Full Length Research Article
Advancements in Life Sciences – International Quarterly Journal of Biological Sciences

ARTICLE INFO

Date Received: 15/02/2023;
Date Revised: 07/03/2022;
Date Published Online: 30/06/2023;

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How to Cite:
Kilp A, Afonyushkin V, Mironova T, Kozlova Y, Cherepushkina V, et al., (2023). Evaluating the Epidemic Risk Posed by Marek's Disease Virus in Russia. Adv. Life Sci. 10(2): 276-281.

Keywords:
Marek's disease virus; Vesicular enteritis; Herpesvirus infection; COVID 19

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Evaluating the Epidemic Risk Posed by Marek's Disease Virus in Russia

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Abstract

Background: The highly oncogenic avian alpha herpes virus known as Marek's disease virus (MDV) raises concerns about its potential oncogenicity in humans. In this article, authors examine the potential epidemic risks associated with MDV, taking into account the current epidemic and epizootic situation in the Russian Federation, with a particular focus on the modern practices of pig and poultry farming. Given its oncogenic properties, MDV remains a cause for concern in the field of avian herpesviruses.

Methods: The study was conducted in 2010-2022 in poultry farms Russian Federation, Republic of Belarus and the Republic of Kazakhstan where authors monitored the rate of vesicular enteritis and MDV. In total, 155 epizootics were examined, including the analysis of 62 epizootics of vesicular enteritis and the population of the studied area exceeded 1 million people.

Results: The authors of the study found that vesicular enteritis, distributed over poultry farms in the Russia since 2011, and its safety for the population remains unknown. The increasing incidence of vesicular enteritis was also accompanied by various health issues in contact persons and veterinary personnel, as well as abnormal and in sync increases in infectious laryngotracheitis and MDV in young birds.

Conclusion: Authors come to the conclusion that the consequences of COVID-19 are accompanied by a deficiency of folic acid, which in turn leads to a risk of developing diseases associated with DNA viruses.It is concluded that MDV may contribute to the development of reproductive and breast cancers, highlighting the need for increased awareness and attention to the health risks associated with poultry farming and further research in this area.

Introduction

According to the World Health Organization, animals have recently become the main source of infections for humans [1]. Zoonoses account for a significant proportion of new and existing human diseases, such as HIV infection [1], which has begun as zoonosis, and Ebola virus disease and salmonellosis [1]. Others, such as the new coronavirus [2], could result in global pandemics [2].

Animal viruses pose a threat to food production and may also have zoonotic potential [3]. RNA viruses are known to have a higher risk of adapting to the human body and causing zoonotic infections [4]. However, the intense contact of poultry and pig farm personnel with farm animals creates a risk for both RNA and DNA viruses to potentially cause epidemics [5]. Among the oncogenic avian herpesviruses, Marek's disease virus is of particular concern as its oncogenicity for humans is still unresolved [6, 7]. It has been found that the virus is capable of replicating in the human body, and there have been reports of cancer cases in individuals who have had contact with this virus (unpublished data).

Marek's disease (MD) is an infectious, highly contagious, chronic disease of chickens, widespread throughout the world, characterized by the development of massive lymphoid neoplasms, decreased immunity, and death of the bird [8]. The scientific literature notes the ability of a person to shed VBM virus within 70 days. We have successfully cultivated VBM on human cell cultures. Other herpesviruses are also capable of immortalizing human lymphocytes causing blast transformation, and many members of this family: Epstein-Barr virus (EBV), human herpesvirus type 6 (HHV-6), type 8 (HHV-8), herpes saimiri monkey virus – prototype models for studying viral carcinogenesis [9].

The sharp increase in the incidence of this infectious disease in broiler chickens, recorded by us over the past decade, in our opinion, significantly increases the risk of human infection.

Therefore, the aim of our research is to analyze the risks of the emergence of epidemic potential in the MDV in conjunction with the current epidemic and epizootic situation in Russia.

Methods

Study Design

Authors aimed to monitor the incidence of vesicular enteritis and Marek's disease. The study was carried out in the period of 2010-2022 by visiting poultry farms and agricultural enterprises throughout the Russian Federation and poultry farms in the Republic of Belarus and the Republic of Kazakhstan.

Studied sample

During the observation period 155 epizootics were examined, including the analysis of 62 epizootics of vesicular enteritis.

The population of the studied area exceeded 1 million people.

An assessment of the incidence of malignant and benign tumors, cases of inflammation of the facial nerves, paresis of the limbs, stomatitis of people working in poultry farms was carried out on condition of anonymity at five large poultry farms in dynamics for 2012-2022.

Methods used

Authors used the methods of pathoanatomical, histopathological studies;

Histological studies of samples of pathological material;

The analysis of the growth of the incidence of ovarian cancer and breast cancer was carried out on the basis of available literature sources.

When choosing literary sources for analysis, we were guided by such criteria as:

- the results of the assessment of the incidence of breast cancer and ovarian cancer in the population belonged to the territory of the Russian Federation;
- scientific literature describes data on the incidence of breast cancer and ovarian cancer in the population for the period from 2011-2014.

Research procedure

Specimens of pathological material are fixed in 10% neutral buffered formalin. After fixation, specimens are transferred to cassettes. Dehydration is then carried out, which involves immersing the specimen in increasing concentrations of alcohol to remove the water and formalin from the tissue. The xylene is used to remove alcohol and provide paraffin infiltration and then the specimens are infiltrated with the paraffin wax Histological sections were stained with hematoxylin and eosin.

Data Analysis

Infection of broiler chickens with the Marek's disease virus of birds unfavorable for this disease was assessed by the results of PCR testing by the generally accepted method. Numerical data on the production indicators of poultry farms, growing periods, productivity were taken from the reporting data of poultry farms, and expert estimates were also used. The data were processed by the methods of variation statistics using MS Excel.

Results

In the period 2011-2021, according to our data, the causative agent of Marek's disease began to infect

younger birds instead of 70 days of age - 30 days. At the same time another herpesvirus infection that affects the respiratory system, ILT (infectious laryngotracheitis), has rejuvenated. The waves of two herpesvirus infections in chickens in the Russian Federation coincide in time with the appearance of the third infection – RSS (runting stunting syndrome / vesicular enteritis).

According to our observations RSS is very often accompanied by the appearance of MD. Mass distribution of RSS has been recorded by us since 2011, probably with breeding birds (spread with live vaccines is not excluded). In the summer of 2013 a new form of vesicular enteritis was recorded by us in the Russian Federation during. The spread through poultry farms likely occurred through humans(those who actively contacted sick birds often had a temperature of 37 ° C during the year, inflammation of the facial nerves was periodically observed).

In 2011-2012, cases of malignant neoplasms of the mammary gland occurred in all employees working with a live MDV , on one of the poultry farms in the Krasnodar region. In 2011-2012 and 2014-2016 two waves of MD (tumors combined with ovarian lesions in birds) were accompanied by an increase in the incidence of benign and malignant ovarian neoplasms in veterinary personnel, which may have been associated with the overall dynamics of the increase in the incidence of ovarian cancer in the country (Fig. 1). At one of the poultry farms in the West Siberian region 21 people fell ill (they were operated on) and 2 people died. So far, there is no way to prove the presence of MD infection in these people, and we can only talk about an indirect connection.

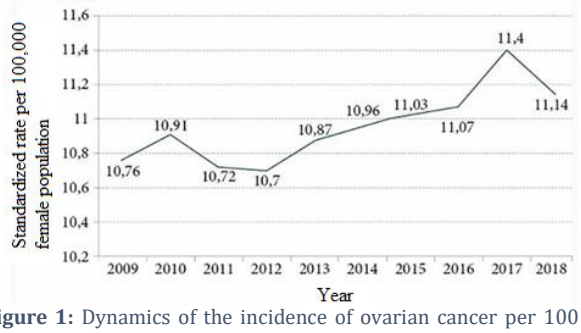

Figure 1: Dynamics of the incidence of ovarian cancer per 100 thousand female population [6].

An analysis of the incidence, mortality, and mortality from breast cancer in the female population of the Omsk region published in the scientific literature in a period from 2007 to 2014 [10] (Figure 2) also does not contradict the data on the incidence of Marek's disease and vesicular enteritis in chickens.

Today, in our opinion, there are additional factors that increase the risk of infection of humans with MDV:

1. BM appeared in broiler chickens of 30 days and older, i.e. henceforth contact with poultry meat carries the risk of infecting humans;
2. The COVID 19 epidemic is accompanied by folic acid deficiency [11], i.e. disruption of the folate cycle in humans which increases the risk of manifestation of diseases associated with DNA viruses, including an increased risk of infection with animal viruses [12,13];
3. COVID 19 reduces the resistance of the population to herpesvirus infections (see also point 2).

It is noteworthy that the dynamics of the incidence of ovarian cancer in the Russian Federation [14], in general coincides with the curve of the incidence of breast cancer [10] which indicates a possible commonality of the mechanisms provoking the development of these diseases (Figure 3).

In view of the fact that the "rejuvenation" of herpesvirus infections in chickens was recorded by us in 2010-2012 and was accompanied, among other things, by inflammatory lesions of the reproductive system of chickens (ovaries) we consider it necessary to test the effect of viral agents from chickens on the incidence of lesions of the mammary glands and ovaries in women.

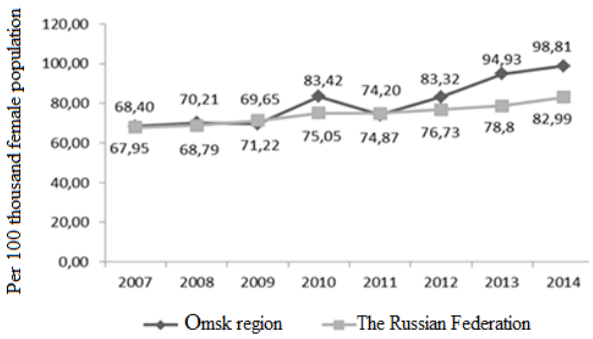

Figure 2: Dynamics of the incidence of breast cancer per 100 thousand female population [10].

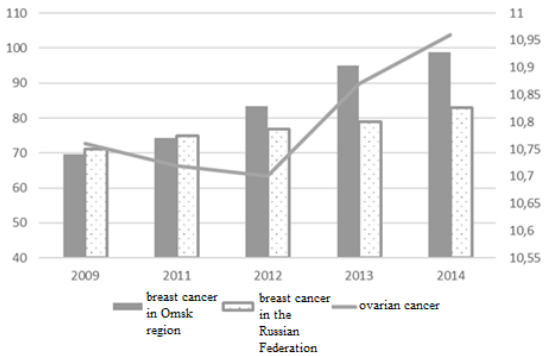

Figure 3: The number of diseases of breast cancer and ovarian cancer in % 2009-2014.

The question is natural - what should be the minimum efficiency of the transfer of an infectious agent from chickens to humans followed by the

manifestation of a neoplasm, so that this fact could be revealed in the course of an epidemiological analysis by medical infectious disease specialists? Thus, we can record an increase in the incidence of breast cancer in the Russian Federation by 14.9 people per 100,000 population from 2007 to 2014 [10]. The increase in the incidence of ovarian cancer was 0.38 per 100,000 people [14] in 2009-2018. That is, even the presence of an additional factor in the form of a viral agent from chickens could provoke the development of a malignant neoplasm from 150 to 3.8 people per 1 million of the population. Correlation coefficient between the incidence of breast cancer and ovarian cancer in the Russian Federation in 2009-2014 was positive and reached 0.61 according to Pearson and 0.486 according to Spearman (not significant). For the Omsk region the correlation coefficient was 0.73, which suggests the presence of a common factor affecting both analyzed parameters.

Infection of broilers with the causative agent of vesicular enteritis, according to our estimates is ~ 30%, similar or greater infection with VBM (up to 60-80% by slaughter according to the results of PCR testing). As a result, during the year the population of the region should come into contact with 4.3 million carcasses of broiler chickens infected with the Marek's disease virus and 1.5 million carcasses infected with the causative agent of vesicular enteritis (excluding cross-contamination of carcasses during processing). With an average annual consumption of poultry meat of 60-80 kg per capita one can expect contact with 24 - 28 broiler carcasses per year of a regular consumer of poultry products, on average. This intensity of public contact with infected poultry should guarantee a high risk of exposure to all viruses for persons involved in the cooking poultry dishes (mainly women, food workers and poultry enterprises). Based on our estimates, we found that BM was present in at least 25% of broiler poultry farms in the Russian Federation, which could potentially lead to increased mortality from neoplasms of the reproductive system. This increase could contribute to the dynamics of oncological diseases of the reproductive organs and breast cancer for the entire Russian Federation.

Since April 2022, we have recorded epizootics of vesicular enteritis at five large poultry farms in the Russian Federation. Accordingly, a forecast was made for an increase in the incidence of breast cancer, ovarian cancer in the population of the Russian Federation in the second half of 2022 and the first half of 2023, compared with 2021-2020. We also predicted an increase in the incidence of Marek's disease and ILT in poultry farms of the Russian Federation. During the autumn-winter period of 2022, we began to record new epizootics of Marek's disease in poultry farms (broiler parent flocks). Further analysis of statistics on the incidence of breast cancer and ovarian cancer in the population of the Russian Federation in 2022 and 2023 will allow us to assess the accuracy of forecasting using data on the incidence of vesicular enteritis in chickens and substantiate the sanitary significance of this nosology.

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An increase in incidence was predicted for Marek's disease and ILT in poultry farms in the Russian Federation. In the autumn-winter period of 2022, we began to record new epizootics of Marek's disease in poultry farms (broiler parent flocks). Further analysis of statistics on the incidence of breast cancer and ovarian cancer in the population of the Russian Federation in 2022 and 2023 will allow us to assess the accuracy of forecasting using data on the incidence of vesicular enteritis in chickens and substantiate the sanitary significance of this nosology.

Discussion

The study found a strong correlation between the incidence of Marek's disease and vesicular enteritis in chickens, and the incidence of breast and ovarian cancer in humans in the Russian Federation. This finding is consistent with studies conducted in Pakistamthat found that people who lived and worked on poultry farms had a significantly higher incidence of respiratory symptoms [15, 16]. Studies in the United States, in turn, found that poultry workers had a higher risk of developing lung cancer [17].Therefore, the study adds to the growing body of evidence that infectious agents in poultry pose a risk to the health of poultry workers and consumers.

While there is a lack of data on the transmission of infectious agents from chickens to humans causing malignant neoplasms in other countries, studies have been conducted on the prevalence and transmission of MD, ILT, and other infectious diseases in chickens. Authors from Serbia in 2022 found a high prevalence of ILT in vaccinated and unvaccinated chickens [18]. This study, along with the current study, indicate the persistence of infectious diseases in chickens and the need for improved control measures.

Moreover, the possible impact of the COVID-19 epidemic on the incidence of infectious diseases is highlighted. Study conducted in India in 2021 found that COVID-19 patients had a higher incidence of herpesvirus infections and an increased risk of

developing malignancies, respectively [19]. This studies suggest a possible relationship between COVID-19 and the incidence of infectious diseases and malignant neoplasms. Thus, the study reinforces the need for increased awareness and attention to the health risks associated with poultry farming, especially in light of the ongoing COVID-19 pandemic [20].

In conclusion, the study provides evidence of a link between infectious agents in chickens and the incidence of breast and ovarian cancer in humans in the Russian Federation, consistent with other studies that suggest a link between poultry farming and human health.

Therefore, there is a need for improved control measures to minimize the risk of transmission of infectious agents from chickens to humans, as well as increased awareness and attention to the health risks associated with poultry farming. Further research is also needed to better understand and mitigate these risks. Vesicular enteritis, a highly contagious form of intestinal pathology, has been widely distributed at poultry farms in the Russian Federation since 2011. However, the safety of this infection for the population remains unknown. During periods of increasing incidence of vesicular enteritis, several cases of inflammation of the facial nerves and subfebrile temperature in contact persons were recorded. There were also bursts of oncological diseases in veterinary personnel, including ovarian and breast cancer, and an abnormal and synchronous increase in the incidence of ILT and BM in chickens under the age of 40 days. These observations highlight the need for additional monitoring studies to assess the safety of this nosology for the population. Furthermore, the spread of COVID-19 indicates an increased risk of human infection with herpesvirus infections from animals, which calls for the monitoring of zoonotic herpesviruses in risk groups among the population of the Russian Federation.

Further research could be conducted in terms to explore the mechanisms by which infectious agents in chickens could contribute to the development of breast and ovarian cancer in humans. Also, additional studies are needed to develop more effective vaccines and treatments for Marek's disease and other herpesvirus infections in chickens. Moreover, it is necessary to assess the safety of vesicular enteritis for the population and take steps to minimize the risk of transmission to humans. Additionally, monitoring of zoonotic herpesviruses in risk groups among the population of the Russian Federation should be conducted to reduce the risk of human infection with herpesvirus infections from animals.

Acknowledgment

This work was supported partially by the Russian Foundation for Basic Research (RFBR) Project 18-016-00045A.

Competing Interest

The authors declare that there is no conflict of interest.

Author Contributions

All authors have contributed equally to this study.

References

1. Wolfe ND, Dunavan CP, Diamond J. Origins of major human infectious diseases. Nature, (2007); 447(7142): 279-283.
2. World Health Organization. Zoonoses. Available at: https://www.who.int/ru/news-room/fact-sheets/detail/zoonoses (access date: September 20, 2022).
3. Wozniakowski G, Samorek-Salamonowicz E. Animal herpesviruses and their zoonotic potential for cross-species infection. Annals of Agricultural and Environmental Medicine, (2015); 22(2): 191-194.
4. Blair A, Zahm SH. Agricultural exposures and cancer. Environmental Health Perspectives, (1995); 103(Suppl 8): 205-208
5. Sharma JM, Witter RL, Burmester BR, Landon JC. Public health implications of Marek's disease virus and herpesvirus of turkeys. Studies on human and subhuman primates. Journal of the National Cancer Institute, (1973); 51(4): 1123-1128.
6. Beasley JK, Patterson LT, McWade DH. Transmission of Marek's disease by poultry bouse dust and chicken dander. American Journal of Veterinary Research, (1970); 31(2): 339-344.
7. Purchase HG, Witter RL. Public health concerns from human exposure to oncogenic avian herpesviruses. Journal of the American Veterinary Medical Association, (1986); 189(11): 1430-1436.
8. Laurent S, Esnault E, Dambrine G, Goudeau A, Choudat D, Rasschaert D. Detection of avian oncogenic Marek's disease herpesvirus DNA in human sera. Journal of General Virology, (2001); 82(1): 233-240.
9. Lvov ND. Human herpesviruses - systemic, integrative, lymphoproliferative immuno-oncopathology. Russian Medical Journal, (2012); 20(22): 1133-1137.
10. Shirlina NG, Stasenko VL, Scherbakov DV. The burden of breast cancer in the female population Omsk region. Modern Problems of Science and Education, (2016); 5: 63-63.
11. Hayashi M, Furuichi T, Ren S, Isogai E, Nonoyama M, Namioka S. Enhancement of mRNA synthesis from Marek's disease virus genome in the lymphoblastoid cell line, MDCC-MSB1, by 5-azacytidine. Journal of Veterinary Medical Science, (1994); 56(2): 287-291.
12. Pejaković S, MbouombouoMfossa AC, Wiggers L, Kheimar A, Coupeau D, Kaufer BB, Muylkens B. Role of DNA methylation and CpG Sites in the viral telomerase RNA promoter during gallid herpesvirus 2 pathogenesis. Journal of Virology, (2020); 94(23): e01488-20.
13. IushkovIuG, Afoniushkin VN, Gorodov VS, Filipenko ML, Boiarskikh UA, Dudareva EV. Issues on evolution of CpG islands in genome of Marek's disease virus. ZhurnalMikrobiologii, EpidemiologiiiImmunobiologii, (2010); 1: 84-86.
14. Leonov MG, Tikhonova EN, Teslenko LG, Shmatkova AM, Belyaeva SA. Onkoepidemiological features, analysis of diagnosis and detectability of ovarian cancer in Russia. Effective Pharmacotherapy, (2020); 16(11): 18-21.

15. Yasmeen R, Ali Z, Tyrrel S, Nasir ZA. Assessment of Respiratory Problems in Workers Associated with Intensive Poultry Facilities in Pakistan. Safety Health Work, (2020); 11(1):118-124.
16. Hamid A, Ahmad AS, Khan N. Respiratory and Other Health Risks among Poultry-Farm Workers and Evaluation of Management Practices in Poultry Farms. RevistaBrasileira de CienciaAvicola, (2020); 20(1): 111-118.
17. Johnson ES, Faramawi M, Chedjieu IP, Delongchamp R, Choi KM, Shen T. Excess lung cancer occurrence in poultry plants. Occupational risk factors: Findings for oncogenic viruses exposure and other occupational exposures. Environmental research, (2018); 167: 393-410.
18. Pajić M, Knežević S, Djurdjević B, Polaček V, Todorović D, Petrović T, Lazić S. Diagnosis of Infectious Laryngotracheitis Outbreaks on Layer Hen and Broiler Breeder Farms in Vojvodina, Serbia. Animals : an open access journal from MDPI, (2022); 12(24).
19. Sinha S, Kundu CN. Cancer and COVID-19: Why are cancer patients more susceptible to COVID-19? Medical oncology (Northwood, London, England), (2021); 38(9).
20. Smolovskaya O, Pleshkov V, Zubova T, Bormina L. Probiotics in Industrial Poultry Farming. American Journal of Animal and Veterinary Sciences, (2023); 18(1): 1-8.