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ORIGINAL ARTICLE

Clinical spectrum of fusariosis from a tertiary care center in India- a retrospective study

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ABSTRACT

Background and Objectives: *Fusarium* spp. is an emerging pathogen that presents with varied clinical presentations but there are very few studies from India that elaborate on the spectrum of infection caused by the fungus. Hence, the present study was conducted in our institute to understand the clinical spectrum of fusariosis.

Materials and Methods: The present study was a retrospective study conducted at a tertiary care institute, in Hyderabad, Telangana, India for four years from January 2018 to December 2022. All the patients with clinically significant isolation of *Fusarium* spp. from various samples were included in the study.

Results: There were 25 cases of fusariosis diagnosed during the study period. *Fusarium* was isolated predominantly from debrided tissue following road traffic accidents in 12/25 (84%) of the cases, nails in 3/25 (12%) and superficial leg ulcer in 1/25 (4%) of the cases. Speciation was done for four patients. Three were *Fusarium incarnatum* and one was *Fusarium solani*. The patients were treated surgically and with/without antifungal therapy and were discharged in a stable condition.

Conclusion: Traumatic injuries were the major cause of infections in the present study. As *Fusarium* is a virulent and highly resistant pathogen, an early suspicion and an appropriate diagnosis would lead to a better outcome in these patients.

Keywords: Traffic accidents; *Fusarium*; Voriconazole

INTRODUCTION

Fusarium spp. is an emerging fungal infection that is commonly found in the environment (1). There are 300 different species of *Fusarium* and the species causing disease in humans are grouped into seven complexes of which *Fusarium solani* complex is the most common cause of infection (2).

Fusarium is one of the most virulent species and with the ability to produce mycotoxins may cause tissue damage. Macrophages and neutrophils play an important role in defense against fungal infections and this explains the reason for disseminated infections in mmunocompromised individuals (3). The portal of entry of the species in humans is the airway, tissue at the site of breakdown, gastrointestinal tract, and central venous catheters (4). Trauma is the key predisposing factor to *Fusarium* infection (5).

The spectrum of infection ranges from superficial, locally invasive lesions in immunocompetent hosts to disseminated infections in immunocompromised individuals (1). Keratitis and onychomycosis are frequent infections caused by *Fusarium* spp. (6). Other infections include sinusitis, pneumonia, endophthalmitis, cellulitis, fungemia, and disseminated infections (3, 4, 7). It is one of the frequent molds isolated from post-traumatic invasive fungal infection (IFI) in military injuries, next to *Mucorales* and *Aspergil-*

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lus spp. (8, 9). However, there are only a few reports of infection due to *Fusarium* in civilian injuries (10, 11).

The infections caused by *Fusarium* spp. present with varied clinical presentations, but there are very few studies from India (12, 13) that elaborate on the spectrum of infection caused by the fungus. Hence, the present study was conducted in our institute, to study the clinical spectrum of fusariosis in all the patients whose culture showed growth of *Fusarium* spp.

MATERIALS AND METHODS

The present study was a retrospective study conducted at a tertiary care institute, in Hyderabad, Telangana, India for four years from January 2018 to December 2022.

Inclusion criteria. All the patients with clinically significant isolation of *Fusarium* spp. from various samples like tissue and nails were included in the study.

Exclusion criteria. All the patients whose sample did not show growth of *Fusarium* spp. in culture were excluded from the study.

Data regarding epidemiology, clinical presentation, risk factors, microbiological findings, management, and outcome of the patients were collected retrospectively from medical records.

Microbiological work up. Samples were subjected to direct examination by KOH, calcofluor white stain, and were inoculated on Sabouraud's dextrose agar and incubated at 30°C for 48 h (14). Phenotypic identification of *Fusarium* was done based on macroscopy and microscopic examination. For morphological identification, the isolates were sub-cultured on potato dextrose agar. The colonies were identified based on macroscopy and pigment production.

Microscopic identification of the isolates was done by slide culture on potato dextrose agar where the shape of the macroconidia; presence or absence of microconidia; shape and mode of formation of microconidia; nature of the conidiogenous cell bearing microconidia; and presence or absence of chlamydospores were taken into consideration.

The isolates were sent to the National Culture Collection for Pathogenic Fungi (NCCPF), PGIMER, Chandigarh, India for species identification. The species were identified phenotypically by slide culture.

Statistical analysis. Descriptive statistics were used for analysis. Categorical data were described as frequencies with percentages. The data were entered into a Microsoft Excel sheet and analyzed using SPSS version 20.0.

RESULTS

There were 25 cases of fusariosis diagnosed during the study period. The male-to-female ratio is 1.7:1(16 males, 9 females). Most of the patients were in the age group of 21-30 years (Table 1).

In the present study, 15/25 (60%) of the patients were immunocompetent. Nine (36%) patients had diabetes mellitus. One patient (4%) had systemic lupus erythematosus (SLE) and was on treatment.

Fusarium was isolated predominantly from debrided tissue from the limbs following road traffic accidents (RTA) in 12/25 (48%) of the cases followed by nails in 3/25 (12%) and superficial leg ulcer in 1/25 (4%) of the cases. The clinical diagnosis of the patient with Fusariosis is given in Table 2.

Table 1. Demographic data of the patients

S. No	Age group in years	No of patients	Percentage
1	0-10	0	0
2	11-20	1	4
3	21-30	8	32
4	31-40	7	28
5	41-50	3	12
6	51-60	4	16
7	61-70	2	8

Direct microscopy showed septate hyphae in all the samples. Culture on Sabouraud's dextrose agar showed growth of *Fusarium* spp. after 48-72 hours of incubation. Colonies are usually fast-growing, pale, or bright-colored (depending on the species) with or without a cottony aerial mycelium. The color of the thallus varies from whitish to yellow, pink, red, or purple shades (Fig. 1). Lacto phenol cotton blue mount (Microscopy) of the slide culture of *Fusarium* spp. showed both macro- and microconidia from slender phialides (Fig. 2). Speciation was done for four pa-

Table 2. Clinical diagnosis of the patient with fusariosis

S.No	Clinical diagnosis	No of patients	Samples	Percentage
1	Traumatic (RTA) injuries	21	Debrided Tissue from the injury site	84%
	Compound fracture	3		
	Avulsion, crush injury	18		
2	Onychomycosis(DM)	3	Nail	12%
3	Superficial ulcer(SLE)	1	Biopsy from skin ulcer of leg	4%

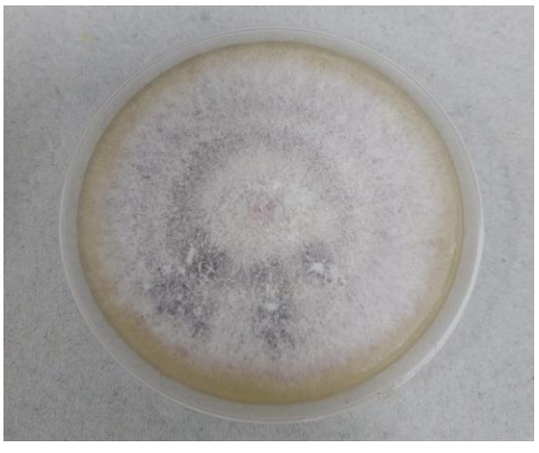

Fig. 1. Culture on Sabouraud's dextrose agar showing white to purple colonies of *Fusarium* spp.

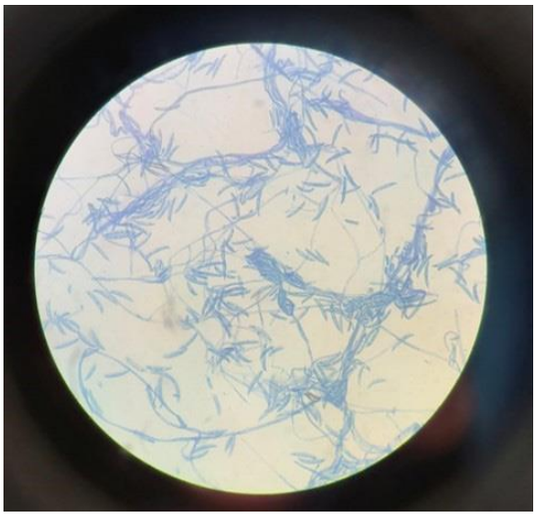

Fig. 2. Lactophenol cotton blue mount showing multiseptate macroconidia of *Fusarium* spp.

tients of RTA of which three were *F. incarnatum* and one was *F. solani.*

The patients were treated surgically and with antifungal therapy (Table 3). Twenty two patients (88%) were treated with both surgical and antifungal therapy, two patients were (8%) treated only surgically and antifungal therapy alone was given in one (4%) patient. All the patients improved clinically and were discharged in stable condition.

DISCUSSION

Fusarium spp. is the second most common cause of invasive mold infection in immunocompromised patients causing disseminated disease (15). The majority of the infections occur in patients with hematological malignancy (3, 6, 15, 16). Fusarium infections are considered rare in immunocompetent individuals (17, 18). In a large review of cutaneous infections caused by fusariosis, only 10% of the patients were immunocompetent (15). But, in a study from Israel 76% of the patients were immunocompetent (19). In the present study, 60% of the patients were immunocompetent.

Fusarium spp. is the third common cause of post-traumatic IFI in military patients (9). Trauma affects the immune system and also impairs the phagocytic function. Following traumatic injuries, the fungus gets inoculated at the site of injury, leading to angioinvasion and tissue necrosis (8). In civilian injuries, the common cause of fungal infection is the contamination of wounds with soil and plant material. Also, underlying conditions such as old age and diabetes will add to the risk of developing invasive infections (9). There were few reports of fusarium infections after RTA, a case of partial flap failure after RTA due to *Fusarium* spp. (10) and necrotizing skin and soft tissue infection due to *Syncephalastrum* species and *Fusarium solani* species complex following open tibia fracture (11). There were 11 cases of Fusarial osteomyelitis reported till now in the literature, of which there was only one case of *Fusarium solani* osteomyelitis after a motorcycle accident and its nosocomial spread to another patient with a similar injury (20). In the present study majority (84%) of

Table 3. Treatment of patients with Fusariosis

S. No	Diagnosis	Treatment	No of patients	Percentage
1	Traumatic (RTA) injuries	Debridement+ Antifungal therapy(Voriconazole)	12	48
		Debridement+ Flap/External fixation	7	28
		Amputation	2	8
2	Onychomycosis	Nail removal + Antifungal therapy(Itraconazole)	3	12
3	Superficial ulcer of the leg	Antifungal therapy(Voriconazole)	1	4

the cases were traumatic injuries following RTA and of them only two patients were diabetics. Necrotic tissue sent immediately after admission from these patients showed growth of *Fusarium* spp.

Onychomycosis is one of the common superficial fungal infections caused by *Fusarium* spp. Diabetes mellitus is one of the predisposing factors of onychomycosis (12). In a review of the onychomycosis cases caused by the *Fusarium* spp. from January 1997 to January 2021, it was found that the toenail was the common site of infection in 46.5% of cases and 28.5% of the cases had diabetes mellitus (21). In a study from Brazil around 90% of cases were Fusarial onychomycosis (6). In the present study, there were three cases of toenail onychomycosis and all of them were diabetics.

Skin lesions are one of the frequent lesions caused by *Fusarium* spp. in immunocompetent and immunocompromised individuals. In a review of 259 cases of cutaneous lesions, the lesions were slowly progressive and preceded by skin breakdown in immunocompetent, but were rapidly progressive without any preceding injury in immunocompromised individuals (15). There are case reports of leg ulcers (17) and lip ulcer (18) with *Fusarium* spp. In the present study, *Fusarium* spp. was isolated from a leg ulcer biopsy in a SLE patient. It was a non-healing ulcer of chronic duration without any recent injury. The ulcer was treated successfully and there was no dissemination.

F. solani complex is the most common cause of infection followed by *F. oxysporum* (2, 7). In the present study, speciation was done for four isolates. *F. incarnatum* was isolated in three patients, and *F. solani* in only one patient. The predominant species could not be determined because the other *Fusarium* isolates were not speciated.

Fusarium spp. shows less susceptibility to antifungal drugs and the susceptibility differs depending on the species isolated (22, 23). *F. solani* complex had shown pan-azole resistance and other species show a wide range of MICs when tested against other azoles and amphotericin B (24). Resistance in *Fusarium* may be due to exposure to antifungal agents used in agriculture (23). In the present study, antifungal susceptibility testing (AFST) was not done.

Treatment of localized disease involves surgical debridement and systemic antifungal therapy to prevent invasive disease. A combination of voriconazole and lipid formulation of amphotericin B can be used in treatment. In immunocompromised individuals, reversal of immunosuppression would be helpful (24). The duration of treatment depends on an individual basis depending on the clinical response (25). In the present study, as the majority (84%) of the patients were cases of traumatic injuries, treatment involved surgical debridement and amputation with/without antifungal therapy with voriconazole. Onychomycosis should be treated carefully with systemic antifungal therapy with voriconazole /itraconazole (26) or else it may lead to disseminated infection in immunocompromised patients (27). In the present study, the patients were treated with itraconazole and removal of the nail. The SLE patient with a superficial ulcer was treated with voriconazole.

The mortality of invasive fusariosis ranges from 50-70% in immunocompromised individuals (16). In immunocompetent individuals, as most infections are superficial the mortality is less (15). However in traumatic injuries, if not treated properly, it may lead to invasive fungal infection. The overall mortality in civilian trauma ranges from 25-41% (9). There was no mortality in the present study as in our institute, the samples from traumatic injuries would be routinely sent for fungal cultures which helped us in early diagnosis and initiation of immediate treatment. Also, most of our patients were immunocompetent. They were treated both surgically and with antifungal therapy.

To the best of our knowledge, the present study highlights the highest number of post-traumatic infections caused by *Fusarium* spp. after RTA.

Limitations. In the present study, speciation could not be done for all the *Fusarium* isolates, and antifungal susceptibility testing was not done. As there were no ophthalmology and ENT departments in our institute the cases of sinusitis and keratitis were not reported. The sample size is also small and hence conducting studies with larger sample sizes would provide a better understanding of the infection.

CONCLUSION

In the present study, fusariosis was seen in the majority of post-traumatic patients. Hence in traumatic injuries, the samples can be routinely sent for fungal cultures which would help in early diagnosis and prevent the delay in treatment. Early initiation of therapy in these patients improves the survival rate in the patients. If the infections are not diagnosed and treated appropriately, the localized infections may lead to disseminated infections causing increased mortality. As *Fusarium* is a virulent and highly resistant pathogen, an early suspicion along with an appropriate diagnosis would lead to a better outcome in these patients.

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