UNIVERSITI PUTRA MALAYSIA

A SYSTEMATIC REVIEW ON THE WORLDWIDE PREVALENCE OF MALIGNANT CATARRHAL FEVER (MCF) IN GOATS, SHEEP, AND DEER FROM 2000 TO 2020

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CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

MCF	malignant catarrhal fever
MCFV	malignant catarrhal fever virus
OvHV-2	ovine herpesvirus-2
AlHV-1	alcelaphine herpesvirus-1
AlHV-2	alcelaphine herpesvirus-2
CpHV-2	caprine herpesvirus-2
CpHV-3	caprine herpesvirus-3
WTD	white-tailed deer
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analysis
C/ ELISA	competitive enzyme-linked immunosorbent assay
PCR	polymerase chain reaction
CFT	complement fixation test

ABSTRAK

Abstrak daripada kertas projek yang dikemukakan kepada Fakulti Perubatan Veterinar untuk memenuhi sebahagian daripada keperluan kursus VPD 4999 - Projek Akhir Tahun.

KAJIAN SISTEMATIK TERHADAP PREVALENS PENYAKIT DEMAM KATAR MALIGNAN DI SELURUH DUNIA DALAM SPESIS KAMBING, BEBIRI DAN RUSA PADA TAHUN 2000-2020

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Penyakit Demam Katar Malignan merupakan satu penyakit penting dalam haiwan ruminan yang disebabkan oleh *Herpesvirus*. Ia adalah penyakit limfoproliferatif yang berpotensi untuk mengundang kerugian pada ekonomi negara. Oleh itu, tujuan kajian ini adalah untuk menjalankan kajian sistematik terhadap prevalens penyakit Demam Katar Malignan di seluruh dunia pada tahun 2000 hingga 2020. Garis panduan oleh PRISMA telah digunakan dalam menulis laporan kajian ini. SCOPUS pula merupakan pangkalan data utama yang digunakan, bagi memilih dan menyaring artikel berkaitan dengan topik kajian ini. Kriteria-kriteria yang termasuk dalam pemilihan artikel adalah (i) tempoh kajian dilakukan adalah di antara tahun 2000-2020; (ii) spesies kajian adalah kambing, bebiri atau rusa; (iii) nilai prevalens direkodkan di dalam artikel, dan; (iv) kajian ditulis hanya menggunakan Bahasa Inggeris. Dua pengarang menilai rujukan yang dipilih secara individu, dan sebanyak 15 daripada 29 artikel telah

dimasukkan di dalam kajian ini. Kemudian, data daripada artikel tersebut telah diekstrak menggunakan Microsoft Excel, dan ringkasan data telah di buat. Daripada ringkasan tersebut, prevalens penyakit demam katar malignan yang tertinggi dalam spesies kambing, biri-biri dan rusa masing-masing merupakan 96% (Turki), 100% (Iraq), dan 3.5% (Norway). Kesimpulannya, prevalens global penyakit ini adalah tinggi, dan ia dikaitkan dengan pelbagai faktor risiko termasuk pengurusan haiwan, umur dan suhu. Kajian ini boleh menyumbang kepada sebarang penyelidikan tentang penyakit katar malignan yang dilakukan pada masa hadapan, dan secara tidak langsung, dapat mengurangkan insiden penyakit ini.

Kata kunci: *herpesvirus, limfoproliferatif, PRISMA, SCOPUS, prevalens global, risiko*.

ABSTRACT

An abstract of the project paper presented to the Faculty of Veterinary Medicine in partial fulfilment of the course VPD 4999 – Final Year Project.

A SYSTEMATIC REVIEW ON THE WORLDWIDE PREVALENCE OF MALIGNANT CATARRHAL FEVER IN GOATS, SHEEP, AND DEER FROM 2000-2020

by

Siti Sarah Ismail,

2021

Supervisor: Wan Nor Fitri Wan Jaafar

Malignant Catarrhal Fever (MCF) is an important disease in ruminants caused by the *Herpesvirus*. It is a lymphoproliferative disease that has a high risk and huge economic losses. Therefore, the goal of this study was to conduct a systematic review on the world prevalence of malignant catarrhal fever between 2000 to 2020. PRISMA guidelines were used in reporting this study. The main database used was Scopus, from which articles relevant to the topic were selected and screened. The inclusion criteria used to select articles were (i) the study period was done between 2000-2020; (ii) species studied were goats, sheep, or deer; (iii) prevalence was recorded in the articles, and; (iv) studies were written only in English. Two authors individually assessed the related references for relevance. A total of 15 out of 29 potentially relevant articles were included in this review. Then, the data were extracted from the articles by the authors using Microsoft Excel, and a summary of the data was created. From the summary, the highest MCF prevalence in goats, sheep, and deer were 96% (Turkey), 100% (Iraq), and 3.5% (Norway) respectively. In conclusion, the global prevalence of MCF was high and it was linked to various risk factors including animal management, age, and temperature. This review can contribute to future research on the occurrence of MCF and disease mitigation.

Keywords: *herpesvirus, lymphoproliferative, PRISMA, SCOPUS, global prevalence, risks.*

1.0 INTRODUCTION

Malignant Catarrhal Fever (MCF) is a high mortality, generalized lymphoproliferative disease of cattle and wild ruminants) caused by *Herpesviridae.* At least 10 viruses belong to the genus *Macavirus* (Maclachlan & Dubovi, 2011). Sood *et al.*, (2013) stated that two major causative agents that contribute to the MCF in domestic and wild ruminants are ovine herpesvirus-2 (OvHV-2) and alcelaphine herpesvirus-1 (AIHV-1). The AIHV-1 is endemic in the wildebeest, which causes wildebeest-associated MCF (WA-MCF) in cattle and susceptible ruminants, which leads to subclinical infection. Meanwhile, the OvHV-2 is enzootic in domestic sheep, and when transmitted to a vast variety of domestic and wild ruminants, causes sheep-associated MCF (SA-MCF). There are six MCF virus members that are associated with the clinical disease: ovine herpesvirus-2 (OvHV-2), alcelaphine herpesvirus-1 (AIHV-1), alcelaphine herpesvirus-2 (AIHV-2), caprine herpesvirus-2 (CpHV-2), caprine herpesvirus-3 (CpHV-3, previously called MCFV-WTD, MCFV- white-tailed deer), and ibex-MCF virus (Chunha *et al.,* 2014).

The MCF virus exhibits different clinical and non-clinical presentations and appears to be virus and species-specific. Since the discovery of the caprine herpesvirus-2 (CpHV-2), there was an increasing trend in the detection of the disease albeit being less virulent (Chmielewicz *et al.*, 2001). The other four viruses in the MCF group have been identified, but so far none of them have been reported in association with clinical symptoms harboured by onyx, roan antelope, muskox, and aoudad. In natural hosts, the viruses cause a subclinical infection, but in susceptible hosts (bison, cattle, deer, and pigs), clinical signs can be observed. This highly fatal disease commonly shows clinical signs in susceptible hosts such as fever, excessive salivation, and nasal and ocular discharges (Neves *et al.*, 2013).

MCF has been described in the past as having several "forms" of the disease. It was categorised as mild, peracute, head and eye, and intestinal (Callan & Lear, 2021). The prolonged use of other terminologies by the society like alimentary, neurological, and cutaneous to describe additional clinical forms of the disease are entrenched and likely ineradicable (O'Toole & Li, 2014). The acute form of MCF is called the "head and eyes" which is characterised by severe clinical signs, and this is the most common of MCF. Acute MCF is most commonly found in pigs (Spickler, 2019), which the clinical signs are high fever and anorexia, weakness, erosion of the buccal mucosa, adenopathy, purulent nasal discharge, dyspnoea, keratoconjunctivitis with progressive opacity of the cornea and ophthalmia, encephalitis with neurological disorders, and death within two weeks in 90% of the cases. Clinically and pathologically, acute MCF cases caused by ovine herpesvirus-2 and alcelaphine herpesvirus-1 are similar (Callan & Lear, 2021), typically resulting in an acute and deadly disease with usual signs such as fever and dyspnea (CABI, 2019).

As for the intestinal type, which is also known as the peracute form, infected animals exhibit few clinical signs before death. Peracute MCF is particularly common in highly vulnerable hosts like bison and deer (CABI, 2019; Callan & Lear, 2021), where after 12-24 hours of depression, weakness, diarrhea, or dysentery, mortality occasionally preceded (Spickler, 2019). It is characterised by liquid and haemorrhagic diarrhoea, as well as ophthalmic symptoms, which indicate that it is milder and which mortality occurs within 1-3 days (SPC Land Resources Division, n.d.). Cases of mild or inapparent infections in asymptomatic cattle, bison, cervids, and pigs, are indicated by the presence of MCF antibodies and/or nucleic acid (Spickler,2019). Ovine herpesvirus-2 (OvHV-2), caprine herpesvirus-2, and white-tailed deer herpesvirus are most often discovered in ruminants in the United States, where the respiratory form of the MCF, which causes keratoconjunctivitis, is most typically found in cattle (MacGavin & Zachary, 2012). Cases in deer and bison are often peracute with sudden death. Deer that survive for a few days and bison usually develop hemorrhagic diarrhea, bloody urine, and corneal opacity before expiring

Two known epidemiological forms of MCF have been well-defined, and each one differs considerably from the others; the AIHV-1 and OvHV-2. The epidemiology of the wildebeest species involves both horizontal and vertical transmission, whereas only horizontal transmission is known for the ovine species (Li *et al.,* 2011). The establishment of lifelong latent infection occurring as early as 29 days old (Wani *et al.,* 2006) in natural hosts such as sheep, nonetheless, usually will not develop any sign. Virtually, the lambs that were born are free from the infection, but under the natural flock's condition, they will become infected as they grow older. Unaffected sheep are still susceptible to being infected when they are adults (O'Toole & Li, 2014). Because the perinatal infection is uncommon in sheep, carrier animals (sheep and goats) play an essential role in viral transmission between sheep and goats. (Khudair *et al.,* 2020). In Malaysia, there is still a lack of information on the presence of AIHV-1 and OvHV-2. There is only a case study that has been published on the presence of OvHV-2 in deer, after being diagnosed using PCR (Ainani *et al.*, 2015). The lack of diagnosis of strains of MCF cases in Malaysia can be due to the diagnostic method used. This can be seen in the case report by Ainani et al. (2015), where they diagnose MCF based on the presence of the pathognomonic lesion of generalized vasculitis and perivascular cuffing in the tissue samples. Thus, the status of AIHV-1 is still unknown in Malaysia.

Control of MCF involves mainly the ability to control the natural host to susceptible host. This implies that separating the virus-free animals from the carrier animals may enable the prevention and control procedures (Khudair *et al.,* 2020). The common route for both entry and shedding of the virus is the respiratory tract (Sood *et al.*, 2013). The virus transmits to the susceptible hosts either by inhalation or ingestion of mucosal secretions of the natural hosts that contain the virus. The aerosol OvHV-2 transmission to susceptible animals has been reported to occur up to about a 5 km radius (Riaz *et al.,* 2021). A natural host, such as the wildebeest calves, who shed MCFV in a cell-free state, can transmit the virus horizontally to cattle, which is a susceptible host (Mushi *et al.*, 1981), but this disease however is unlikely to have horizontal transmission between susceptible hosts, even they have clinical signs and live in the same enclosure. This is because susceptible host species are considered as impassable and dead-end hosts for the virus (Moore *et al.*, 2010; Callan & Lear, 2021), which shed extremely fragile cell-associated viruses in their nasal and ocular secretions host (Sharma et al., 2019). Due to this, sick susceptible animals do not need to be separated from healthy animals (Sharma *et al.*, 2019). However, susceptible hosts should be kept separate from natural hosts for a certain time, as wildebeest calves are most infectious during their first 90 days of life, and infectious OvHV-2 is shed in large amounts in ovine nasal secretions particularly in 6–9-month-old lambs (Spickler,2019).

Malignant Catarrhal Fever is also known as a lymphoproliferative disease and has complex pathogenesis. Its pathogenesis is characterised by the accumulation of lymphoid cells in the non-lymphoid organs, vasculitis, and T-lymphocyte hyperplasia in the lymphoid organs (Sood *et al.*, 2013). The tropism of the virus in vivo includes CD8+ T cells and epithelial cells. In sheep lungs, this tropism is mostly shown in alveolar type II epithelial cells.

Detection of nucleic acid techniques such as polymerase chain reaction (PCR) and competitive enzyme-linked immunosorbent assay (cELISA) can be used to detect Malignant Catarrhal Fever. By using cELISA however, does not differentiate the MCF viruses. It can only detect seropositive subclinical carriers and hosts of the virus (Sharma *et al.*, 2019). Serum neutralising test can also be used in the detection of AlHV-1 (OIE, 2020) and OvHV-2 (Giangaspero *et al.*,2013).

MCF viruses are found worldwide, but illness only arises when a virus is passed from a carrier species to susceptible hosts. MCF associated with AlHV-1 has been documented primarily in sub-Saharan Africa where cattle and wildebeest comingle (OIE, 2020). In zoological parks where carriers and susceptible species cohabitate, AIHV-1 can cause disease. OvHV-2, on the other hand, is an emerging disease of domestic animals, captive ruminants, and wildlife outside Africa. In Indonesia, sheep-associated MCF is common among Bali cattle; however, cases in cattle are uncommon in countries where *Bos taurus* and *Bos indicus* are the major species. This is because domestic cattle (*Bos taurus* and *Bos indicus*) are quite resistant compared to American bison (*Bison bison*) which are approximately 1,000 times more likely to develop clinical illness, and may not become ill as a result of exposure to OvHV-2 (Sharma *et al.*, 2019). Thus, OvHV-2 is a serious concern in countries with bison and cervid farms, as they are very susceptible (OIE, 2020).

The lack of information on the overall true seroprevalence of MCF in the world makes it necessary to do further and thorough investigations, which then the data can be helpful to mitigate this disease in Malaysia. Thus, the goal of this review is to estimate the prevalence of MCF infection in goats, sheep, and deer in the world from 2000-2020, and to understand the risk factors that affect the prevalence of MCF. The outcome of this study can boost the herd health program in small ruminant farms in Malaysia by adding new knowledge and data and improving the welfare of the animals.

2.0 MATERIALS AND METHODS

The study was conducted based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) checklist. (Moher et al., 2010). The checklist was used to ensure that all relevant data was included in the analysis. The outcome of interest was the prevalence of malignant catarrhal fever. Related articles published by any reliable scholars and institutions were systematically searched

2.1 Search strategy

SCOPUS was the database used in this study for literature searches in order to find relevant papers.

The research question was "what is the prevalence of MCF infection among small ruminants and deer in the world?", where searching terms used were (malignant AND catarrhal AND fever) OR (ovine AND herpesvirus) OR (ovine AND gammaherpesvirus) OR (caprine AND gammaherpesvirus) OR (caprine AND herpesvirus) AND (prevalence OR seroprevalence OR molecular AND detection OR PCR OR seroepidemiology OR epidemiology). Any articles in the database containing related keywords in its title or abstract were selected.

2.2 Study eligibility and application of inclusion and exclusion criteria

Studies that were considered for systematic review were identified based on a few criteria. The inclusion criteria of the studies were (i) the study period was done between 2000-2020; (ii) species studied were goats, sheep, or deer; (iii) prevalence was recorded in the articles, and; (iv) studies were written only in English if they were conducted in any parts and reported the prevalence of MCF infection in goats, sheep, and deer. The studies will be excluded if (i) the data was insufficient, or; (ii) the studies had a different outcome of interest.

2.3 Study selection and data extraction process

All potentially related articles were imported to Mendeley Reference Manager software to organize and remove any duplicates.

A standardized data collection format had been prepared to extract necessary data from the articles. The data included were the title of the study, the first author's last name, the study population where the study was conducted (goat/sheep or deer infected), study design, year of publication, sample size, and main findings of prevalence. After that, the student and supervisor screened the title and abstracts with predefined inclusion criteria. The student and supervisor collected the full texts and evaluated their eligibility for final inclusion. Any data discrepancy was resolved by referring back to the original study.

2.4 Data synthesis and statistical analysis

Extracted data from the selected articles were entered and organized into a Microsoft Excel spreadsheet. Figures and tables were used to show the summarized and descriptive results.

3.0 RESULTS

3.1 Literature search

Initially, 57 potential articles were retrieved from Scopus. However, after carefully reviewing the title and abstracts, 28 articles were found irrelevant for this study and were removed from consideration for the following step. Then, 29 articles were considered for full-text reading, and later 14 articles were excluded because they lacked sufficient information or had a different outcome of interest. Only 15 papers met the inclusion requirements in the end, and the data was extracted accordingly. The PRISMA flow chart is used to show the study selection process (Fig. 1)

3.2 Study characteristics

All the 15 included studies were conducted using a cross-sectional study design with convenient/purposive, stratified, systematic, cluster, multistage, and simple random sampling procedures and published between 2000 and 2020. The studies were undertaken from all parts of the world. The 12 countries that were included in this study were the United States, Canada, Norway, Turkey, Iraq, South Africa, India, Pakistan, China, Mongolia, Philippines, and Japan. Fig. 2 shows the prevalence of Malignant Catarrhal Fever in the world divided by 4 degrees of prevalence. Fig. 3 shows the number of times the risk factors that were stated in the 15 articles. Management, which was mentioned in all 15 articles, is the largest risk factor related to the spread of MCF.

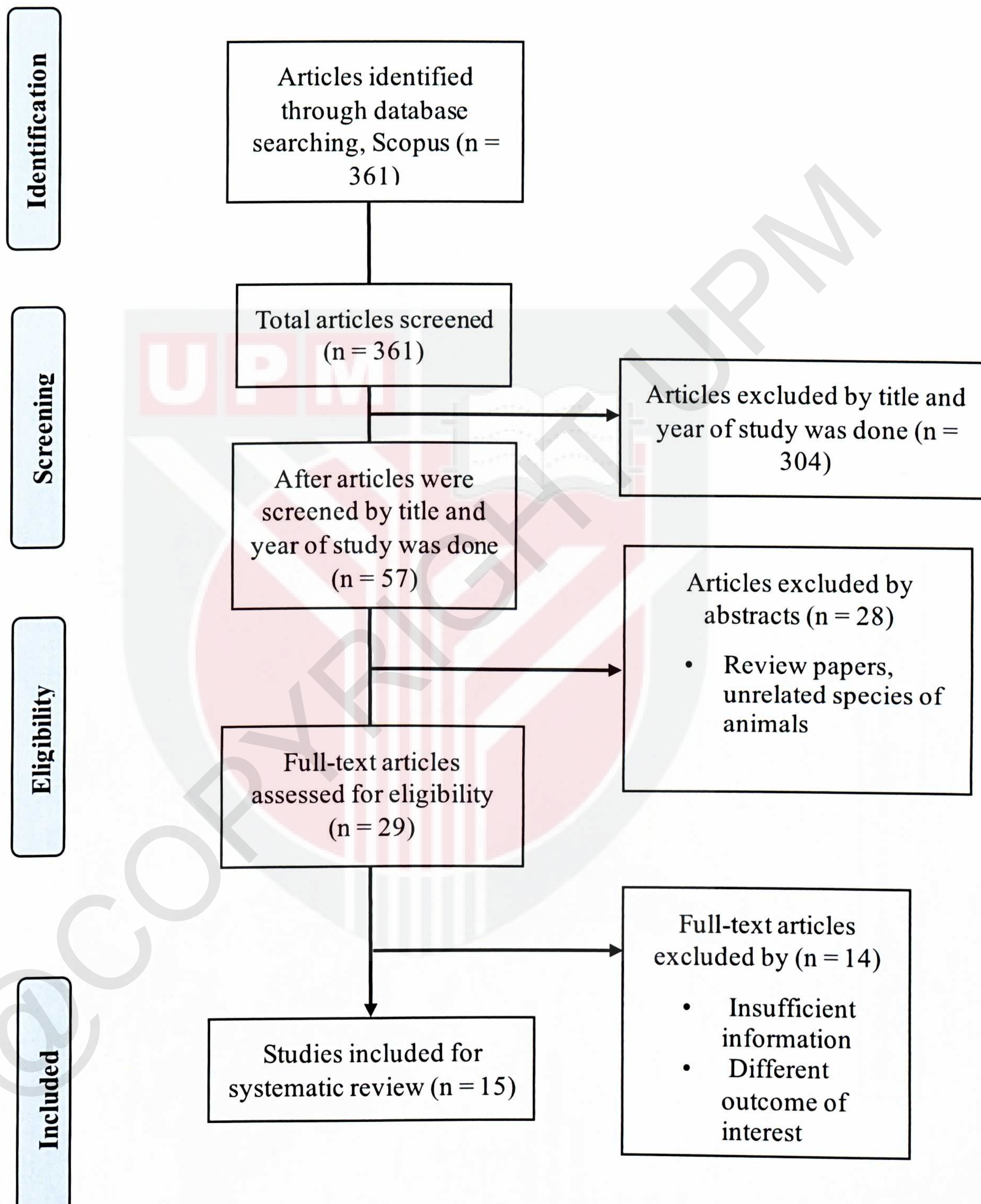

Fig. 1 Flow chart explaining the number of included and excluded articles in the systematic review on the worldwide prevalence of malignant catarrhal fever (MCF) in goats, sheep, and deer from 2000 to 2020, based on the PRISMA 2009 guideline.

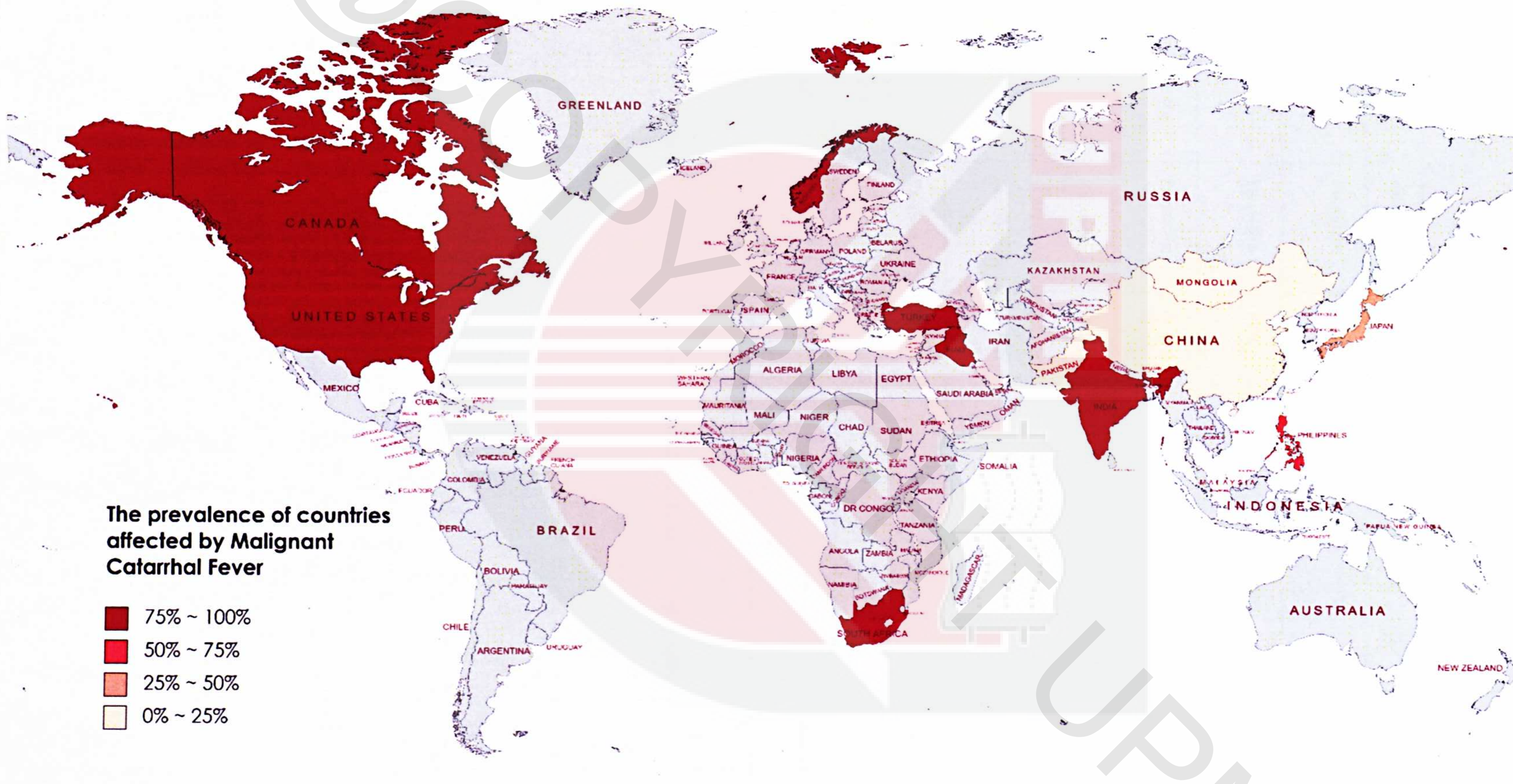

Fig. 2 Map of the prevalence of malignant catarrhal fever in the world.

Authors	Region	Sampling method	Diagnostic test	Sample size	Prevalence	Risk factor
Li et al., 2003	United States	Purposive	ELISA	15	86.7%	Management
Wani *et al.*, 2006	India	Purposive	PCR	26	61.5%	Temperature, age
Løken *et al.*, 2009	Norway	Purposive	ELISA & IFAT	4	100%	Management
Riaz *et al.*, 2021	Pakistan	Random	PCR	50	44%	Management
Yeşilbağ, 2007	Turkey	Random	ELISA	200	96.0%	Management
Li et *al.*, 2001	United States & Canada	Random	ELISA	142	87.0%	Management
Khudair *et al.*, 2020	Iraq	Random	PCR	60	86.6%	Management

Table 1. Prevalence of Malignant Catarrhal Fever in the goat species.

Author	Region	Sampling method	Diagnostic test	Sample size	Prevalence	Risk factor
Riaz *et al.*, 2021	Pakistan	Purposive	PCR	54	50%	Management
Løken *et al.*, 2009	Norway	Purposive	ELISA & IFAT	75	95%	Management
Yazici *et al.*, 2006	Turkey	Purposive	ELISA	160	6.3%	Management
Khudair *et al.*, 2020	Iraq	Random	PCR	60	100%	Management
Mananguit *et al.*, 2021	Philippines	Random	PCR	89	65.2%	Management, age
Giangaspero *et al.*, 2013	Japan	Random	SN	272	37.7%	Management
Orchikuu *et al.*, 2017	Mongolia	Random	PCR	211	5.7%	Management, age
Yeşilbağ, K. 2007	Turkey	Random	ELISA	200	97.5%	Management
Bremer, 2010	South Africa	Stratified	PCR	85	76.5%	Management
Wani *et al.*, 2006	India	Stratified	PCR	Adult sheep: 33 Lambs: 21	Adult sheep: 84.8% Lambs: 95.2%	Temperature, age
Premkrishnan *et al.*, 2015	India	Cluster	PCR	356	24.4%	Management, age

Table 2. Prevalence of Malignant Catarrhal Fever in the sheep species.

Author	**Region**	**Sampling method**	**Diagnostic test**	**Sample size**	**Prevalence**	**Risk factor**
Li *et al.*, 2003	United States	Purposive	ELISA	28	46.3%	Management
Zhu *et al.*, 2020	China	Purposive	PCR	NA	3.8%	Management
Neves *et al.*, 2013	Norway	Random	ELISA	3339	3.5%	Age

Table 3. Prevalence of Malignant Catarrhal Fever in the deer species.

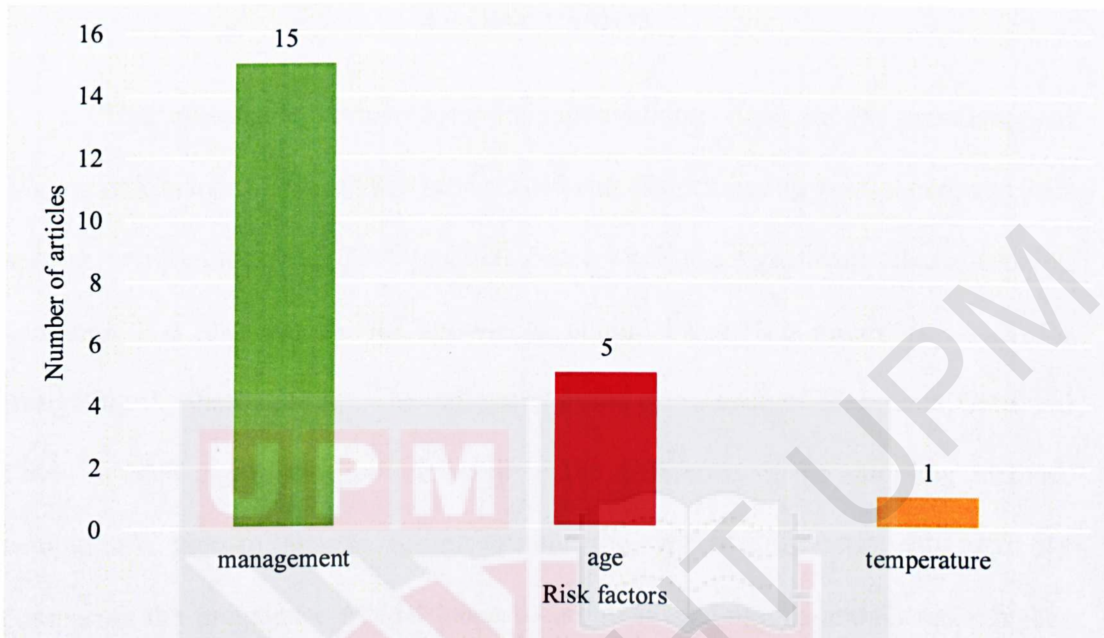

Fig. 3 Total risk factors

4.0 DISCUSSION

This systematic review compiled all available data on the prevalence of Malignant Catarrhal Fever (MCF) and related risk factors among goat, sheep, and deer species between the years 2000 to 2020. Since MCF is a significant disease-causing economic loss to a country, the knowledge obtained from this review is critical for mitigating the disease's risk. The variations in the prevalence of Malignant Catarrhal Fever in each region may be attributed to the difference in the sampling method, sample size, type of sample, age group, and the type of diagnostic tests used. By comparing the prevalence of Malignant catarrhal fever in goats and sheep, a higher prevalence of MCF can be observed in the sheep species. This can be due to the earlier discovery of OvHV-2 in sheep, which leads to more studies being done on it, compared to the later discovery of the CpHV-2 in goats. The difference of prevalence in the studies can also be caused by the no standardized diagnostic method, where PCR, ELISA, c-ELISA, CFT, and SN tests were used. The lower prevalence reported in some studies might be due to the use of the SN test (Giangaspero *et a.l*, 2013) or usage of c-ELISA, where the specificity of it was 94% in cattle, bison, and deer (Li *et al.*, 2001)

4.1 Risk factors

According to the articles, animal management, age, and temperature of the environment were the risk factors associated with Malignant Catarrhal Fever (Fig. 3). These risk factors are important dynamics to the prevalence of this disease in an area.

4.1.1 Management

Intermixing of flock species is the highest associated risk factor of MCF (Managuit *et al.,* 2021; Premkrishnan *et al*., 2015; Zhu *et al.,* 2020). A farm that rears only cattle has a 0% prevalence of MCF, compared to farms that rear both natural host (sheep and goat) and susceptible host (cattle and deer), at 25% prevalence reported on the cattle population (Løken *et al*., 2009). Natural hosts (sheep and goats) have important roles in virus transmission (Khudair *et al.,* 2020) by releasing and transmitting the cell-free virus horizontally to the susceptible hosts (Sharma et al., 2019). Differentiating and isolating virus-free animals from virus-carrier animals would help with the prevention and control of MCF (Li et al., 1998).

The stocking density of the farm has a pivotal role in the spread of MCF. A high stocking density farm (Neves *et a.l*, 2013; Ochirkuu *et al.,* 2017) will cause MCF to spread faster. Similarly, it would lead to an uncontrollable outbreak compared to a low stocking density farm (Neves *et al*., 2013). The same study found that a high population density (16 animals per area) farm has a higher MCF prevalence at 6.7% compared to the low population density farm (1 animal per area) at 3.2% (Neves *et al*., 2013). Density-dependent issues, such as infection risk, may increase as population density rises.

It is unclear why animals do not always get sick after being exposed to carriers, but stressors that increase virus shedding in the carrier and/or susceptibility in the incidental host, as well as environmental factors (e.g., high humidity) that increase virus survival or concentrate the virus, have been suggested as possible factors. In one outbreak in subclinically infected bison, clinical cases tended to occur 3-14 days after the animals were stressed by handling (Spickler, 2019). Resource constraints may cause stress and have a direct impact on the biological parameters of the susceptible hosts. The parameters impacted such as body mass, survival, and recruitment will cause the susceptible host to become more prone to illnesses and disease as their fitness declines and their stress levels rise among their herd (Neves *et al*, 2013). As a result, appropriate husbandry practices, such as limiting stressor exposure, may help to prevent major illnesses in animals who are subclinically infected or mildly affected (Spickler, 2019).

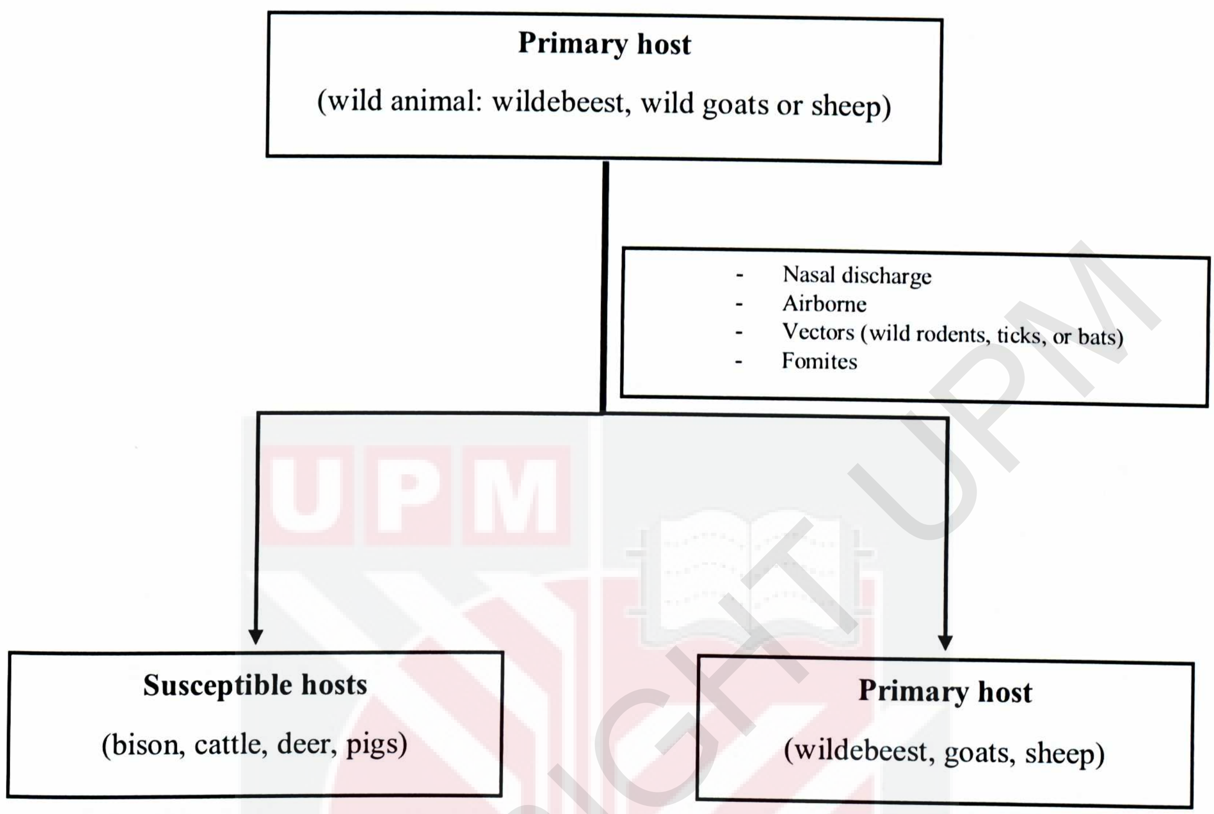

Fig. 4 Horizontal transmission of MCF from wild animals.

Finally, wild animals such as the wildebeests are known as the reservoir host of the MCF virus, which is common, the AlHV-1. Thus, allowing livestock to come into contact with wild animals (Premkrishnan *et al.,* 2015) that are possible carriers are also an example of a management risk factor. Refer to Fig. 4 to see a simplified horizontal transmission of the MCF virus. Free-range livestock is often at risk of coming into contact with wild animals that act as a reservoir host, or other possible MCF vectors, such as wild rodents, ticks, or bats (Zhu et al., 2020). The herding approach of co-rearing sheep in a free-range backyard or pasture among other animals such as buffalo, cattle, and goats in the Philippines (Mananguit *et al.,* 2021) could enhance the risk of OvHV-2 transmission from sheep to sheep, as well as other livestock and wildlife. This identical management practice was also recorded by Ochirkhuu et al. (2017) and Khudhair et al. (2019, 2020) in Mongolia and Iran, respectively (Mananguit *et al*., 2021). The farm management risk factor is applicable in Malaysia because when it comes to raising free-range animals, it is a regular sight that in the rural areas such as Johor, Kedah, Kelantan in which the farmers allow the livestock to graze freely around the village area. However, in Kedah, letting livestock graze freely in a reserved forest, a place that has the potential of getting in contact with a wild animal, will be fined RM10,000 or a 3-year prison sentence or both. Therefore we are at a high risk of MCF outbreak due to the nature of our production system of mostly Integrated and extensive farming, However, since the virus is not transmitted horizontally in the final host, the virus is self-limiting which explained the status of the disease is under-reported The less number of reported cases in Malaysia can also be caused by the type of commonly reared livestock in Malaysia the domestic cattle, *Bos Indicus,* which is different to the other higher MCF cases countries that rears a high number of bison (*Bison bison*) like in the United States. This is because domestic cattle (*Bos taurus* and *Bos indicus*) are quite resistant compared to American bison (*Bison bison*) which are approximately 1,000 times more likely to develop clinical illness, and may not become ill as a result of exposure to OvHV-2 (Sharma *et al*., 2019).

Thus, the prevalence of MCF among the livestock in Malaysia should be investigated due to our free grazing management system in the country. In conclusion, the management of the farm is the ultimate factor for the spread and control of MCF.

4.1.2 Age

The second risk factor, which has been mentioned in five articles is the age of the animal. In the article by Wani et al. (2006), where lambs did not become infected during the neonatal period, and only started to get infected as early as 29 days old can be caused by the decreasing of passively transferred maternal immunity that used to be protecting the lambs since they were born. Malignant catarrhal fever was noticed to be lower prevalence in young animals, which may indicate that these adult animals have acquired the infection as they grew older (Premkrishnan *et al,* 2015). Zhu et al. (2020) documented that deer aged 4–6 years old were most easily vulnerable, accounting for 76.5% of the affected deer in the study. This statement can also be supported by Neves *et al,* 2013, in his study which stated that adult has more time exposed to the virus and develop it as time passes by. Adult animals, on the other hand, could escape infection as adults by avoiding contact with diseased natural hosts like sheep from a young age. This technique is used by sheep producers and zoos in America and Europe to keep OvHV-2-free sheep populations (Ochirkuu *et al.,* 2017).

A national policy in the form of a law directing the sheep farmers to separate lambs at an early age and nurture them separately to develop OvHV-2-free sheep flocks would be an ideal way to control this risk (Premkrishnan *et al,* 2015).

4.1.3 Temperature

The last risk factor which had been mentioned is temperature. The study by Wani et al, (2006) shows that as the environmental temperature increases, the rate of infection of Malignant catarrhal fever in the farm also increases, where the rate of infection increases by 9.3% by the increase of temperature. The lambs in the farm become positive in a short period when the ambient temperature increased from 7.5 °C to 22.7 °C. Crawford et al. (1999), reported a significant number of cases in late summer and autumn, several months after the end of the lambing season, which can be a great agreement as to all the cases in cattle in this study were recorded during the spring, summer, and autumn. In summer where the environmental temperature is higher, the migration of sheep and goats to highland pastures puts them at risk of in contact with the hangul or Kashmir stag, which can be a carrier of the MCF virus. In another study by Zakharova et al. (2020), the prevalence of MCF in cattle was timed to coincide with unusually warm temperatures in Kharchev, ranging from 31°C to 35°C. During the sampling period, there were eight days with such high temperatures, where after each very hot day, one or two infected animals were discovered. However, no additional cases of the disease were reported in the village after mixed grazing of cattle and sheep ended in August and the air temperatures returned to normal at 17°C–22°C. Drought and intense vegetation and pasture depletion were caused by the temperature anomalies, resulting in a shallow pond at the pasture's edge. Therefore, grazing animals had a substantial feed and water shortages, resulting in dehydration in cows and heat stress, which then the MCF develops (Zakharova *et al.,* 2020).

5.0 CONCLUSION

This study is the first systematic review on the worldwide prevalence of malignant catarrhal fever (MCF) and the associated risk factors in goats, sheep, and deer from the year 2000 to 2020. However, there was an issue with insufficient data to conclude the true prevalence of the disease in the world. The limitations include the dearth of studies to conclude the true prevalence suggesting the importance of further expansion of research in this area. Another limitation in this study was the lack of uniformity of diagnosis between ELISA, PCR, complement fixation test (CFT), and serum neutralisation test (SNT). Similarly, the sampling method and the type of samples tested may have a different outcome to the prevalence. Some articles used nasal swabs, while the others take from the blood test. The risk factors associated with MCF are animal management, age, and environment temperature, where the highest risk factor is management practice. Therefore, it is recommended to do more research on the prevalence of Malignant Catarrhal Fever (MCF) in goats, sheep, and deer in the future to determine the true prevalence of the infection in other countries and the world. The information gained from this study elevates the importance of understanding the prevalence and risk factors of the disease in cattle, sheep, goats, and deer.

6.0 FUTURE RECOMMENDATIONS

I would recommend that for future studies on Malignant catarrhal fever, a standardised protocol suggested by OIE should be followed on obtaining, keeping, and processing samples with less inaccuracy to produce reliable data that can benefit other researchers. Awareness of this disease among farmers is also required to gain more workforce to mitigate this high mortality disease.

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APPENDICES

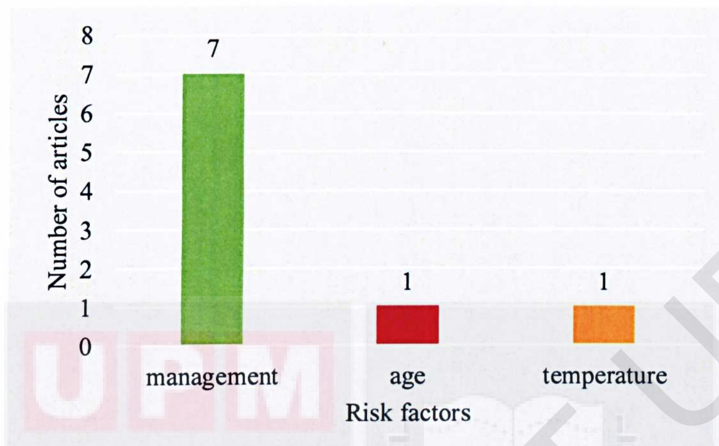

Fig. 3 Risk factors of Malignant Catarrhal Fever in goat.

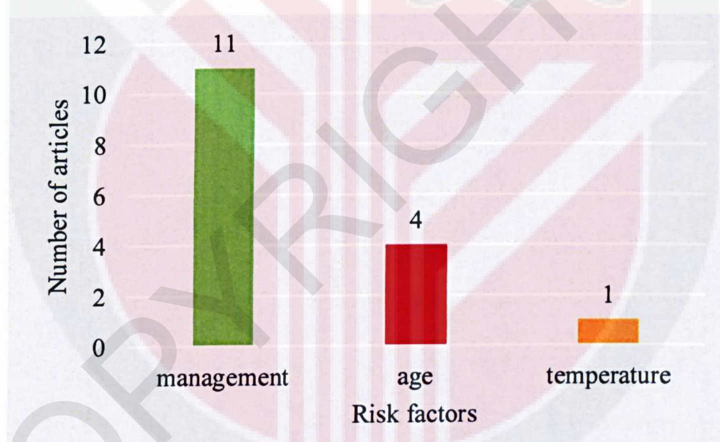

Fig. 4 Risk factors of Malignant Catarrhal Fever in sheep.

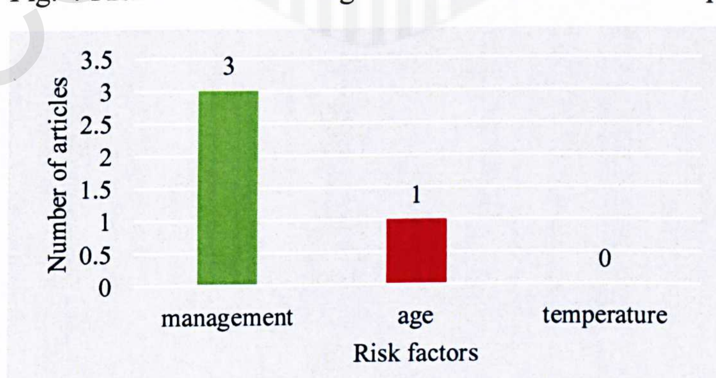

Fig. 5 Risk factors of Malignant Catarrhal Fever in deer.