

Caprine Cancer: Etiology, Types and Metanalysis of 21-Years of Case Reports

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Abstract

Caprine carcinoma is relatively rare, which is often confused with other pathological conditions. We also provide, brief etiology and development mechanism of carcinoma which were more abundant in goat. In this study we meta-analyzed the data, from 2000-2021, on the basis of type of cancer, breed, age and region. The purpose of this review was to gather all current available case studies involving different forms of caprine carcinomas to provide a basis for its occurrence, what is already known and what is to be explored in future. The meta-analysis of twenty years (2001 - 2021) was performed with following indexing terms: "goat" AND "cancer" in PubMed and Google. Incidence of 94 cases of goat carcinoma were identified from 48 articles, the majority of them were reported from the US and China. Most cases were of adenocarcinoma (n = 35), and squamous cell carcinoma (n = 18) while remaining incidences belong to other types of cancer. Though the occurrence of caprine cancer is less reported but not rare. Thorough research is required to further understand caprine carcinoma for developing efficient methodology for its identification, control and prevention.

Keywords: Goat Cancer; Etiology; Meta-Analysis

Introduction

Cancer is the state where cells lose their ability of organized cell growth. They show peculiar properties like unrestricted control of development, invading the local tissues, and the potential to spread to other parts. They are differentiated into two types based on their propagative property: - Benign and Malignant cancer. Benign that remains confined to one region and another is Malignant, spreading to other parts. Common cancers include bone marrow, prosthetic cancer, cancer in the lungs, and mammary. Any single factor does not cause cancer. The changes in gene sequences or mutation are the main reason, but in many cases, cancer develops due to abiotic factors that may cause disturbance in cellular processes. So, for this reason, we can't solely call genetic cancer disease.

The commonness of mammary tumors differs from species to species. In humans, females are highly subjected to breast cancer. In contrast, in the case of domestic ruminant animals, the rate of mammary cancer is meager, instead of the fact that the morphology of human mammary glands is on par with bovine [1]. Due to the infrequent mammary tumors in dairy animals, mammary cancer's probable threat, physiological and anatomical traits are still unspecified. It was observed that meat-eating animals are more prone to mammary cancer as they consume carcinogenic substances via their diet. The number of domestic meat-eating animals like dogs with mammary cancer is high compared to domestic plant-eaters like cattle, which have zero incidences of development of mammary cancer [2]. Previous studies

have also shown that a high parity rate reduces the time of subjection of estrogen, and increased lactation reduces the risk of mammary carcinoma, nevertheless, the process behind this suppression is still not clear.

Goat also develops some types of cancer especially on location of skin which are less covered with hair and exposed to sun. Like skin on nose, eyelid, udder, under the tail and ears are the common spots for the goat that may develop cancer. Many other factors that can cause carcinoma in goats are, aflatoxins have been reported to cause cancer in goats [3]. Aflatoxins are produced as a secondary metabolite by the fungus *Aspergillus paraciticus*, and are a potent carcinogen for both humans and ruminants. Its exposure is highest in the tropical and subtropical regions, where conditions are suboptimal for food storage. There is also a viral etiology. When virus-like particles (compatible with type-D retrovirus) isolated from the nasal fluid of unhealthy goats are transferred to the healthy goat, the latter develop the tumor [4]. Thus, exposure to ultraviolet rays, type of skin pigmentation, age, and viral infection. U.V. radiation is now classified as a complete carcinogen, and it is harmful to humans and ruminants. Chronic exposure to U.V. radiation acts as a tumor initiator and tumor promoter [5]. In small domestic animals, tumors induced by U.V. rays are found where the skin is directly exposed, like eyes, nose, the tail [6,7].

Common cancer types in goat

Adenocarcinoma

In caprine, the most common cancer found is adenocarcinoma, according to data from 2000 to 2022, and among Adenocarcinomas, Enzootic Nasal Adenocarcinoma (ENA) found most of them [8-13]. Adenocarcinoma is a subtype of carcinoma that begins from the glands [14]. Enzootic nasal adenocarcinoma (ENA) is also known as enzootic nasal tumor and infectious nasal adenopapillomatosis. It is a contagious tumor of the glandular cells of the nasal mucosa and histopathologically classified as low-grade adenocarcinoma [13,15,16]. This type of tumor rarely metastasizes to other organs [17]. Several studies showed that ENA is etiologically associated with the caprine nasal adenovirus (CNAV) [15] or enzootic nasal adenocarcinoma virus (ENAV) [17] or enzootic nasal tumor-2 (ENTV-2) [9] that are the type of retrovirus and closely related with Jaagsiekte Sheep Retrovirus (JSRV). These retroviruses prompt neoplastic growth of the mucosal gland from the ethmoidal part of the nasal cavity [17]. At necroscopy, the tumors which arise from the ethmoid mucosa can be unilateral or bilateral [13,18].

The incidence of mammary tumors in *caprine* is considered rare [19]. The low incidence of mammary tumors in ruminants is probably due to the high pregnancy rate [20]. Hormone such as estrogen is essential for the appropriate development of the mammary gland as it promotes epithelial cell proliferation and differentiation in healthy mammary glands [21]. Despite estrogen exposure being a significant risk factor for mammary tumors [23]. About 3 out of 4 cases of mammary tumors express E.R. (estrogen receptor) [24]. It plays a vital role in neoplasia and hyperplasia of mammary tissues, and increased parity reduces estrogen exposure. Hence, low exposure to estrogen reduces the incident rate of mammary cancer in goats [22]. A survey from 1935 to 1974 of screening cancer in goats was conducted in Africa, and none of the cancers were found as mammary cancer [25]. Another study in Veterinary Diagnostics Laboratory at Oregon State University examined only seven mammary adenocarcinomas out of 100 goats from 1987 to 2011 [26]. However, papilloma of the skin of the udder and teat is very common in goats [20].

Clinical evaluation of cancer

The goats were clinically examined at different parameters. In a study by G. Yi and co-workers, the clinical analysis included nasal discharge, coughing, difficulty breathing, swelling in body parts, and weight loss [13]. In many cases after the death of an animal, the autopsy was performed to examine the animal solely. The enlargement of organs was observed with other processed lesions for Histopathological examination. The microbial assessment was also done to determine the microbial source that may result in cancer development. A rare development of cancer and tuberculosis of the mammary gland was seen in 7 years old doe of breed Serrana which showed symptoms

like fever, coughing, udder enlargement, and dissection of mammary, lung, spleen, and mesentery showed the growth and similar kind of lesions [27]. A doe of age eight was found to have vaginal discharge, but no deformity was detected. It was further examined by ultrasound, which showed the presence of 2 types of tumors simultaneously: uterine adenocarcinoma and leiomyosarcoma [10]. A 4 years old goat was found to have malignant lymphoma with clinical signs of posterior ataxia that later resulted in paralysis [28]. A female goat two years of age could not conceive instead of breeding; usually, no defect in the estrous cycle can be seen with further ultrasonic examination. The right ovary was found to have increased in size and have multiple cysts [29].

As different forms of rare scientific information accumulate regarding the caprine carcinoma, scientist haven't hypothesized about their potential role in affecting caprine health. There are published case reports on different forms of caprine carcinoma. Limited literatures are available on caprine carcinoma. The purpose of current meta-analysis was to gather all current information on caprine carcinoma and evaluate its occurrence globally.

Metanalysis of 21 years of cancer reports of goat

The literature search was conducted between February and march 2022 with restrictions on the timeline. We included articles from the year 2000 onwards only. Online electronic databases of PubMed and Google scholar were used for searching the required articles using search terms of *goat, cancer, tumor, metastasis* and, it was limited to carcinoma in goats. Using the "case reports" filter of PubMed, we further filtered our search results and narrowed them down to 74 articles, and after going through title and abstract we got only 48 articles related to our work.

Data collection and study selection

The papers were evaluated to determine whether they reported any case of caprine carcinoma. The defined search strategy gave 673 literatures from PubMed and 3000 literatures from Google scholar for a total of 3673 literatures analyzed for review. We analyzed incidents of caprine carcinoma from the year 2000 to 2022. After review of title and abstract, 3599 articles were removed for not aligning with our selection criterion (original case reports on caprine carcinoma)- leaving 74 articles for whole literature review. A complete analysis of all 74 publications lead to the removal of 26 literatures due to the major deficiency of analysis on caprine carcinoma (they were based on sheep carcinomas or, having inadequate information). The remaining 48 literatures were thoroughly reviewed for finding different types of carcinomas in goats. The references record of selected literatures were reviewed for additional information on its development, but no such information was figured out by this scheme. In summation, we present our review focused on caprine cancer, a first in the queue of meta-analysis. A flow chart of the data collection procedures and filters applied to sort out the relevant articles is given in figure 1.

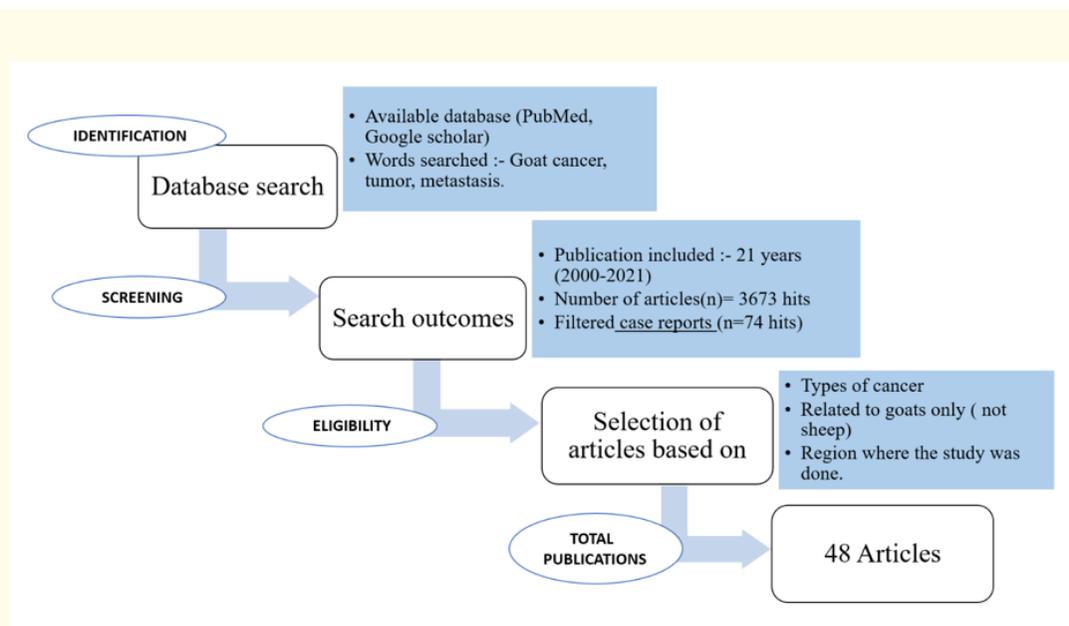


Figure 1: Methodology of data collection for the meta-analysis of caprine cancer of the last 21 years.

Results and Discussion

Cancer is relatively rare in goats, and therefore most of the cases included in our study reported carcinoma for the first time. For meta-analysis investigation, we included only the cases reported from different parts of the world. The initial search got 1888 hits from PubMed, which was reduced to 673 after using the timeline filter (2000 - 2021). On selecting case reports the hits restricted to only 74. After a brief review of the title and abstract, 24 articles were eliminated because they were not suitable for our study. The remaining 48 articles were analyzed to find the type of cancer, breed, age, country and year summarized in table 1.

Forty-eight studies were reviewed that particularly addressed caprine carcinoma and are summarized in table 1. Studies included in the review were published from 2000 to 2021. Existing study were mainly evolved from case reports.

Year	Case #	Country
2000	1	USA [30]
2001	8	S. Africa [31], USA [32]
2005	3	Italy [33,34] Click or tap here to enter text.
2006	1	Germany [35]
2007	5	Spain [36,37], Iran [38], Switzerland [39]
2008	7	USA [40,41], Spain [42,43], Netherlands [44], Switzerland [8]
2009	24	USA [45], Germany [46,47], China [13]
2010	1	Germany [48]
2011	4	Germany [28,49], Turkey [50], USA [51],
2014	4	USA [12,29,52], Spain [27]
2015	13	USA [53,54], Italy [55], Switzerland [56]
2016	1	USA [57]
2017	2	USA [10], Japan [11]
2018	2	USA [58,59]
2019	3	USA [39,40,41,42] Austria [61]
2020	3	Germany [62], USA [63], Egypt [64]
2021	12	Iran [65], Egypt [66], Spain [9]

Table 1: Summary of the reports (year wise) of caprine cancer retrieved from the databases ranging from 2000 - 2021.

The systematic review of 48 studies and meta- analysis of 94 cancer affected goats from 2000 to 2021 is the thorough meta-analysis to the best of our awareness evaluating the occurrence of carcinomas in the goats. Our meta-analysis indicates the higher occurrence of adenocarcinoma (37.2%), which was majorly reported in Nanjiyang breed [8-10,12-15,36], followed by squamous cell carcinoma (19.1%) reported in Tswsana breed [32,33,54] and other forms of cancer (43.7%) in different breeds. No direct and indirect correlation was observed in breed and type of cancer or breed and region. Most common clinical symptoms reported in different cases was nasal discharge and loss of appetite. Most of the affected goats were subjected to euthanasia, due to deterioration of goat health. There was inadequate data to establish any possible cause and development of carcinoma in goats. Despite the non-uniform and irregular variations in different data, this analysis can guide further clinical and oncological studies.

The occurrence of carcinomas in goats are not well documented in the literatures; However, there is so much to know about the cancers in goats. As exploration in the goat cancer development and its possible factors will be done, novel evidences will bridge the gaps in

its full understanding, it will be vital for veterinarians as well as goat farmers to be aware of their occurrence and to decode their possible implications on the health of their livestock. On identification of possible cancer triggering factors in goats and its elimination can be practiced and a pivotal contribution can be made in improving their growth and health. Meta-analysis of incidence of goat carcinoma in last 21 years reported in the literature has been shown in figure 2.

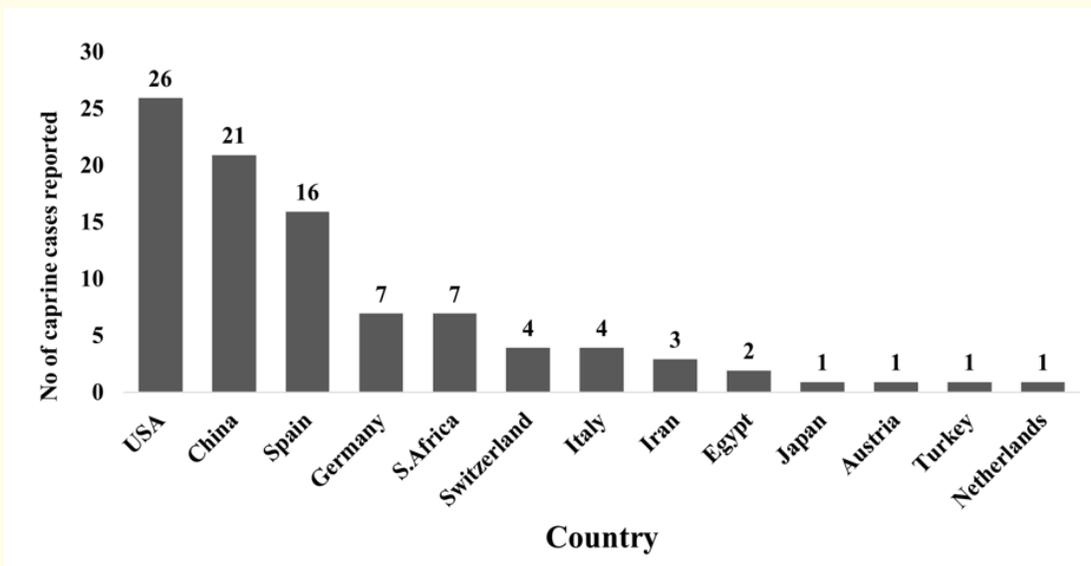


Figure 2: Country wise number of goat carcinoma reported in the literature in the last 21 years.

Different forms of cancers in goats have been reported since long and, there still left a strong need for ample research to further identify and characterize the development of different carcinomas during the life time of goats, most paramount is their development and possible treatments for protecting goats. Because of scarcity of study in this domain, there is more to be done in coming years. Our review team is currently addressing the gaps in different literatures majorly focused on different types of carcinomas and starting to address questions linked to factors influencing carcinoma development and its scarce occurrence. Although wide variety of carcinomas were reported in different goats. But the mechanism surrounding their occurrence is still not known and has promising possibilities of further scientific interpretation and encourage future research ventures targeted on improving goat health. As more information is decoded on caprine cancer, we can initiate to answer the newly developed questions: What triggers cancer development in goats, how are they involved in development of cancer, how different forms of cancer occur in goats, why scarce occurrence of cancer in goats, what is the cancer age of goats? More specifically, how they develop in different organs of goat’s body? Do poor managing practices and epigenetic factors influence its development? As observed in area graph the uneven representation of carcinoma occurrence indicates the lack of data or might be goats utilized for meat purposes at early age.

The occurrence of different forms of carcinomas in goats and its rare reporting opens new avenues for exploration and creation of advance scientific knowledge in caprine carcinoma. However uneven reporting of data creates a big pothole in understanding its development and possible ways of finding its cure. To date, most records are only restricted to its occurrence in different forms and has further required to dig in to the exact mechanism of development that results due to the different external as well as genetic factors. In future, most researches likely to be centered on its development and root causes triggering it.

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