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## A Review Study on The Effect of Fungi and Aflatoxin on Stem Cells

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#### ABSTRACT

Infection with pathogenic fungi, such as invasive *Aspergillosis*, remains a major infectious disease. Causes of death after transplantation of hematopoietic stem cells (HSCT), although a new antibody to bacteria has been present in recent years. The increase in deaths due to infection with fungi such as *Aspergillus* is mainly due to the difficulty of diagnosing invasive fungi in the early stages of development because laboratory tests require a combination of multiple procedures, low-quality tests and other surgical procedures in the case of detection of fungi. This study sheds light on Research that has dealt with focusing on the relationship between fungi and the toxins they produce, such as aflatoxin toxins, and the deaths that occur after stem cell transplantation in many patients who need this type of treatment. Shedding light on these studies can take a positive turn to saving the lives of many patients by discovering the reasons behind the occurrence of deaths after a stem cell transplant. It was found through the studies covered in this report that most of the antibodies in the blood of patients were Positive ring against fungi that were present in-patient samples such as sputum, blood, diuresis and other samples in addition to false positive rings, as well as negative rings, but at lower rates.

**Keyword:** Fungi, Aflatoxin, stem cell, *Aspergillus*

#### INTRODUCTION

Aflatoxins are a type of carcinogen and are secondary metabolites produced by a number of *Aspergillus flavus*-like *Aspergillus* <sup>(1)</sup>. The importance of these toxins lies because they can infect a group of economically important crops such as corn, tree nuts, nuts and peanuts, and they appear in the case of deteriorating discoloration and a foul odor that may be contaminated with aflatoxin, and these toxins are characterized by a very high acute toxicity. <sup>(2)</sup> There are many factors that can affect aflatoxin production during storage, such as temperature, oxygen availability, moisture,

and lipids. There are four types of aflatoxin (B1, B2, G1 and G2), and aflatoxin B1 is the most dangerous toxic type <sup>(3)</sup>. The distinction between aflatoxin and non-aflatoxin strains from the *Aspergillus* section has long been the subject of controversy <sup>(4)</sup>. Conventional methods used to detect aflatoxin are microbiological identification, high-performance liquid chromatography (HPLC), enzyme-linked immune-sorbent assay (ELISA) and thin layer chromatography. (TLC) These procedures are time consuming and are reliable techniques for detecting aflatoxins <sup>(5,6)</sup>. The polymerase chain reaction (PCR) is easy to

use, costly, fast and accurate. According to our simple knowledge, there is no report in Iraq regarding the use of real-time PCR as a diagnostic tool to differentiate the production of the different strains of isolated aflatoxins as well as the molecular assay and expression of aflatoxin-coding genes (*ver1*, *nor1*, and *aflR*)<sup>(7)</sup>. On the other hand, aflatoxins are broadly classified as a carcinogen by the International Agency for Research on Cancer (IARC)<sup>(8)</sup>. These toxins have many effects such as cytotoxicity, immunotoxicity and carcinogenicity, genotoxicity and hepatotoxicity,<sup>(9)</sup>. Thus, the present study aims to make a comparison to the studies that refer to the study of the cytotoxic effect of aflatoxin on the hematopoietic stem cells taken from the human umbilical cord and the detection of its toxic dose.<sup>(10,11)</sup>

## STEM CELL

A stem cell is a cell that has the ability to reproduce itself for long periods or the ability to renew itself at high levels and is characterized by the ability to generate distinct cell ancestors of different strains in agricultural conditions (*in vitro*) and after transplantation into the host tissue (*in vivo*). It also can develop into specialized cells that comprise tissues and organs of the body as embryonic cells (ESCs)<sup>(12,13)</sup>. The term “stem cell” can be found in botanical studies

documenting the regenerative competence of cells such as the plant meristem<sup>(13)</sup>.

These general definitions may suffice for embryonic stem cells. But this definition collapses when trying to distinguish between adult progenitor cells that have a low capacity for self-renewal and adult stem cells<sup>(14)</sup>. Therefore, it is important when adult stem cells are described that this definition be reduced to cells that self-renew and serve as a stockpile for regenerating damaged tissues or replacing short-lived cells<sup>(15)</sup>. For example, CSCs are a blood cell replacement center and are present at a frequency of 1 in 10,000 to 100,000 per blood cell<sup>(16)</sup>. Hematopoietic stem cells (HSCs) are the cells responsible for the formation of blood cells such as white and red blood cells and platelets<sup>(17)</sup>. At present, researchers have found through animal experiments that CSCs have some flexibility<sup>(18)</sup>. Moreover, this type of cell has the ability to undergo apoptosis<sup>(19)</sup>, in which spontaneous destruction of unnecessary cells occurs and, unfortunately, HSCs are difficult to recognize<sup>(20)</sup>.

## MATERIALS AND METHODS

The first step was to conduct an electronic search. For a body of research on the effect of aflatoxin mycotoxins on stem cells, I collected more than 20 articles on the effect of mycotoxins on stem cells. Various articles

on the diseases caused by fungi and the toxins they produce on this type of cells, in addition to the research that relied on HPLC and PCR, the detection of aflatoxin B1 from *Aspergillus flavus* strains and its cytotoxic effect on hematopoietic stem cells and the treatment AFB1 taken from the umbilical cord Human.

## RESULTS

**Study cohort characteristics** The total group of 173 patients, according to (22), was stimulated by a set of treatments, namely: Treatment for AML or MDS is high risk. Of these, there were 87 They were males with an average age of 54 years. It was a relapse of blood diseases It occurred in 27 patients, including 17 patients He was treated in our hospital during the first and second period Of their disease, adding an additional episode to the patient population. Which included the other ten patients with relapsing disease at the beginning were They are treated in another hospital and contribute only to the second A circle of study samples, as indicated by the researcher above (.), But none of these patients was diagnosed With invasive aspergillosis during the period of their first treatment ring. The treatment was recorded between 2005 and 2012. Show database That, before SCT, treatment with voriconazole and / or liposomal Amphotericin has been described as approximately 68 (36%) of those reported

Total patients. Prescribing fungicide medications for many reasons Other than treatment for IA, the following are included: Chemoprophylaxis For IA (n = 1), he also indicated that the experimental treatment was stopped (N = 4), and fungal infections other than IA (n = 1). From Of the remaining 62 episodes of the total patients with probable IA, approximately 18 were added to Patient group without an IA because IA has occurred and He was cured after SCT. The researcher also indicated that one patient with a possible IA died Before processing is complete and has been added to IA patient group. This resulted in 184 episodes (45 Where IA and 139 were diagnosed and without a diagnosis IA) included in the analyzes.

Studies indicate that the use of chemotherapy to treat patients whose stem cells were transplanted was one of the steps to prevent infection with fungi or being affected by toxins that may be produced by these fungi during their recovery periods, and the risk of death before transplantation was much higher during the period of transplantation of stem cells, It was found through examination of sputum samples and blood samples that several genera of fungi were obtained, ranging between *A. fumigatus* and *A. flavus*, which contains strains that produce mycotoxins, as shown in Table (1).

Table No. 1 shows the strains that produce mycotoxins and the genes responsible for producing the aflatoxin toxins <sup>(23)</sup>:

Aflatoxin genes			Isolate organ	Isolate No.
AfR	AfD	AfM		afR
+	+	-	Fishes	AFL1
+	+	+	Lung	AFL2
+	+	+	Spices	AFL3
+	+	+	nuts	AFL4
-	-	-	waste	AFL5
+	+	+	Corn	AFL6
+	+	+	oil	AFL7
+	+	+	Barley grain	AFL8
+	+	+	Wheat	AFL9
-	-	-	Milk	AFL10
+	+	+	Fruits	AFL11
+	+	+	Nuts	AFL12
-	-	-	Poultry lung	AFL13
+	+	+	Peanut seeds	AFL14

The diagnostic procedures included, as indicated by the researcher <sup>(21)</sup> samples of blood, sputum, and urine, and also included

other procedures such as x-rays, tomography, and chest and nose scans, especially for patients with clinical signs or



symptoms suggesting the existence of clinical suspicion of injuries during the stem cell transplantation process. In a tomography it cannot be Refused due to use of targeted or anti-fungal treatment Antifungal treatment for other fungal infections. The researcher indicated that a total of 3296 serum samples from 157 patients were analyzed Overall, 50 patients (31.9%) showed genetically positive blood antigens An average of 107 days With a one-year cumulative incidence of 32.2%. While Five of the patients had second positive episodes with an average interval 358 days between the first and the second Episodes. Four positive attacks occurred in one patient. So my total was 58 positive episodes, Plus seven were considered positive and inconclusive. In all seven episodes, the searcher was unable to conclude if it was Abnormalities in CT are attributable to IA in specimens that did not contain piperacillin / tazobactam or amoxicillin / clavulanate treatments and which were not administered to antigen-positive In general, it can be said that fungi and the toxins they produce have negative effects on stem cells in the transplantation or post-transplant stage, which may cause a relapse in the patient, especially in people with weak immunity or who complain of various cancers.

## **DISCUSSION**

This study showed, according to previous studies, that fungi and mycotoxins produced by them can be a major reason for the failure of the transplantation of stem cells in patients. It was comparable with the reports referred to in the above study, as it was found, according to previous studies, a group of false positive and positive antigens that have clear indications of occurrence A statistically significant correlation between the occurrence of a pseudo-positive antigen of genetically modified blood and a false positive in most of the previous studies and there was another false positive episode in which GVHD was found absent upon detection of genetically modified positive blood antigens, and it included the occurrence of such cases in a case not given. Other anti-fungal and anti-fungal treatments include piperacillin / tazobactam or amoxicillin / clavulanate in addition to the occurrence of a range of infections and reactions that were only mildly mentioned in such studies, and both are treated as risk factors that may cause relapse of the stem cell transplantation process In the sick.

**Conflict of Interest – Nil**

**Source of Funding- Self**

**Ethical Clearance – Not required**

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