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RESEARCH ARTICLE

THE NOVEL CORONAVIRUS: A SYSTEMATIC LITERATURE REVIEW WITH A FOCUS ON ANIMAL TRANSMISSION

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Abstract

The novel Coronavirus is currently the center of medical and media concerns worldwide, with crucial effects not only on the human health, but also on the global economy. Although a wide range of information is available in regards to other SARS strains and especially in humans, very few reports have been published in connection to animals. The present paper attempts to summarize the latest studies on SARV CoV-2 in an effort to capture not only the broad state of knowledge in the field, but, most importantly, what information is available about the virus' transmission via animal sources. The current undertaking begins with a discussion on the specificity of SARS CoV-2 and continues with a content analysis of research articles published on this issue during January-April 2020 in the Scopus and Springer databases. The findings indicate that animal-to-human transmission remains poorly documented, although it represents the source of this pandemics.

Introduction:-

The emergence of SARS CoV-2 of has produced major transformations in everyday realities, changing travelling practices, economic environments, as well as research and media interests. Since the beginning of 2020, the international medical community has been focusing on the new coronavirus, SARS-CoV-2, and the disease it determines, COVID-19. Despite current allegations that the pandemic would be based on the intentional laboratory manipulation of SARS CoV-2, there seems to be a general agreement that the virus first appeared in Wuhan City, Hubei Province, in China, and that it's rapid spread worldwide remains zoonotic, in essence [19].

Due to the fact that SARS CoV-2 has determined not only lockdowns with vital effects on economies worldwide, as well as others', but, most importantly, unprecented life losses, we deem that its effects on the Romanian rural economy are undebatable. Ultimately, the management of various sectors in agronomy and agriculture is virtually impossible with people. That is why the present paper approaches a potential perspective of the veterinary medicine studies in the debate on SARS CoV-2.

Because it is a new virus, the state of knowledge in this regard is dynamic, as new data is validated and published. The viral genome has been identified in a record time for a newly discovered organism, in just 30 days, but recent studies suggest that there are many more details to understand about this virus and how it works. While the latest numbers indicate a total of over 1 million, and 200,000 cured, the death toll has reached over 50,000 deceased inividuals worldwide, with France reporting over 1,000 deaths per day [18] at the date of this research paper (April 2nd). It is widely known fact that no vaccine or treatments are available, although multiple attempts are in progress at the moment [4], [6]. What is less known is that COVID-19 vaccine strategies will imply vaccinating at-risk human

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populations including frontline healthcare workers, individuals over the age of 60, and those with underlying and debilitating chronic conditions [3]. Because whole virus vaccines will be considered and, as outlined, immuno-compromised individuals will be less likely to opt out [3], this means that vaccination itself might pose important risks for some vulnerable groups. Thus, prevention at all levels is compulsory and remains the core measure to reduce the impact of the virus.

Since the first outbreaks in China and Italy, the scholarly and media attention has focused extensively on human-to-human transmission [12], [14], despite the fact that the roots of the SARS CoV-2 spread have been documented as zoonotic [1], [7]. In this context, we argue that it is vital to address the animal sources that may function as hosts and transmitters of the virus in order to actually stop its spread. To this point, the only perspective genuinely targeting at all sources of contamination, both human and animal, remains the One-Health approach. In a theoretical undertaking aimed at capturing the important forms of prevention, Zowalaty and Järhult [22] outline that 4 important actions need to be taken in order to stop the transmission: reducing all possible contact with bats, currently considered the virus' natural host; eliminating live animal markets as much as possible; isolating different animal species in different areas of markets where complete elimination of live markets is not possible; and, of course, limiting human-to-human transmission. Otherwise, in the absence of comprehensive prevention actions, prophylaxis will remain solely an ideal. The role of intermediary hosts, such as cats, sheep, goats, dogs remains equally important in this process (figure 1, below), which is why the World Health Organization has recommended limiting the contact with house pets [20].

The present paper attempts to summarize the latest studies on SARV CoV-2 in an effort to capture not only the broad state of knowledge in the field, but, most importantly, what information is available about the virus' transmission via animal sources.

Particularities of SARS-CoV-2:

Between 2002 and 2019, mankind has undergone two coronavirus-related health crises: the Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) which developped in China in 2002; and the Middle East Respiratory Syndrome coronavirus (MERS-CoV), occurring in 2012 in Saudi Arabia [22]. The new, Wuhan-emerged coronavirus was firstly named 2019-novel coronavirus (2019-nCoV) and thenceforth, the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

SARS-CoV-2 stems from a viral family that mainly affects animals: bats, pigs, mice and even beluga whales [1]. The seven species of coronaviruses that infect humans (most recently SARS-CoV-2) have also been identified in various animal species. In addition, the onset of the COVID19 epidemic and the first cases in Wuhan were closely linked to an agri-food wet market, before they spread through inter-human transmission. All this suggests that SARS-CoV-2 is a zoonotic virus, which has crossed the species barrier from animal to human. Genetic studies have traced the virus from animal hosts to humans, tracking the genetic variations of the S spike protein [15].

Comparing the genetic code responsible for the construction of this protein from different coronaviruses allows for the identification of the origin of SARS-CoV-2. Both the SARS virus and SARS-CoV-2 have high affinity for the receptor in human cells, but the structure of the S protein is significantly different between the two viruses. This observation indicates that S SARS-CoV-2 protein appeared by natural selection, a long process of accumulation of genetic mutations in successive generations of viruses. The unlikely hypothesis of the emergence of the new coronavirus by human manipulation involves the use of an already known viral structure [1]. SARS-CoV-2 is similar to the other SARS coronaviruses and MERS respectively (which have evolved in an epidemic manner in the past) only in a proportion of 79% and 50% respectively). Another aspect that differentiates SARS-CoV-2 from other known coronaviruses is the presence of a cleavage site between two of the three subunits of protein S. This protein fragment, consisting of a series of basic amino acids (polybasic cleavage site), may be be split by a furin, an enzyme found in many tissues in the body. Like the unique structure of S protein among coronaviruses, the cleavage site is different from other protein fragments with similar function from other coronaviruses (SARS virus not showing any such site) [1].

The genetic structure of SARS-CoV-2 indicates the bat as the zoonotic source of the infection: it is 96.2% identical with a coronavirus from the bat population in China. However, important fragments of the S protein differ. The intermediate host between the bat and the human has been indicated as being the pangolin, a mammal with a body covered in scales, which is illegally marketed in food markets such as Wuhan, due to its use in traditional Chinese

medicine. Coronaviruses isolated from these animals have in common with SARS-CoV-2 highly specific S-protein fragments responsible for cell binding. These two observations indicate the history of SARS-CoV-2: a bat-specific coronavirus, which was transmitted to pangolin in the Wuhan agri-food market, accumulating mutations that increase infectivity in this process [1].

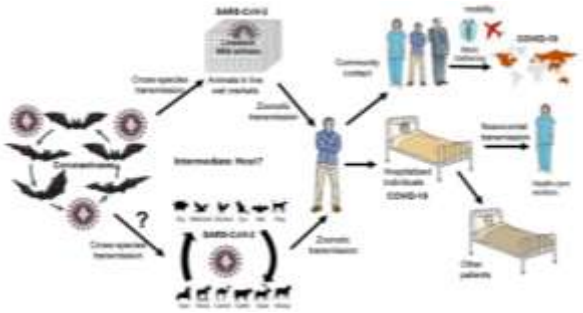

Figure.1:- Estimated circuit of SARS COV-2 contamination [22].

Materials and Methods:-

As outlined in the introduction, the aim of this research is to explore the topics concerning SARS-CoV-2 and, more specifically, to assess the information available about animal to human transmission, otherwise understood as the zoonotic circuit of the virus.

In order to do so, all papers that have been published since January until April 2020 in the Scopus (Elsevier) and Springer databases were analyzed. Primarily, an exploratory content analysis was carried out to explore the main topics around SARS CoV-2. The main key-word to filter the articles was „SARS CoV-2". Articles focusing on MERS and articles published anytime before 2020, as well as research written in any other language than English were ruled out. The topics were grouped in clusters of meaning and a special consideration was given to pieces of research mentioning the word „animal"- in order to capture the available information on animal to human transmission.

The research articles were firstly inventoried in Excel and coded in SPSS afterwards. The analyses were based on Frequencies commands, as well as qualitative content analyses.

The following categories of topics were associated with the virus, as shown in table 1:

1. Prevention or treatment of the disease
2. Human-to-human transmission
3. Virus' implications on humans
4. Economic implications of the virus
5. Animal-to-human transmission
6. SARS CoV 2 in social media

Table 1:- Excerpt of the inventory of research articles and associated topics with SARS CoV-2, during January-April 2020.

Research data base	Name of research article	Article main topic associated to SARS CoV-2
Scopus	Structural basis of SARS-CoV-2 3CLpro and anti-COVID-19 drug discovery from medicinal plants	Prevention or treatment of the disease
Scopus	First known person-to-person transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the USA	Human-to-human transmission
Scopus	Composition of human-specific slow codons and slow di-codons in SARS-CoV and 2019-nCoV are lower than other coronaviruses suggesting a faster protein synthesis rate of SARS-CoV and 2019-nCoV	Virus' implications on humans

Scopus	The spread of novel coronavirus has created an alarming situation worldwide	Economic implications of the virus
Scopus	YouTube as source of information on 2019 novel coronavirus outbreak: a cross sectional study of English and Mandarin content	SARS CoV-2 in social media
Springer	From SARS to COVID-19: A previously unknown SARS- related coronavirus (SARS-CoV-2) of pandemic potential infecting humans – Call for a One Health approach.	Animal-to-human transmission
Springer	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges.	Virus' implications on humans

Results And Discussions:-

In the analyzed period, a total of 226 articles discussed the problematic of the virus, 199 in Scopus, and 27 in Springer.

	Frequency	Percent
Prevention or treatment of the disease	93	41,2
Virus' implications on humans	90	39,8
Human-to-human transmission	34	15,0
Economic implications of the virus	3	1,3
Animal-to-human transmission	5	2,2
SARS CoV 2 in social media	1	0,4
Total	226	100,0

Fig. 2 Overall distribution of topics associated to SARS CoV-2 in research articles published between January-April 2020.

As it would be predictable in a time of pandemics, most of the article concerned prevention strategies and treatment of COVID-19 (41.2%, SD=.93, figure 2). The perspectives were quite different in this regard: some authors addressed alternative therapies such as acupuncture and moxibustion [9], medicinal plants [17],[21], while others highlighted either clinical trials with classical pharmacological substances such as hydroxychloroquine, azithromycin [6] or remdesivir [4]; doubled by genetic analyses indicating different proteins that can be enforced in order to reduce the virus' impact [8]. Management measures proposed to practitioners in Radiology represent an important part of the "prevention and treatment" category and consist of staff protection and medical care initiatives.

The virus' implications on humans are discussed in relation with different comorbidities such as cardiovascular diseases [16], diabetes [5] and cancer [11]; in conditions like pregnancy [13]; and the negative effects of isolation on sexual health, and STI specifically [2]. While human-to-human transmission is third-rankly debated (15%, N=226, SD=.93), animal-to-human transmission remains poorly discussed (2.2%). The differences lie not only in numbers, but also in the depth of information available. The articles outlining animal-to-human transmission in the beginning of the zoonotic cycle solely mention bats or the pangolin as main virus source and the Huanan wet market. Chen et al. [3] mentions birds and rabbits as potential intermediary hosts. Liu et al. [10] emphasize the fact that pangolins have a high degree of viral infectivity and pathogenicity, with the potential of transmitting coronavirus disease both directly and indirectly, to humans. The authors also highlight the devastating effects of coronaviruses on the pangolids' quality of life. Hemida and Abduallah recommend the following measures to stop the virus' transmission from animals to humans:

1. Regular monitoring to bat virome for the potential emergence of any new zoonotic viruses;
2. Surveillance of SARS-CoV-2 among various species of animals and birds
3. Banning live markets;
4. Rising the hygienic thresholds and standards for the supply chain in poultry and animal slaughter houses [7];

Hemida and Abduallah's study was present both in the Springer and Scopus databases and is representative of the One-Health approach. Zowalaty and Järhult [22], previously mentioned in the introduction of this article, point to similar courses of action, as Hemida and Abduallah, while stressing on limiting the contact with hosts of the virus, such as bats.

To summarize, the information regarding animal-to-human transmission remains scarce, although further contamination along this circuit is possible. Our anaylsis showed that prevention and treatment among humans was discussed in proportion of 41.2%, the virus' implications on humans, in 39.8%, human-to-human transmission, in 15%, and animal-to-human, in 2.2%. In the case of this last topic, the available information was poor not only quantitavely, but also qualitatively.

Although all the information indicated in the abovementioned studies are particularly important and may represent the basis of much more nuanced studies, no further data are known, such as: the extent to which the initial transmission routes can be repeated through other intermediary hosts; the type of intermediate hosts more likely to contract the virus and pass it on to humans; the COVID-19 symptomatology in animals and birds (whose knowledge may also be useful in predicting potential contamination to human hosts); environmental conditions that support the life span of the virus, etc. Therefore, future studies will need to bring some extra knowledge awareness around these issues, at least tangentially, in order to make room for a three-dimensional type of prevention.

Conclusions:-

To conclude, the data with respect to animal-to-human transmission remains lean both quantitavely, and qualitatively. Our study indicated that many of the topics around the virus focused on humans and very little, on animals. The accessible data showed some potential animal hosts, both source and intermediary, and a few counter-measures in the fight against spread of the virus from animals to humans - most of which were the product of the One-Health approach, and not a veterinary perspective. The need of reliable information and scholastic consideration in this respect is compelling on future contamination routes, which are very likely to repeat, if animal sources of the infection are to be ignored.

Future studies should address the virus' transmission routes and impact on the quality of animal life from a veterinary medicine perspective. This way, we would gain not only a broader knowledge over the current pandemics, but also a closer step at stopping the contamination.

Last but not least, a more detailed perspective from the view of veterinary medicine in the preventive approach of SARS CoV-2 could reduce the existent death toll and, consequently, a better involvement of people in agriculture.

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