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Zoonotic fungal diseases and animal ownership in Nigeria

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ABSTRACT

Background: The growing interest in keeping animals as pets in Nigeria and other resource-poor countries highlights the possibility of transmission of zoonotic infections to humans. These zoonoses which are usually caused by viruses, bacteria, parasites and fungi, are naturally transmitted to humans, causing various degrees of morbidity and mortality with attendant economic and or public health consequences.
Materials and method: In the present review, a computerized search of existing literature was conducted using the Google search engine and PubMed electronic database to identify and download relevant publications on zoonotic fungal infections in Nigeria. The key words used were zoonotic fungal disease and Nigeria while the Boolean operator 'AND' was used to combine and narrow the searches. Additional information was obtained by searching the medical and veterinary libraries for journals not listed in the database. The available publications were thereafter reviewed and findings qualitatively described.
Results: Our findings revealed that fungal diseases with zoonotic potential lack sufficient attention in Nigeria. This suggests that fungi are yet to be considered as major causes of morbidity and mortality in animals and humans in Nigeria, and may account for the few reports available on zoonotic fungal diseases in the country.
Conclusion: There is a need to raise awareness of the extent of health problems caused by zoonotic fungal diseases in Nigeria in order to better appreciate their burden and public health consequences, and also provide an integrated platform for development of effective prevention and control strategies.

Contents

1. Introduction

Zoonoses are diseases of animal origin, usually caused by viruses, bacteria, fungi and parasites which can be naturally transmitted to humans.[1] They have been known for many centuries, and account for the majority of emerging and re-emerging infectious diseases, globally.[2,3]. It has been reported that 75% of all emerging

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infectious disease pathogens are zoonotic, originating principally from wildlife.[2,4] Indeed, zoonotic infections have emerged as a burden for millions of people in recent years, due to re-emerging or novel pathogens often causing outbreaks in the developing world in the presence of inadequate public health infrastructure.[5] The growing demands for food availability, development and industrialization have resulted in encroachment on wildlife habitats and increased contact between humans and animals, resulting in a dynamic upward trajectory of these diseases.[6,7] Many zoonotic diseases have significant impact on human health as well as livestock productivity, thereby undermining livelihoods both by causing illness in the household and threatening its livestock and their output.[8]

Fungi are a group of non-photosynthetic microorganisms which live as saprophytes in the soil and on dead organic matter or as parasites of plants and animals including man. There are approximately 1.5 million different species of fungi on Earth, but only about 300 of those are known to cause diseases in humans.[9] Fungal diseases are often caused by fungi that are common in the environment. Zoonotic fungi can be naturally transmitted between animals and humans, and in some cases cause significant public health problems. However, some fungal diseases with zoonotic potential have been given little attention in international public health efforts, leading to insufficient interest in the development of strategies for their prevention and control.

In Nigeria, some zoonotic diseases such as rabies, avian influenza, Lassa fever, toxoplasmosis and tuberculosis have been given priority attention.[10–14] However, it is noteworthy that fungal diseases with zoonotic potential have attracted inadequate interest in the country, probably due to the fact that fungi are yet to be recognized as major causes of morbidity and mortality in animals and humans. In the present review, a computerized search of existing literature was conducted using the Google search engine and PubMed electronic database to identify and download relevant publications on zoonotic fungal infections in Nigeria. The key words used were zoonotic fungal disease and Nigeria while the Boolean operator 'AND' was used to combine and narrow the searches. Additional information was obtained by searching the medical and veterinary libraries for journals not listed in the database. The available publications were thereafter reviewed and findings qualitatively described.

2. Dermatophytosis

Dermatophytosis is an integumentary mycotic disease prevalent in both sporadic and epidemic forms in over 145 countries of the world, and is of public health and economic significance. It is an important occupational mycozoonoses of dairymen, animal handlers, livestock farmers, pet owners, veterinarians, etc.[15] caused by a group of highly specialized pathogenic fungi collectively referred to as "dermatophytes", which are the most common agents of superficial mycoses in animals and humans, and are thus recognized as a public health menace worldwide.[16–20] This group of closely related fungi comprising 40 identified species in the dermatophytic genera that include *Microsporum*, *Trichophyton* and *Epidermophyton*[21] cause infection of the stratum corneum of the epidermis and keratinized tissues such as skin, hair and nails of humans and animals.[22,23]

Ecologically, dermatophytes are classified as zoophilic, anthropophilic or geophilic depending on their major reservoir in nature (animals, humans and soil, respectively). Zoophilic dermatophytes may result in zoonoses when humans are exposed to these organisms.[18] Majority of zoonotic dermatophytes are caused by four species: *Microsporum canis* (usually derived from pet animals, particularly cats and dogs), *Trichophyton verrucosum* (usually derived from cattle), *Arthroderma vanbreuseghemii* (usually derived from cats and dogs) and *Arthroderma benhamiae* (usually derived from guinea-pigs). Human infection results most often from direct contact with an infected animal, but may also be acquired indirectly through contact with a contaminated environment,[18] such as fungus-bearing hair and scales from infected animals. The prevalence of superficial mycoses caused by zoophilic dermatophytes was found to be significant in different parts of the world[24] especially in the tropical countries with warm and humid climate, crowded living and poor sanitary conditions.[25]

Several studies have indicated that domestic animals (including cats, dogs, sheep, goats, pigs, rabbits, horses, donkeys, ducks and chickens) constitute important reservoir of human dermatophytic infections in Nigeria.[21,26–32] The most common agents of infection identified were the zoophilic species: *Microsporum canis*, *Trichophyton mentagrophytes* and *T. verrucosum*. In addition, these studies revealed that close interactions of humans with domestic animals through nomadic lifestyle, animal farming, domestic livestock keeping or pet ownership promote the prevalence of dermatophytic infections.

3. Basidiobolomycosis

Basidiobolomycosis is a rare but emerging fungal infection caused by *Basidiobolus ranarum*.[33] The causative agent is an environmental saprophyte found worldwide and isolated from decaying plant materials, foodstuff, fruits, leaves of deciduous trees and soil. Also, it is occasionally present in the gastrointestinal tracts of amphibians (e.g. frogs and toads), reptiles (e.g. garden lizards and geckos), fish, and mammals (e.g. horses, dogs, insectivorous bats and humans) as well as in the faeces of Kangaroos and wallabies.[34–38] It is usually a subcutaneous infection but gastrointestinal involvement has also been described.[39,40]

The disease has been reported in tropical countries of Africa, Asia, South America, the USA and Europe, and occurs sporadically as a result of traumatic implantation or inhalation of the fungus that is present in plant debris in tropical environments.[41,42] The fungal spore enters the tissue of man through cuts in the skin and grows slowly to produce a hard and enlarged lump under the skin, often in the legs and arms.[34] Ingestion of food contaminated with soil or animal faeces is another likely route of infection with the disease.[33] If not treated, basidiobolomycosis may spread to the deeper tissues sometimes affecting vital organs like the brain and resulting in death of the patient.

The first case of basidiobolomycosis was reported in 1964 from Nigeria.[43] However, since that report, there have only been few studies on this disease in the country with most of them reported over two decades ago.[44–46]

4. Histoplasmosis

Histoplasmosis is an infection caused by *Histoplasma capsulatum*, a dimorphic fungus with two known varieties: *H. capsulatum* var. *capsulatum* and *H. capsulatum* var. *duboisii*. The two varieties have been identified in Africa. African histoplasmosis caused by *H. capsulatum* var. *duboisii* is a deep mycosis endemic in the African continent, essentially between the Tropics of Cancer and Capricon[47,48] as well as in the island of Madagascar.[49] It has been detected in about 20 countries in tropical Africa located between 20° North and 20° South of the Equator and extending from Senegal in the West to Tanzania in the East.[47,48,50,51] This region is characterized by high average rainfall, high humidity and little variation in diurnal temperature.[48]

Histoplasma capsulatum var. *duboisii* lives in the environment particularly in soil that contains large amounts of bird or bat droppings.[9] The fungus has been isolated from the intestinal contents and various organs of domestic animals (dogs, cats, cattle, sheep and horses) and wildlife (bats and wild rodents).[52,53] Also, natural infections due to this fungus have been reported in baboons (*Cynocephalus babuin, Papio cynocephalus papio*) detected in France and USA, although they had mostly originated from West African countries.[54] Interestingly, birds are not susceptible to histoplasmosis, possibly because their high body temperature does not allow the fungus to develop.[55]

Although the portal of entry of the fungus has been a subject of speculation, it has been suggested that the fungus may be inhaled and then haematogenously transferred to a favourable site such as the skin, subcutaneous tissue, bone or lymph node for proliferation.[48,56] Indeed, transmission via inhalation and deposition in alveoli of the microscopic fungal spores from the air has been reported.[57] Transcutaneous transmission following trauma as well as the possible role of insect bites has also been suggested.[58] Consequently, the population at risk includes farmers, poultry keepers, especially when cleaning chicken coops, pigeon roosts and bat-infested caves, barns or lofts, and construction workers especially those who work around old buildings with roosting birds.[59]

Although the incidence of African histoplasmosis is rare, approximately 50% of recorded cases have occurred in Nigeria while 25% of cases have been recorded in Niger, Senegal, Congo, Zaire and Uganda.[60] Following an investigation conducted in a bat cave in a rural area of Anambra state, southeast Nigeria, Gugnani et al.[52] discovered a natural reservoir of *H. capsulatum* var. *duboisii* in soil admixed with bat guano. The fungus was also recovered from the intestinal contents of a hairy-tailed slit face bat with long ears (*Nycteris hispida*) examined from the cave.[61] Additionally, these workers detected a high prevalence (35%) of skin sensitivity to histoplasmin among the cave guides, traders and farmers as well as precipitating antibodies to histoplasmin in the sera of 9.4% of young adults (farmers and palm oil workers) resident in the vicinity of the cave.[61] Subsequently, antibodies to histoplasmin have been detected in human immunodeficiency virus (HIV)-infected patients and carriers, indicating the existence of co-infections with *H. capsulatum* var. *duboisii* and HIV in Nigeria.[62]

5. Sporothricosis

Sporotrichosis, caused by the dimorphic fungus *Sporothrix schenckii*, is distributed throughout the world, especially in tropical and subtropical zones, with the main areas of endemicity located in Japan, India, Mexico, Brazil, Uruguay and Peru (reviewed in [63]). The fungus lives naturally as a saprophyte on living and decaying vegetation, animal excreta and soil.[51,64–66] Infection generally occurs by traumatic inoculation of soil, plants and organic matter contaminated with the fungus. Certain leisure and occupational activities such as floriculture, horticulture, gardening, fishing, hunting, farming, mining, wood exploitation and others that facilitate exposure to the fungus, are traditionally associated with transmission of this mycosis.[63,67] Although zoonotic transmission to humans is not the predominant mode of human sporotrichosis development, it has become increasingly recognized, not only in professionals in contact with infected animals, but also in pet owners and particularly in childhood. Zoonotic transmission has actually been described in isolated cases or in small outbreaks. Presently, veterinarians, technicians, caretakers and owners of cats with sporotrichosis are regarded as a new risk category for the acquisition of the disease.[63,68] It has been suggested that the armadillo (*Dasypus septemcinctus*) may be a reservoir of *S. schenckii*, since armadillo hunting was reported by several patients with sporotrichosis in Uruguay.[69] Transmission of *S. schenckii* has also been associated with bites or scratches from animals such as rodents, cats, dogs, squirrels, parrots, horses, and birds.[51,70] Moreover, *S. schenckii* was isolated from aquatic animals, primarily fish and dolphins,[71,72] as well as from insects that had been in direct contact with the fungus.[51] Some authors have reported sporotrichosis cases due to mosquito bites.[73] The largest epidemic of zoonotic transmission of this mycosis ever recorded occurred from 1998 to December 2009 in Rio de Janeiro, Brazil and involved more than 2000 cases in humans and over 3000 cases in cats.[74]

In Africa, the first case of Sporotrichosis was described from South Africa following an outbreak among native miners,[75] while the largest outbreak occurred between 1941 and 1944 with more than 3000 gold miners infected by the fungus, which was present in the mine timber.[76] Some other African countries with reports of sporotrichosis include Ghana,[77] Sudan,[78], Tanzania[79] and Congo.[80]. In Nigeria, Jacyk et al.[81] documented the isolation of *Sporothrix schenckii* from lesions on a Fulani herdsman and a farmer while Dalis et al.[82] recently reported concurrent infection with sporotrichosis and dermatophilosis in a bull showing severe generalized skin lesions.

6. Other fungal diseases with potential for zoonotic transmission to humans

6.1. Paracoccidioidomycosis

Paracoccidioidomycosis (PCM) is an acute to chronic systemic infection caused by a thermally dimorphic fungus, *Paracoccidioides brasiliensis*.[83] The natural habitat of *P. brasiliensis*, its environmental niche and life cycle in nature remain unknown, but it is presumed that the fungus is able to survive and proliferate in the soil,[83] from where it has previously been isolated.[84,85] Geographically, the disease occurs most commonly in Latin America with Brazil accounting for 80% of reported cases, followed by Colombia and Venezuela. In countries where the disease is endemic, cases are not distributed homogeneously around the territory but tend to concentrate around humid forests (subtropical or tropical).[86] However, according to Martinez,[87] factors such as human migration, expansion of agricultural frontiers, climate and environmental changes, as well as modifications in agricultural and social practices are beginning to influence the occurrence of infection and disease induced by *Paracoccidioides* spp. For instance, an increased incidence of cases of acute/subacute PCM was detected within one to two years after the observance of climate changes caused increased soil and air humidity in Sao Paulo State, Brazil,[88] while an increase in *Paracoccidioides* spp. infection in the population of North eastern Argentina was linked to the construction of the Yacyreta hydroelectric plant.[89]

Paracoccidioidomycosis is transmitted in an air-borne manner, in both humans and animals, by inhalation of infective conidia present in the environment or through injuries of the skin and mucous membranes.[90,91] The disease has been shown to occur in several species of domestic and wild animals including cows, horses, armadillos, sheep, monkeys, guinea-pigs, raccoons, porcupine and chickens (reviewed in [92]). Natural PCM has also been reported in dogs[91,93] and cats[94]; dogs living in rural areas have been reported to have a higher rate of infection than those living in the urban areas.[95] Furthermore, PCM has been associated with residence and professional occupation in the rural area and may be favoured by contact with coffee cultures, armadillos and bats.[96–98] In addition, serological surveys or skin tests with *P. brasiliensis* antigens have revealed the existence of PCM infection in cats, dogs, chickens, pigs, cattle, horses, sheep, goats, rabbits, monkeys, and in other free or captive wild animals.[99].

Although PCM has not been demonstrated persuasively to be a zoonosis, a zoonotic role has been suggested for it based on the following facts: (i) it has been demonstrated in wildlife (armadillos and monkeys) and domestic animals; (ii) the habitat of the causative fungus remains elusive[100]; (iii) the epidemiology of the disease indicates a rural predilection, consistent with most zoonotic infections[101]; and (iv) it has been shown, in areas of endemicity, that infected armadillos and humans share genetically similar strains of *P. brasiliensis*.[102]

Paracoccidioidomycosis is rare in Africa. However, Lawande et al.[103] reported a case of paracoccidioidal granuloma in a female from Kano, northern Nigeria. The causative fungus was demonstrated to be *P. brasiliensis* by culturing.[81]

6.2. Penicilliosis

Penicilliosis is an emerging infectious disease caused by the fungus, *Talaromyces (Penicillium) marneffei*, which is an important pathogenic and thermally dimorphic fungus causing systemic mycosis in South-East Asia.[104–106] *T. marneffei* is a member of the family Trichocomaceae and the only member in the *Talaromyces* genus which is considered to be an important human pathogen. *T. marneffei* infection is endemic in tropical regions, especially Thailand, Vietnam, north eastern India, Southern China, Hong Kong, Taiwan, Malaysia, Myanmar, Cambodia and Laos.[105] The fungus was first isolated from the hepatic lesions of a bamboo rat (*Rhizomys sinensis*) which died spontaneously from the infection in 1956[107] while the first human case occurred as a laboratory-acquired infection in 1959 when a laboratory researcher accidentally inoculated the fungus into his own finger during experiments with hamsters; a localized small nodule was produced at the inoculation site.[108] Subsequently, it has been shown that bamboo rats (*Rhizomys* spp. and *Cannomys* spp.) and soil from their burrows were important enzootic and environmental (natural) reservoirs of *T. marneffei*, respectively.[107,109–111] Recently, dogs have been suggested as a possible reservoir for this fungus.[112]

Historically, *T. marneffei* infection in humans has been considered to be exclusively associated with acquired immunodeficiency syndrome (AIDS) caused by HIV infection.[105,113] In South-East Asian populations, penicilliosis is the third most common HIV-related opportunistic infection (after tuberculosis and cryptococcosis), with thousands of cases being reported from Thailand in particular.[105] Multilocus genotyping shows that *T. marneffei* isolates from humans are similar to those infecting rats and are in some cases identical,[114] thus strengthening speculations of zoonotic transmission of this fungus.

7. Fungal diseases and animal ownership in Nigeria

In the last few years, the interest in keeping of animals as pets has increased considerably in Nigeria and other resource-poor countries with a growing number of such pets co-habiting and feeding with their owners and members of their households in the majority of cases.[115,116] This is more common especially in the rural and peri-urban areas of many developing countries. Owing to such close interactions between pets and their owners and or household members, the possibility of transmission of zoonotic pathogens to humans, especially from pets that are asymptomatic carriers is high.[29,116]

According to Karesh et al.,[117] these animals can constitute either reservoirs or mechanical vectors of zoonotic fungal pathogens, thus their transmission may be direct or indirect. In most cases, many wild and domesticated animals (including their faeces and the soil in their burrows) play essential roles in maintaining these zoonotic infections in nature and contribute in varying degrees to the distribution and actual transmission of infection in human and animal populations.[118] This fact is corroborated by findings in Nigeria which show that enzootic dermatophytosis from domestic animals commonly causes sporadic disease among owners or caretakers of these animals or their children.[19,30] Additionally, a case of histoplasmosis in a Nigerian poultry farmer was reported after 6 months of treatment for tuberculosis with little or no improvement.[59] In this particular report, the occupational history and exposure to poultry roost were overlooked; this further points to the fact that fungi are yet to be considered as major causes of morbidity and mortality in humans, and possibly animals, in Nigeria.

8. Conclusion

Zoonotic fungal diseases constitute social and occupational hazards for humans that are exposed to and closely interact with infected animals. Contact with fungus-contaminated environments as well as objects of animal rearing and restraint are considered important in natural dissemination of these diseases. However, although the global burden of zoonotic fungal diseases is steadily increasing, the scientific and public health attention given to them in Nigeria is abysmally low. Apart from dermatophytoses which are prevalent among humans and animals in the country, many of these zoonotic fungal diseases are ‘neglected’ and thus may be misdiagnosed because of physicians’ and veterinarians’ lack of awareness and familiarity with them. Thus, there is a need to raise the level of awareness of zoonotic fungal diseases in Nigeria in order to better appreciate their burden and public health outcomes. Consequently, we advocate that they should be given priority attention by relevant animal and human health authorities through aggressive public enlightenment programmes and that the One-Health approach should be adopted to overcome the health challenge that they pose.

Moreover, routine screening of livestock animals and pets followed by commencement of anti-fungal treatment where an infection is detected could be very useful in reducing infection with these fungal pathogens and subsequent transmission from animals to humans. Adequate treatment of affected pets and their environments will thus help in the prevention of recurrence or new infections. In addition, it is advisable that pet owners in Nigeria take proper care of their animals as poor management has been reported to increase the number of infected pets.[119]

Furthermore, in view of the fact that pet animals, especially cats and dogs, may be the most susceptible to zoonotic mycoses, and might constitute the main source of human infections which are very difficult to treat,[120] it is imperative that studies be conducted on the prevalence and distribution of these diseases among pet animals and their owners in Nigeria. Considering the potential of zoonotic transmission of these diseases to humans especially occupationally exposed persons such as pet owners, veterinarians, herdsmen, agricultural workers, zoo keepers and horticulturists, there is a compelling need for continuous research into zoonotic mycoses in Nigeria using a combination of classical and molecular surveillance and diagnostic tools. These may include laboratory isolation and identification, polymerase chain reaction and sequencing to identify prevalent genotypes of these fungi in both human and animal populations. The findings of such studies will not only help to bridge the knowledge gap and increase awareness of these diseases among veterinarians, physicians and the general public, they will also provide a platform for the development of more effective prevention and control strategies against these zoonoses.

Conflict of interest

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