Incidences of *Aspergillus* sp infections in Brazil

Incidências de infecções por *Aspergillus* sp no Brasil

DOI: 10.55905/revconv.16n.12-004

Recebimento dos originais: 27/10/2023
Aceitação para publicação: 30/11/2023

**Felipe José Ferreira Gomes**
Master in Clinical and Environmental Pathology
Institution: Universidade Paulista
Address: São José dos Campos - SP, Brasil
E-mail: felipe.jogfer@gmail.com

**Rondinele Ribeiro Motta**
Specialist in Clinical Pathology
Institution: Universidade Paulista
Address: São José dos Campos - SP, Brasil
E-mail: rondinele.ribeiro@hotmail.com

**ABSTRACT**
The main objective of this research was to analyze the incidence of *Aspergillus* sp in Brazil, as well as to research the species that cause the most infections and the impacts caused by fungi on Brazilian humanity. This is an exploratory descriptive research from reviews and bibliographic research in scientific articles from the database Scientific Electronic Library Online - Scielo, in the periods 2013 to 2023; Given the above, the need arose to research this subject from the questions: What are the incidences of infections caused by *Aspergillus* sp in immunosuppressed patients in Brazil? And which fungal species cause more infections? In which Brazilian population? The dissemination of these infections is due to the ingestion of contaminated food, produced without observations as to Good Agricultural Practices (GAP), affecting immunosuppressed patients, senile and hospitalized patients, causing serious neoplasms in humans, by these mycotoxin-emitting fungi, triggering aspergillosis, responsible for major complications in Brazil, and the most affected human organs are the lungs, heart, kidneys, gastrointestinal tract, liver, etc. The *A. flavus*, *A. brasiilienses* and *A. fusarium* are the ones that most affect the essential organs and the Brazilian population, especially the lung, which is responsible for serious neoplasms, leading to death in a few days.

**Keywords:** *Aspergillus*, fungal infections, aspergillosis.

**RESUMO**
O objetivo principal desta pesquisa foi analisar a incidência de *Aspergillus* sp no Brasil, bem como pesquisar as espécies que mais causam infecções e os impactos causados pelos fungos na humanidade brasileira. Trata-se de uma pesquisa descritiva exploratória a partir de revisões e pesquisas bibliográficas em artigos científicos da base de dados Scientific Electronic Library Online - Scielo, nos períodos de 2013 a 2023; Diante do exposto, surgiu a necessidade de pesquisar este tema a partir das questões: Quais são as incidências de infecções causadas por...
Aspergillus sp em pacientes imunossuprimidos no Brasil? E quais espécies de fungos causam mais infecções? Em qual população brasileira? A disseminação dessas infecções se deve à ingestão de alimentos contaminados, produzidos sem observações quanto às Boas Práticas Agrícolas (BPA), afetando pacientes imunodeprimidos, senis e hospitalizados, causando neoplasias graves em humanos, por esses fungos emissores de micotoxinas, desencadeando a aspergilose, responsável por grandes complicações no Brasil, sendo que os órgãos humanos mais afetados são os pulmões, o coração, os rins, o trato gastrointestinal, o fígado etc. Os A. flavus, A. brasilienses e A. fusarium são os que mais afetam os órgãos essenciais e a população brasileira, principalmente o pulmão, responsável por neoplasias graves, levando à morte em poucos dias.

**Palavras-chave:** Aspergillus, infecções fúngicas, aspergilose.

1 INTRODUCTION

The fungi Aspergillus sp, are opportunistic classes, which in most cases generates respiratory infections, so the fungi of the genus are characterized by their filaments with hyaline hyphae, septa and branch at an acute angle and differentiate into reproductive structures called conidia, there are six types of species causing major infections are they: A. flavus; A. Niger; A. nidulans; A. terreus; A. fumigatus; A. fusarium. The most aggravating mycotoxins and the most worrying Aspergillus sp are those that release the aflatoxins B1; B2 and the Ochratoxin A, respectively produced by A. flavus; A. fumigattus; A. brasilienses; A. funsarium, are the four most worrying for the Brazilian health. Aflatoxin B1 possess high ionization chemical instability, being a potent cause of chronic intoxication with the first symptoms of fever, fatigue, pain in the abdominal region, lack of appetite, allergic manifestations, skin aspergillosis, fungal endocarditis, cerebral aspergillosis, among other pathologies. [1]

The Aspergillus sp, has wide distribution in nature and is responsible for serious infections, its contagion occurs by airborne route, and the immunosuppressed patients are the most compromised, such as HIV carriers, prolonged neutropenia and primary immunodeficiency and lung and bone marrow transplanted, complicating the picture of immunosuppressed patients, the worsening can lead to death in a few hours, at this point before the above, in this main point then arose the great need to research the subject from the question: Among these species, the one that causes more infections are Aspergillus flavus and Aspergillus fumigatus, being responsible for 90% of them. Therefore, the objective of this literature review work is to analyze the incidence of aspergillosis in Brazil and the impacts caused by Aspergillus sp fungi in
immunocompromised patients in Brazil shows about 51% of Brazilian humans infected with HIV virus; 25.43% with Hepatitis A, B, C; 8.8% of patients undergoing hemodialysis in Brazil commonly also patients with comorbidities, cancer patients about 16.56% of the Brazilian population, about 18% immunosuppressed in general genetic or acquired aspects being serious rates of immunosuppressed patients in Brazil, showing to have only 78.6% healthy.

The Brazilian population, and of this percentage 45% are rates of people over 55 to 60 years, according to data from (IBGE,2022).[2]

Below are the percentages of the Brazilian population that are Immunosuppressed; Healthy and Senile in chart 1 below:

Graph1. Total percentage of immunosuppressed, senile, and healthy Brazilian population.

Source: Prepared by the author, 2023

2 METHODOLOGY

This work was carried out using the knowledge of scientific research that has as one of its principles to conceive north to the daily experience, requiring, therefore, skills regarding the rigor of planning, knowledge and data collection of hospital articles of fungal infections. Thus, the importance of the literature review study is centered on the opportunity of deepening research that gives the opportunity to verify a certain subject, comparing it in time. Therefore, we chose to use the electronic database Scielo, using a time frame of 2013 to 2023. The articles were selected according to the following descriptors: Aspergillus; Fungal Infections; Aspergillosis.
3 RESULTS

3.1 WIDE URGENCY WITH ASPERGILLOSIS

Aspergillosis is necessarily invasive and acquired through inhalation of the spores, spreading, and as a result of ingestion of contaminated food, is rapidly disseminated to other organs. The toxins are accumulative and ionizing with low molecular weight. Recently published studies indicate a 40% to 90% mortality rate from Aspergillosis and a high chance of neoplasms. Aspergilloses constitute one of the largest silent infections, it also contributes to serious infections such as chronic obstructive pulmonary disease (COPD), with a high risk of cardiorespiratory arrest, and the high risk of cancer due to the high ionic rate and mortality related to the lack of cure and rapid diagnosis in the face of disease. [3]

3.2 INCIDENCE OF INFECTIONS BY ASPERGILLUS SP SPECIES

The main aflatoxins are B1, B2, G1 and G2, among which B1 is the one with the greatest toxigenic and carcinogenic power to humans, because its teratogenic and mutagenic properties are of great ionization of intracellular DNA chain, so in general clinical findings in Brazil it was found, among infections, persistent fevers in about 70.8% of the Brazilian population, 33.3% in radiographic images showed pleural effusion by Aspergillus fusarium and Aspergillus sp. The greatest concern is with infections by A. flavus, where it was found that about 47.50% of the population develop cancer when contaminated by this fungus and there were also histories of infections in nosocomial immunosuppressed patients. It has been found that 34.10% develop pneumonia due to Aspergillus fumigatus leading to pulmonary ephysema, 18.30% develop chronic obstructive pulmonary disease due to Aspergillus fusarium and 28.10%; fungal meningitis caused by Aspergillus brasilienses. About 120 cases of infections in Brazil occur in the lungs in immunosuppressed patients, with neutropenias, left shift, medullary compromises with probability of bone marrow transplantation without specific antifungal drugs to treat these fungi with mycotoxic load of neoplastic power. [4.5]

Among patients infected with Aspergillus, 7% to 20% are immunosuppressed and are on treatment with antifungals without specificity, of these patients, 1% to 15% develop pulmonary cystic fibrosis, in total 36% immunosuppressed. Of the fungi reported as invasive we have: Aspergillus fumigatus and Aspergillus nidulans, as Aspergillus flavus has a substance called aflatoxin B1, considered one of the most toxic substances ever produced by microscopic beings.
compared to the ionization power equal to that of a snake. In humans, aflatoxicosis, develops mycotoxin found in food products being produced by filamentous fungi and has been a major cause of nephrotoxic, hepatotoxic, teratogenic, carcinogenic, and because it has immunosuppressive properties, it can lead the individual to death. Thus, we can understand that on top of these percentages of infections we have healthy populations, immunosuppressed populations, and senile populations that also enter for future immunosuppressions, then based on this we establish the percentage according to the data from IBGE (Brazilian Institute of Geography and Statistics). In Brazil today, food contamination is becoming more and more of a problem, because together with the lack of control in public stores, there is a lack of control of fungal prevention, collection and evaluation of all bulk food points for microbiological analysis. [6,7]

Below is chart 2 for the better understanding of the incidences of Aspergillus sp infections, specific to each species of the genus Aspergillus sp:

Graph 2. Percentages of fungal infections by species and pathologies caused in immunosuppressed, senile and healthy patients.

![Graph 2](image)

Source: Prepared by the author, 2023

Already the aflatoxins B1, are under study, but it triggers serious risks to humans, being of the same family of toxin of fungi called Aspergillus flavus, excretor of a powerful mycotoxin called aflatoxins B1, obtained large rates of lung infections in acute form, The estimate is that it should manifest in up to 47% of the immunosuppressed Brazilian population and patients with acute myeloid leukemia, i.e., immunosuppressed patients aggravating the cancer to metastasis with infections by these fungi, knowing that the aggravation also occurs in healthy patients. According to the research and survey conducted in eight public hospitals in the country, Aspergillus fumigatus can proliferate in the lungs through different strategies, because of the
ability to escape the body's defenses and the main antifungal drugs, the azoles resulting in the excretion of high mycotoxins called Aflatoxins B2, about 34% of infections in immunosuppressed and healthy populations in Brazil. On the other hand the infection by Aspergillus brasilienses has been increasing, about 27% of immunosuppressed and senile patients have been suffering attacks of fungal infections, emitting a strong and chronic toxin called Ochratoxin A, inhibiting protein synthesis in the elderly, favoring early fading, and organ failure before the permitted life span. [8]

In addition, twelve clinical reports on cases of Aspergillus infection in immunosuppressed patients found in the database on the Scielo platform were surveyed. In table 1 below we can see the significant percentages in Brazil of their infections and pathologies triggered in the most affected senile and immunosuppressed populations:

Table 1. Clinical complication rate on Aspergillus species in Brazil.

<table>
<thead>
<tr>
<th>Genus and species</th>
<th>Clinical complications</th>
<th>Percentage of cases in the population Brazilian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspergillus sp</td>
<td>Persistent fevers</td>
<td>70,80%</td>
</tr>
<tr>
<td>A. flavus</td>
<td>Cancer</td>
<td>47,50%</td>
</tr>
<tr>
<td>A. fumigatus</td>
<td>Pneumonia</td>
<td>34,10%</td>
</tr>
<tr>
<td>A. Brasilienses</td>
<td>Fungal meningitis</td>
<td>28,30%</td>
</tr>
<tr>
<td>A. Fusarium</td>
<td>Renal failure and petechiae</td>
<td>18,30%</td>
</tr>
</tbody>
</table>


Thus we have assigned through much international research and international library bibliographies, the following most potent fungi and their definitions of pathologies developed after infection and contamination with the mycotoxins from each of the aspergillus sp species, we then describe each type of mycotoxin from their respective species and assign them to the diseases caused, following table 2 below:
Table 2. Major infections caused by mycotoxin factors genera and species.

<table>
<thead>
<tr>
<th>Gender and species</th>
<th>Mycotoxins</th>
<th>Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspergillus flavus</td>
<td>Aflatoxin B1 (hypercarcinogenic)</td>
<td>Necrosis; Renal insufficiency; Hepatocarcinogenic; Neoplasms; Renal necrosis.</td>
</tr>
<tr>
<td></td>
<td>Trichothecenes; Fungal acid; Fumonisins.</td>
<td>Hepatic, renal, cardiac hypertrophy, interstitial fibrosis of the testicle, estrogen-level effect, atrophy of the testicles and signs. In men they first affect the gastrointestinal tract and the oral cavity, giving a burning sensation in the mucous membranes; in the second phase appear leukopenia followed by fatigue, petechial hemorrhage of the skin, increased capillary fragility, appearance of necrosis of the throat, oral mucosa (contamination via oral, inhalation or food route).</td>
</tr>
<tr>
<td>Aspergillus nidulans</td>
<td>Sterigmatocystine (xanthine-coupled hydrophenobenzofuran ring)</td>
<td>It affects bile duct proliferation, nuclear pleomorphism, kidney necrosis, hemorrhage, and liver necrosis. It is also considered hepatocarcinogenic (alimentary route).</td>
</tr>
<tr>
<td>Aspergillus brasiliensis</td>
<td>Ochratoxin A</td>
<td>Ochratoxin A, in its contaminating action via the diet, passes into the blood in both animals and humans, and accumulates in various organs, such as the kidney, brain, reaching mainly the cerebellum. This toxin also produces an inhibition of protein and DNA synthesis (contamination via the diet).</td>
</tr>
<tr>
<td>Aspergillus fumigatus</td>
<td>Aflatoxins B2</td>
<td>Abortions; acute lung infections; necrosis of placentas in immunosuppressed patients, lungs, bones, eyes, cardiovascular system and central nervous system (via inhalation, ingestion of tap water and shower).</td>
</tr>
</tbody>
</table>


Knowing that the "Aflatoxins B1" is a concentrated toxin, known as the most carcinogenic natural agents due to its high hepatoxicity and its higher concentration in the substrate, having chemical structure that allows it to undergo bioactivation through p450 enzymes, further activating the mycotoxins, forming the major carcinogenic metabolites after bioactivation. Thus, "Fumosins, Fungary Acid and Trichothecenes", are the three substances that inhibit protein synthesis "RNA and DNA", inhibit mitosis and cell lysis. [9] Sterigmatocystin is usually causing acute or chronic diseases these effects can be carcinogenic, mutagenic, teratogenic, estrogenic, hemorrhagic, nephro and hepatotoxic, neurotoxic and/or immunosuppressive, depending on the metabolism, mycotoxins can undergo changes that are reflected in different forms and degrees of toxicity, mycotoxins will have a distinct influence on humans due to the multiple susceptibilities proper in each individual. Sterigmatocystin has a very similar structure to aflatoxin B1, since it is its biosynthetic precursor, thus to Ochratoxin A, as the phenylalanine substance, being the hydroxyl catalyzes the hydroxylation of phenylalanine into tyrosine, this toxin binds to plasma proteins causing the mycotoxins to remain in the blood, intoxicating the body, because they adhere to the tissue for a long period preventing the development of their
functions and normal maintenance of the body and cellular repair, causing organ failure in an accelerated time. [10,11]

Graph 3: Incidence of healthy humans compared to the percentage infected by Aspergillus sp according to the years.

Source: Prepared by the author, 2023

4 DISCUSSION

When an individual is infected with Aspergillus flavus, after 24 to 48 hours, aflatoxicosis is triggered, resulting in serious pathological problems such as necrosis, hemorrhages in the liver, proliferation of the bile duct, gastrointestinal hemorrhages, jaundice, and lethargy, in case of ingestion of large oleogenic grains, for example: Contaminated peanuts, pico grain, beans, corn, peas, etc; Could lead the individual to aflatoxicosis, leading the patient to liver cancer or lethal death, getting the fungi A. Flavus fungi have the ability to grow in moderate and high temperatures with low water activity, in this respect invasive pulmonary aspergillosis is now one of the main causes of death, as well as neoplasms. The fungi most responsible for the highest incidences of infections in Brazil are A. flavus; A. fumigatus; A. brasilienses; A.nidulans; A. funsarium, as shown in the figure of colonies and microscopy of the fungi of the genus Aspergillus spp, stained by lactophenol aman blue of the highest incidences of infections, demonstrated in figure 1 below:
However, antifungal therapies have been deficient by medical teams in patients with aspergillosis, neutropenic, with fever manifestation who do not respond to the use of broad spectrum antifungal drugs prescribed by physicians. Another factor, is that also the identification of the fungi is time consuming, as it depends on their growth in culture medium from 7 to 10 days. The most used antifungal drugs are "Amphotericin B and Vanconazole", about (68.8%).
The use of these having 45% efficacy only in patients outside the margin of immunosuppressed. [12,13]

Contamination by Aspergillus flavus through ingestion of contaminated oleogenic grains, allows the filamentous fungi to invade liver, kidney and endocrine tissues, where they perform mitoses there, produce and release aflatoxins constantly, consequently, will produce toxicogenic effects in the individual's organism, where after the first metabolism of passage through the liver, the formation of toxic active metabolites will occur, increasing the transformation of the toxic agent into a toxicogenic agent leaving its toxigenic power twice as powerful as pure aflatoxin. In this aspect, it is called an indirect contamination by toxin performing at all times the great blood circulation, damaging liver and kidneys by overload of toxicogenic agent and some days may occur kidney lesions by circulation of aflatoxin that binds to nucleic acids mainly DNA, where then occurs a covalent connection between the aflatoxin molecule and the mitochondrial DNA of the liver cell after the attack of millions of aflatoxins that are present in the bloodstream and hepatic portal vein and by itself located in the liver, with this connection mutations occur where they change the codons, DNA-dexoribonucleotide proteins, thus altering the DNA sequence.
With this altered sequence the cell totally changes its behavior, becoming a neoplastic cell, increasing its protein synthesis constantly with frequency and performing uncontrolled mitoses, causing liver cancer. Knowing that the major source of contamination to humans of Aspergillus sp is food, and the second source is hospitals and immunocompromised patients. Thus we have the fungus A. fumigatus; A. nodulans is nowadays the major cause of the main invasive pulmonary deaths and chronic fungal osteomelitis, knowing that the infections by Aspergillus spp still constitutes a great challenge for medicine, causing great impact in the Brazilian health.[14,15] The image below of pulmonary aspergillosis sp:

![Bronchopulmonary aspergillosis with bronchial parental spacing indicated by arrows](image)

Source: Torres PPTS et al., 2022/ Doenças fúngicas: sinais e padrões tomográficos.

In graph 1, it shows in red the healthy Brazilian population, over the percentages in blue of the immunosuppressed populations over the senile population that can be converted over time into the percentage of immunosuppressed, which are patients with chronic or acute comorbidities, hospitalized patients and patients with HIV, patients susceptible to nosocomial and urban fungal infections. Then in chart 2, we observe the screening of hospital and IBGE data surveys of fungal infections genus and specific species identified in each pathology by fungal contamination, we observed large infections by A. flavus 47.50% of infections, A. fumigatus 34.10% of infections; A brasilienses 28.30% of infections on 100% of the Brazilian population, affected.

We can follow the graph 3, noting in the years 2022 to 2023, the year after Covid-19, that humanity has gained an advance in healthy humans due to vaccines against Covid-19, even so we still do not escape the advances of fungal infections of Aspergillus sp, still showing small differences in the rates of healthy humans and humans with infections called aspergillosis, data
47.5% of humans with aspergiloses to 60% only of healthy humans, outside these rates of infections, only 12.5% the difference demonstrates of the two rates, awakening that the researches to take measures for larger studies in the creation of anti-aspergiloses vaccines or serums with therapeutic effects anti mycotoxins denominated aflatoxins B1, B1, Ochratoxins A, with objective of reduction and control of these fungal infections in Brazil. [16]

5 CONCLUSION

Therefore it must be emphasized that the main microbial source of primary fungal contamination comes from food to senile, immunosuppressed and healthy humans, the second source of contamination comes from immunosuppressed and senile intra-hospital nosocomial environments, thus knowing that Aspergillus flavus is one of the major first ranking fungal infections. However, its pathological causes are the most urgent and of great impact to patients with the infections, causing necrosis and invasive neoplasms in organs. It should be noted that Aspergillus furmigatuns has been the second in the ranking of systemic infections, fungal bronchitis and obstructive lung infections, and in the third place in the ranking of fungal infections is Aspergillus brasiilenses with its mycotoxins that adhere to the organs, gradually inducing physiological stops of the organs early. In this context, the indexes in the year 2023 can already alert the sanitary surveillance to a better inspection in food industries, the research of new and deeper studies for the possible creation of antimycotoxins serum and specific antifungals for these four most aggravating genera and species, as a therapeutic source against these pathologies and fungal infections by aspergillus sp in Brazil, which will motivate new researches, in Brazilian.

ACKNOWLEDGMENTS

We would like to thank the Paulista University - UNIP; Campus: São José dos Campos -SP; Brazil; for the support and the concession of the multidisciplinary laboratories II NB-2 for the execution of this great research.
REFERENCES


