5-25 nm in size,

icosahedral, non-enveloped virus having a 2.3 kbp circular single stranded DNA genome (Figure. 1).

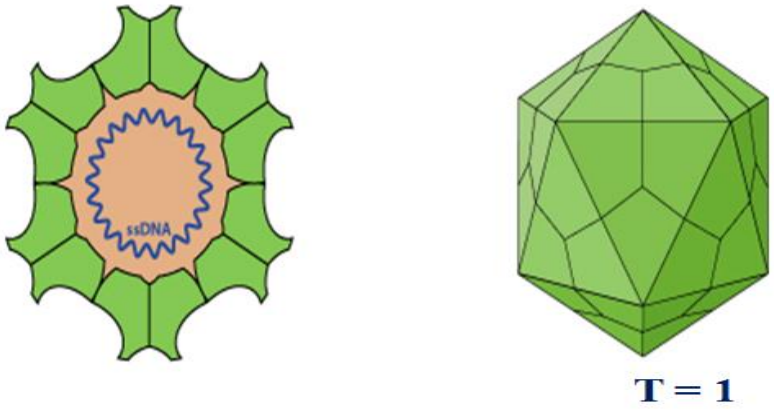

Figure 1: CIAV virion; Non-enveloped, round, T= 1 icosahedral symmetry, 23.5-25 nm in diameter. The capsid consists of 12 pentagonal trumpet-shaped pentamers

The genome codes for three viral proteins (VP1, VP2 and VP3) transcribed from single major transcript of 2.0 kbp size from three overlapping reading frames (ORF1, 2 and 3) (Figure. 2).

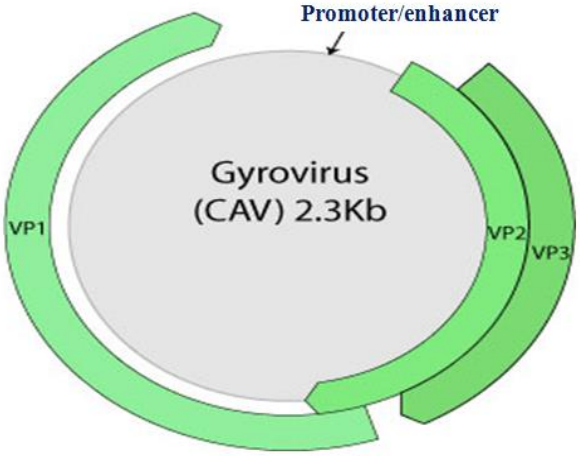

Figure 2: Diagram of the genome codes of CIAV

It is believed that CIAV genome replicates through rolling circle model [5], and is very hardy, difficult to inactivate thermally or with common disinfectants, which limits the utility of normal sanitization practices.

CIAV is generally considered to be omnipresent in both egg and meat-type chickens worldwide. Affected young birds appear anorexic, depressed, and with aplastic anaemia, which is characterised by PCV values ranging from 6 to 27%, with consequences including generalized lymphoid depletion and immunosuppression [6]. In the breeding periods, CIAV is responsible for increased mortality, reduced performance and decreased resistance to viral and bacterial diseases [7, 8]. The effect of immunosuppression was increased when the chicken populations infected with several infectious diseases.

Epidemiology

The only host for CIAV is chickens, it is spread throughout the world mainly in countries of industrial production, the susceptibility of birds decreases with age [3]. After CIAV infection, viraemia and spread of the virus to the bone marrow, lymphoid organs, liver, heart, lung etc occurs [9]. Due to the hemocytoblastosis in the bone marrow, the depletion of lymphocytes in the cortex of thymus and the alterations in other organs of the immune system, the birds will suffer from anaemia and immunodeficiency [2, 10].

When a flock of breeders is negative to CIAV becomes infected during the laying period, vertical transmission occurs, which will start from 7 to 14 days after infection and may last from 3 to 9 weeks depending on the spread of the virus within the flock [9], and when the breeders seroconvert and reach sufficiently high levels of neutralizing antibodies, to avoid vertical transmission [11]. Breeders will not have clinical signs or lesions while the congenitally infected hatching bird will suffer from the disease, the first sign is an increase in mortality from 10 to 14 day of age with the peak at 21 day, and by horizontal transmission a second peak between 30 and 33 day [10].

Pathogenesis

The entry route of the virus is determinant in the severity of the infection and time of appearance of the clinical signs and generation of immunity [12]. The experimental inoculation of CIAV intramuscularly in chicken birds of specific pathogens free (SPF) less than 4 weeks of age determines anaemia that begins 8 to 10 days post inoculation (PI) while birds inoculated by the oral route show a less severe reduction that starts at day 14 PI [12].

Anaemia occurs as a result of the destruction of erythroblast cells in the bone marrow. Affected chickens show yellowish bone marrows instead of red characteristic of normal bone marrow [9]. Hematocrit has usually been restored to normal levels in surviving chicken birds around day 28 PI [13]. CIAV is also characterised to produce aplastic anaemia, intramuscular and subcutaneous haemorrhages, with causing atrophy of the thymus and the immunosuppression of young chickens [14]. It is

common to observe haemorrhages in different parts of the carcass of chickens affected by CIAV, including the musculature. The cause of the haemorrhages is thrombocytopenia, which by reducing the platelet concentration decreases the coagulation capacity [15].

Weight gain is reduced following a temporal pattern similar to that observed in the hematocrit [15]. Thus, chicken birds inoculated intramuscularly reduce weight from 8 to 10 days PI while oral inoculation decreases weight gain from day 14 PI [14]. Weight loss is more drastic in chickens infected by the parenteral route. Unlike hematocrit, weight loss has not been restored until day 28 PI with differences of up to 35% lower compared to non-inoculated controls [15].

CIAV induces destruction of lymphoblasts particularly in the thymus. Histopathological lesions in the thymus are characterised by lymphoblastoid depletion, particularly in the cortex of the shy lobe, presence of intranuclear inclusion bodies and cells with apoptotic alteration [16].

Hosts and worldwide distribution

The only hosts for the virus are *gallinaceous*, it is spread throughout the world, mainly in the countries of industrial production. The virus has been isolated from Japan, USA, Brazil, Germany, Denmark, England, Libya, Mexico, Argentina, Chile and among others. In other countries, seroconversion has been recognized as evidence of the presence of the virus (Colombia, Peru, Ecuador, Australia, New Zealand and Malaysia) [17]. In 2010, antibodies against CIAV were found among free-range chickens in the northeastern area-Libya after conducting a serological evaluation survey of the virus [18].

In Granada, an island country of the Caribbean sea, CIAV is widely distributed in commercial chicken (broilers and layers) lines [19]. In Spain in 2009, the positivity of CIAV was determined in the provinces of Catalonia and Aragon [20]. There is a wide distribution of the CIAV and a considerable high prevalence of infection (82.28%) among commercial broiler breeders and broilers flocks in Libya [11]. Consequently in 2014, PCR analysis detected CIAV-DNA in all tested tissue samples (100%) of backyard chickens in Libya [21]. Based on this finding in 2012, Gerish find that, CIAV-DNA in embryonic tissues (embryonic organs and egg shell membrane) from broiler hatchery, originated from hens (parent stock) with virus neutralizing antibodies [11]. This outcome supports the previous evidence that CIAV may remain in the gonads of antibody positive chickens and can be vertically transmitted to their progeny [13]. The finding by Schat and Santen [2] indicated low level of viral transcripts can be detected in the developing embryo during specific developmental periods supporting the this hypothesis that, it may be possible that a limited viral replication occurs in the embryos, but if the embryos have virus neutralizing antibodies, the virus neutralizing antibodies prevent the development of viremia in the embryos [22]. In addition to the widespread use in chickens of live vaccines produced with CIAV contaminated eggs or cells may have played a role in the dissemination of CIAV to chickens due to the previously undetected CIAV infection of SPF flocks [23]. Examination of tissues from embryos obtained from hens positive for viral DNA in the gonads showed that the embryos can carry the viral DNA without signs of virus replication, thus continuing the transmission cycle [24]. These data strongly support the suggestion, first made by McNulty (1991) that CIAV can establish a latent infection [25]. A periodic testing of egg shell membrane residues at hatch by PCR assay can be used to identify the flocks carrying CIAV-DNA [24].

Transmission

The horizontal transmission is produced by direct contact with diseased and indirect birds with infected material. The route of entry of the virus is by ingestion or inhalation [10]. The virus, when transmitted through the transovarial route, can cause severe offspring disease, characterised by anaemia, subcutaneous haemorrhage, and a decrease in resistance to secondary bacterial diseases such as gangrenous dermatitis [26]. Affected birds, if coinfected with the Infectious Bursal Virus, can develop deep immunosuppression with increased susceptibility to a wide range of viral and bacterial pathogens [3].

Clinical form of the disease it occurs when susceptible chicks are infected very early (breeders with active infection) [27]. It is of acute presentation, occurs between 7 and 14 day of age. Birds show depression and mortality It can be more than 60%, more commonly between 5 and 10%. There is a peak mortality between 17 to 24 day of age. There may be a second peak of mortality at 30 to 34 day of age, probably due to horizontal transmission [2].

Subclinical form of the disease

Maternal antibodies remain for 2 to 3 weeks, after which the birds become susceptible to infection [28]. Subclinical infection leads to a decrease in productive performance with consequent economic losses [29]. Subclinical infection of CIAV results in immunosuppression. Indirect evidence includes inadequate responses to vaccination such as Newcastle Virus Disease (NVD), Infectious Laryngotracheitis (ILT) and Marek's Disease (MD) [30]; high initial mortality and Marek's disease in pullets, as well as an increase in the pathogenicity of several agents such as Marek's Disease Virus (MDV), Reovirus, Infectious Bursal Virus (IBD), Newcastle Disease Virus (NDV), Inclusion Body Hepatitis (IBH), *Staphylococcus aureus* and *Cryptosporidium* spp [17].

The virus inoculated in birds older than 6 weeks of age can be found in several organs. It is very difficult to isolate the virus after 2 weeks of infection. After the natural atrophy of the thymus it is more difficult to find the virus or lesions. Bursectomized birds may suffer from the clinical form for longer [17].

Clinical semiology and lesions

In birds infected at very early ages, the manifestations they present are not specific to the disease such as: depression, growth retardation, ruffled feathers, increase in dead and culls from 10 to 14 days after infection [31]. Mortality is usually between 5 and 10%, although depending on the pathogenicity of the strain, simultaneous infections can cause much higher levels; the morbidity within the flock is almost 100% with the consequent production decreases [10].

Macroscopic lesions are more frequently observed at necropsy, with a pale or yellowish bone marrow due to anaemia, severe atrophy of the thymus, haemorrhages in the proventriculus mucosa as well as muscular and subcutaneous [30]. In the latter case they may appear in the wing, and may be complicated by secondary bacterial infections and gangrenous or blue wing dermatitis. The hematocrit, which under normal conditions is around 27%, will be below 20% in birds suffering from anaemia from 8 to 10 days after infection [10].

Diagnosis

For the diagnosis CIAV we must take into account some factors such as: that the signs and lesions are suggestive to CIAV, the age of presentation, the productive parameters, among others. Being a virus of global distribution is relatively easy to find [10].

As direct methods of diagnosis, viral isolation and detection of genetic material can be performed by molecular biology (PCR) or direct immunofluorescence (DIF) [32]. We can also diagnose it using serological techniques such as virus neutralization (VN), ELISA and indirect immunofluorescence (IIF). Of the three the most sensitive and effective is VN but too complex as a routine technique, the ELISA test is reliable and practical for bird monitoring [10].

Prevention and control

The control of immunosuppressive diseases depends on biosecurity to avoid exposure to the causes of immunosuppressive diseases, and the increase of resistance to withstand the challenge of immunosuppressive agents through immunization and genetic selection [33]. Today, with the expansion of the chicken flock batches, the litter (bedding) is reused due to economic and environmental limitations, cleaning and disinfection must become seasonal events instead of occurring after each batch [32].

Strategies for the control of immunosuppression in commercial chickens (broilers and layers) are largely based on vaccination programs for broilers breeders progeny, and management to minimize stress during breeding [33]. The available vaccines are live attenuated viruses, which must be delivered between 6 and 18 weeks of age.

References

[1]- **Yuasa, N., Taniguchi, T. and Yoshida, I. (1979).** Isolation and some characteristics of an agent inducing anemia in chicks. *Avian Diseases*. 23: 366-385.

[2]- **Schat, K. A., and Santen, V. (2013).** Chicken infectious anemia. In: Diseases of Poultry. (13th Edn). Swayne DE, Glisson JR, McDougald LR, Nolan LK, David Suarez, L.D, and Nair, V. (Editors), Blackwell Publishing, Ames, Ch. 8, pp: 248-264.

[3]- **Rosenberger, J. K., and S. S. Cloud. (1997).** Chicken anemia virus. *Avian Diseases*, 33, 707-713.

[4]- **Bhatt, S., Shukla, K., Mahendran, M., Dhama, K., Chawak, M. and Kataria, M. (2011**). Prevalence of Chicken infectious anemia virus (CIAV) in commercial poultry flñocks of Northerm India: A serological. *Transboundary and Emerging Diseases*, 58, 458-460. doi: 10.1111/j.1865-1682.2011.01215.x.

[5]- **Meehan, B. M., Todd, D., Creelan, J. L., Earle, J. A. P., Hoey, E. M. and McNulty, M. S. (1992).** Characterization of viral DNAs from cells infected with chicken anaemia agent: sequence analysis of the cloned replicative form and transfection capabilities of cloned genome fragments. *Archives of Virology*. 124: 301-319.

[6]- **Toro, H., Ramirez, A.M., Larenas, J. (1997).** Pathogenicity of chicken anemia virus (isolate 10343) for young and older chickens. *Avian Pathology*. 26: 485-499.

[7]- **Rosenberger, J.K., and S.S. Cloud. (1989).** The isolation and characterization of chicken anemia agent (CAA) from broilers in United States. *Avian Diseases*. 33: 707-713.

[8]- **McIlroy, S.G., McNulty, M.S., Bruce, D.W., Smyth, J.A., Goodall, E.A., Alcorn, M.J. (1992).** Economic effects of clinical chicken anemia agent infection on profitable broiler production. *Avian Diseases*. 36: 566-574.

[9]- **Zhang, X., Liu, Y., Wu, B., Sun, B., Chen, F., Ji, J., Ma, J., and Xie, Q. (2013).** Phylogenetic and molecular characterization of chicken anemia virus in southern China from 2011 to 2012. *Scientific Reports*, 3(1) .doi:10.1038/srep03519.

[10]- **Biarnés, M. (2014).** Revisión de la anemia infecciosa del pollo. Portal Veterinario albeitar, Recuperado de http://www.wpsa-eca.es/articulo.php?id_articulo=2055.

[11]- **Gerish, E. KH. (2012).** Epidemiological Study on Chicken Infectious Anaemia Virus in Broiler Breeders in Libya. Thesis (*M.V.Sc*), Department of Preventive Medicine, Faculty of Veterinary Medicine, Tripoli University.

[12]- **van Santen, V., Joiner, K., Murray, C., Petrenko, N., Hoerr, F., and Toro, H. (2004**). Pathogenesis of chicken anemia virus: Comparison of the oral and the intramuscular routes of infection. *Avian Diseases*, 48: 373-388.

[13]- **Cardona. C., Wendelin, B., and Schat., K. (2000).** Distribution of chiken anemia virus in the reproductive tissues of specific-pathogen-free chickens. *Journal Genetic Virology*, 81: 2067-2075.

[14]- **Oluwayelu, D., Todd, D. and Olaleye, O. (2008).** Sequence and phylogenetic analysis of chicken anemia virus obtained from backyard and commercial chickens in Nigeria. Onderstepoort. *Journal of Veterinary Research*, 75: 353-357.

[15]- **Toro, D., Van Santen, V., Hoerr, F., and Breedlo, T. (2009).** Effects of chicken anemia virus and infectious bursal disease virus in commercial chickens. *Avian Diseases*, 53(1), 94-102 Recuperado: http://www.ncbi.nlm.nih.gov/pubmed/19432010.

[16]- **Toro, H. (2011).** Control de anemia infecciosa aviar.Argentina: Congreso Latinoamericano de Avicultura. Recuperado de http://www.elsitioavicola.com/articlesw/2095/control-de-anemia-infecciosa-aviar.

[17]- **Cardoso, B. (2006).** Anemia infecciosa aviar: El control de la inmunosupresión. Estados Unidos. Recuperado de http://detodounpoco2021.bligoo.es/media/users/24/1220632/files/356618/ANEMIA_INFECCIOSA_Control_de_inmunosupresion.pdf.

[18]- **Gerish, E., Mansour, L., Gawas, A., Al-Kateb, A., Al-Khallab, E., Skeeb, A., and Al-Ghriany, O. (2017).** Prevalence of Antibodies Against Chicken Infectious Anaemia Virus Among Free-Range Chickens in Northeastern Libya. *Alq J Med Hum Sci.*;1(2):14-19.

[19]- **Sharma, R., Tiwari, K., Chikweto, D., Thomas, D., Stratton, G., and Muhammad, I. (2013).** Serological evidence of chicken infectious anemia in layer and broiler chickens in Grenada, West Indies. *Veterinary World*, 7(2), 59-61.

[20]- **Biarnés, M., Blanco, A.,Camprubí, Q., Canals, N. and Porta, R. (2009).** Anemia infecciosa del pollo en sistemas de producción con elevada bioseguridad. *XLVI Symposium científico de avicultura, Recuperado de* http://www.wpsa-aeca.es/articulo.php?id_articulo=2055.

[21]- **Al-Kateb, A., Mansour, L., Skeeb, A., Al-Khallab, E., Dardour, A., and Gerish, E., KH. (2017).** Molecular Detection of Chicken Infectious Anaemia Virus from Backyard Chickens in Libya *Alq J Sci Res.*;6(1):70-76.

[22]- **Brentano, L., S. Lazzarin, S. S. Bassi, T. A. P. Klein, and K. A. Schat. (2005).** Detection of chicken anemia virus in the gonads and in the progeny of broiler breeder hens with high neutralizing antibody titers. *Veterinary Microbiology*, 105: 65-72.

[23]- **Barrios, P.R., S.Y. Marin, M. Resende, R.L. Rios, J.S. Resende, R.S. Horta, M.P. Costa and N.R.S. Martins. (2009).** Occurrence of chicken anemia virus in backyard chickens of the metropolitan region of belohorizonte, Minas Gerais. *Brazilian J. Poult. Sci.* 11: 135-138.

[24]- **Miller, M. M., K. A. Ealey, W. B. Oswald, and K. A. Schat. (2003).** Detection of chicken anemia virus DNA in embryonal tissues and eggshell membranes. *Avian Diseases*. 47: 662-671.

[25]- **Miller MM, and Schat K.A. (2004).** Chicken infectious anemia virus: an example of the ultimate host parasite relationship *Avian Diseases*. 48: 734-745.

[26]- **Smuts, H. (2014).** Novel Gyroviruses, including Chicken Anaemia Virus, in Clinical and Chicken Samples from South Africa. *Advances in Virology*, 1-7. doi: 10.1155/2014/321284.

[27]- **Sawanta, P., Dhamab, K., Rawoolc, D., Wania, M., Tiwarid, R., Singhb, S. and Singhe R. (2014).** Development of a DNA vaccine for chicken infectious anemia and its immunogenicity studies using high mobility group box 1 protein as a novel immune adjuvant indicated induction of promising protective immune responses. *Vaccine*, 32, 315-325. doi:10.1016/j.vaccine.2014.11.020.

[28]- **Rollano, M., Lewandowska, M., Stetefeld, J., Ossysek, K., Madej, M., Bereta, J., Sobczak, M., Shojaei, S., Ghavami, S. and Los, M. (2014).** Apoptins: selective anticancer agents. *Trends in Molecular Medicine*, 20(9), 519-528. doi:10.1016/j.molmed.2014.07.003.

[29]- **Carter, G., Wise, D. and Flores, E. (2005).** Virología Veterinaria. (International Veterinary Information Service), Recuperado de http://www.vet.unicen.edu.ar/html/Areas/Virologia/Documentos/Cd/VIROLOGIA%20VETERINARIA.pdf.

[30]- **Eregae, M., Dewey, C., McEwen, S., Ouckama, R., Ojkić, D. and Guerin M. (2014).** Flock prevalence of exposure to avian adeno-associated virus, chicken anemia virus, fowl adenovirus, and infectious bursal disease virus among Ontario broiler chicken flocks. *Avian Diseases*, 58(1), 71-77.

[31]- **Rimondi, A., Pinto, S., Olivera, V., Dibárbora, M., Pérez, M., Craig, M. and Pereda, (2014).** A Comparative histopathological and immunological study of two field strains of chicken anemia virus. *Veterinary Research*, 45(1), doi:10.1186/s13567-014-0102-y.

[32]- **Craig, M., Rimondi, A. and Delamer, M. (2009).** Molecular characterization of chicken infectious anemia virus circulating in Argentina during 2007. *Avian Diseases*, 53(3), 331-335.

[33]- **Hoerr, F. (2010).** Clinical aspects of immunosuppression in poultry. *Avian Diseases*, 54, 2-15.