International Journal of Dermatology, Venereology and Leprosy Sciences

E-ISSN: 2664-942X
P-ISSN: 2664-9411
www.dermatologypaper.com
Derma 2019; 2(2): 35-43
Received: 05-05-2019
Accepted: 08-07-2019

Dr. Pranshu Mishra
Assistant Professor, Department of Dermatology Prasad Institute of Medical Sciences, Lucknow, Uttar Pradesh, India

Dr. Neeraj Kumar Mishra
Assistant Professor, Department of Surgery Mayo Institute of Medical Sciences, Lucknow, Uttar Pradesh, India

Corresponding Author:
Dr. Pranshu Mishra
Assistant Professor, Department of Dermatology Prasad Institute of Medical Sciences, Lucknow, Uttar Pradesh, India

Role of fungal infection in burn wounds influencing the morbidity and the mortality in burn patients

Dr. Pranshu Mishra and Dr. Neeraj Kumar Mishra

DOI: https://doi.org/10.33545/26649411.2019.v2.i2b.81

Abstract

Background: The burn wound represents a susceptible site for opportunistic colonization by organisms of endogenous and exogenous origin. Fungal wound infection is a leading cause of burn wound infections. Most of the fungal infections are missed owing to lack of clinical awareness and similar presentation as bacterial infection coupled with paucity of mycology laboratories. Expedient diagnosis and treatment of these mycoses can be life-saving as the mortality is otherwise very high.
Objective: To study the incidence and type of fungal infection in burn patient and to evaluate its role in morbidity and mortality of burn patients.
Method: This was an institution-based, prospective, non-randomized study. Skin swabs were collected from 50 patients who were admitted under department surgery with >15% burn surface area. Patients below 18 years and those with any systemic comorbidities were excluded.
Results: Of total 50 patients 28 cases (56%) were positive for fungal elements, total negative cases were 22. GMS stain and 10% KOH stain (Smear test) were positive in 25 patients and culture was positive in 23 cases out of 56% of total positive cases, 33.33% were in 15-29% TBSA group, 66.7% were in 30-59% TBSA group and 78.6% were in 60% or above TBSA group. This showed a clear increase in fungal positive cases with increase of total body surface area involvement. Candida fungi were seen in the greatest fraction of patients (60.7%), Mucor-like in the smallest fraction (7%), and Aspergillus-like in an intermediate fraction (21.4%). There was higher observed mortality with deeper fungal involvement.
Conclusion: This study showed that fungal infection influenced mortality and morbidity of burn patients. Also mortality due to fungal infection in these patients was significantly associated with Total body surface area (TBSA %) of burn and age of patient.

Keywords: fungal infection, burn, burn intensive care, burn morbidity, mortality

Introduction

Burn wound infection (BWI) is a major public health problem and globally the most devastating form of trauma [1]. Infection is the leading cause of morbidity and mortality in burns and remains one of the most challenging concerns in the management of burn patients. Fungal wound colonization with the possibility of invasive infection is a probability in burn patients, in view of use of antibiotics for prolonged periods and immunosuppression associated with burn injury [2].

BWI is primarily caused by bacteria (70%) followed by fungi (20–25%), anaerobic and virus (5–10%). Fungi cause BWI as part of monomicrobial or polymicrobial infection, fungaemia, rare aggressive soft tissue infection and as opportunistic infections [3].

Consequent to the availability of topical and systemic antimicrobial agents in 1960s, near eradication of universal BWI was witnessed. Subsequently, emergence of fungal infections in burn wound patients was seen [1, 3].

The omnipresence of fungi in environment coupled with suppression of normal bacterial flora promotes fungal super infection in these patients.

Though burn constitutes an important and independent risk factor for invasive fungal infection, most of the infections are misdiagnosed due to lack of clinical awareness and similar presentation as bacterial infection coupled with paucity of mycology laboratories.

Nonetheless, early diagnosis and treatment of these mycoses can be life-saving as the mortality is otherwise very high [4, 5, 6].

In the developing countries, the scenario with regard to BWI is grim owing to lack of surveillance laboratories and dearth of well-equipped burn centres. Consequently, the clinical data pertaining to fungal BWI are scarce [5]. There is worldwide decrease in bacterial infections due to better care of burn patients and availability of effective antibiotics. Consequently, the fungal BWI has shown an increasing trend [7-12].

Traditionally, burn area and patient´s age have been employed as the primary predictors of mortality after thermal injury. Other factors identified during the course of hospitalization also may help to predict accurately those patients who are likely to die [13].

Thus, it seems unlikely that mathematical models based solely on these two, or on any other two indices of burn mortality, can fully describe this complex problem. Clinical research pertaining to fungal infection has largely been a neglected area in India.

The purpose of this study is to determine the fungal profile in burn wounds and to evaluate the role of fungal infections in morbidity and mortality of burn patients.

Materials and Method

This was an institution-based, prospective, non-randomized study. Skin swabs were collected from 50 patients who were admitted under department surgery with >15% burn surface area.

The following patients were excluded from the study population

a) Those patients who did not give consent to take part in the study
b) Patients with
- Uncontrolled Diabetes Mellitus
- HIV and other co morbid illness
- Patients admitted and treated initially outside & referred later,
- Patients less than 18 years of age,
- Electric or chemical injuries, or with no burn skin diseases,
- Pregnant females.

Parameters studied

a) Age
b) Sex
c) Percentage of total body surface area involved
d) Duration of burn
e) Nature of burn -superficial and deep
f) Sequential burn wound inspection

Study tools

a) History of illness
b) Clinical examination
c) Routine Investigations
d) Wound swab and biopsy from lesions for:
- Gram staining, Gomori Methenamine Silver (GMS) staining & KOH preparations
- Fungal culture media like SDA, SDACC, BHI Agar, BHI Broth.

All the patients with burn >15% of total body surface area admitted in our casualty burn ward were subjected to a detailed history using a structured questionnaire and examined clinically.

a) Baseline investigations of the patients were done which included Hb, TLC, DLC, ESR, platelet count, Na+/K+, random blood sugar, urea, creatinine, total protein / Albumin / Globulin, A:G ratio, ECG, chest X ray.
b) Swabs and biopsies were taken from various burn wound sites at the time of admission and also on day 8th, 15th and 21st respectively.
c) Blood samples were taken from the burn patients at the time of admission.

Results and Analysis

This study was conducted on 50 patients admitted in Burn ward of Department of Surgery. 50 burn patients met inclusion criteria for analysis from whom swabs and biopsies were taken from various burn wound sites at the time of admission and also on day 8th, 15th and 21st respectively.

Specimens in which fungal elements were observed on KOH mount or Gram’s stain or GMS stain were further confirmed by histopathological examination by using periodic acid Schiff’s stain and culture on various Mycological media.

Table 1: Total number of Fungus positive cases

Total no. of cases	No. of positive cases	No. of negative cases	Percentage of positive cases (%)
50	28	22	56

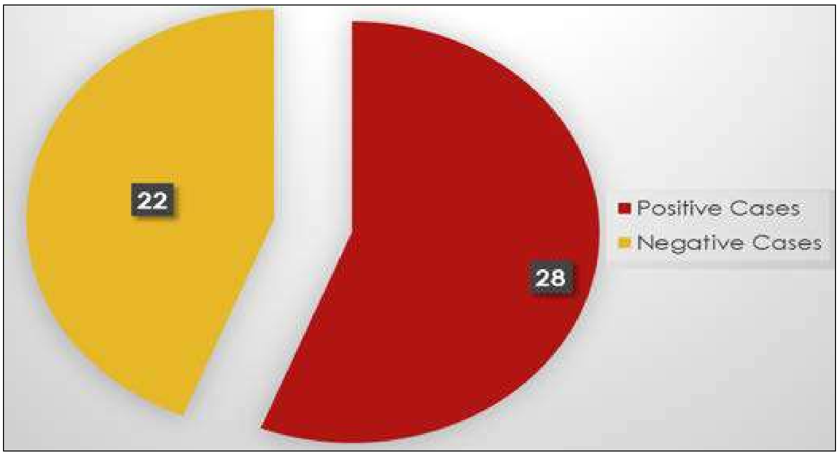

Chart 1: Pie chart showing fungal positive and negative cases

Table 2: Outcome of investigations in patients with clinically suspected fungal colonization

	Culture Positive	Culture Negative	Total No. of patients
Smear Positive (KOH, GMS)	20	05	25
Smear Negative	03	22	25
Total	23	27	50

Table 1 &2 shows that out of total 50 patients 28 cases were positive for fungal elements, total negative cases were 22. GMS stain and 10% KOH stain (Smear test) were positive in 25 patients and showed 89% sensitivity{(25/28) x 100}and 81% specificity while culture was positive in 23 cases & showed sensitivity of 82% {(23/28) x 100}& specificity approximately 90%. Thus smear tests showed acceptable sensitivity and specificity comparable to culture test. This contingency table shows corelation between smear and culture, on calculation of Chi Square test = 23.27. P value for this contingency table is .0001 (highly significant) it means culture positivity and smear positivity are positively co-related and the co-relation is statistically significant. Therefore smear test alone can be used to establish early diagnosis of fungal wound infections reliably.

Table 3: Fungal positivity in relation to total burn surface area (%)

TBSA%	Total No. of Patients	Total No. of positive Patients (%)
15-29	21	07 (33.3%)
30-59	15	10 (66.7%)
>60	14	11 (78.6%)
Total	50	28 (56%)

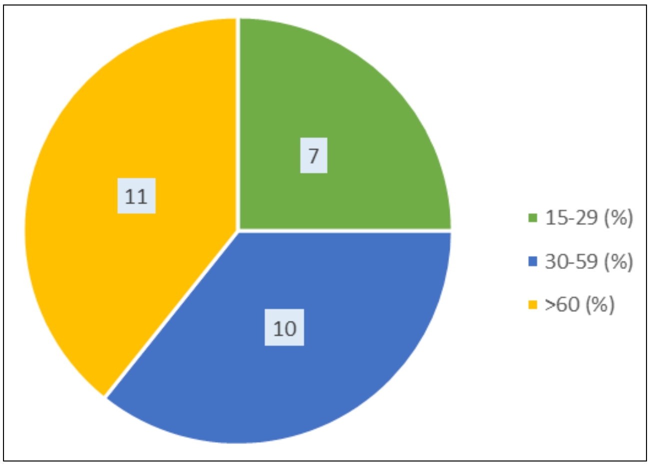

Chart 2: Pie chart showing relation between in TBSA% and fungal positive cases

Total 50 cases were further divided in 3 groups as per the total body surface area of burn as 15-29%, 30-59% and 60% or more. 56% of total cases were found to be positive for fungal elements of which 33.33% were in 15-29% TBSA group, 66.7% were in 30-59% TBSA group and 78.6% were in 60% or above TBSA group. This showed a clear increase in fungal positive cases with increase of total body surface involvement. P value was 0.01% (statistically significant). So significant association was present.

Table 4: Incidence of fungal positivity in relation to sex of the patients

Sex	No. of cases	Positive cases	Percentage of positive
Male	19	11	57.9%
Female	31	17	54.8%

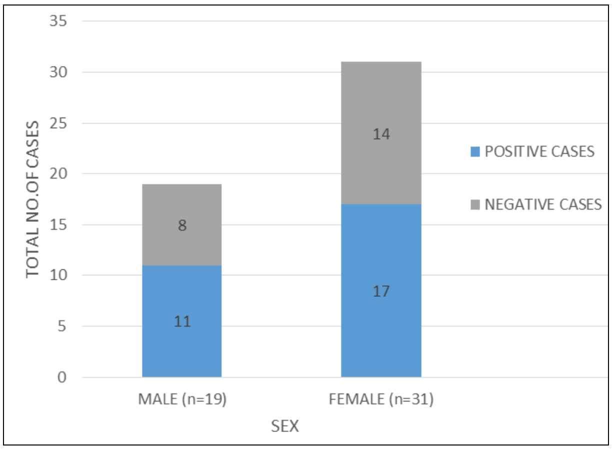

Chart 3: Chart showing incidence of fungal positivity in relation to sex of the patients

Out of total 50 cases 19 cases were male and 31 cases were female. Total number of male patients tested positive for fungal elements were 11(57.9%) and total number of female patients positive for fungal elements were 17(54.8%).This showed that incidence of fungal positivity was approximately similar in both sexes. P value was 0.7823 (non-significant). Thus no significant association was present.

Table 5: Incidence of fungal positivity in relation to age group

Age (years)	No. of cases	Infected	Percentage (%)
18-29	09	03	33.3%
30-39	11	06	54.5%
40-49	12	07	58.3%
50-59	11	07	63.6%
>60	07	05	71%
Total	50	28	56%

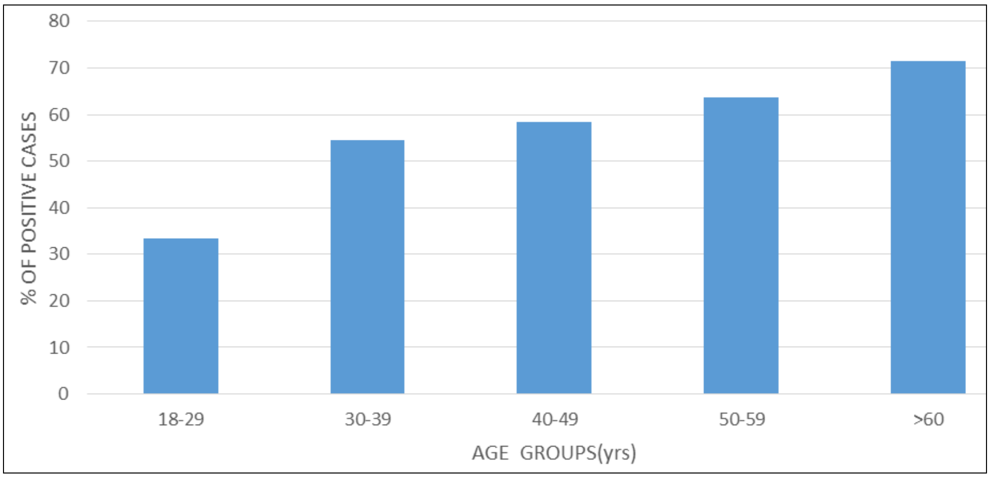

Chart 4: showing incidence of fungal positivity in relation to age groups

Of the total 56% of infected cases 33.3% were in the age group of 18-29 years, 54% cases in age group 30-39 yrs, 58.3% cases in age group 40-49 yrs, 63.6% cases were in age group 50-59 yrs and 71.4% cases were in age group 60yrs or more. Thus showing a clear trend of increasing fungal positivity with increase in age. Each patient's fungal-status category was defined according to the deepest level of fungal involvement observed during the hospital course: no fungus (22 patients), fungal wound colonization (FWC, 16 patients), or fungal wound infection (FWI, 12 patients).

Table 6: Numbers of Patients and Observed Values in Relation to Fungal-Status Category in 3 TBS Group

TBS Groups (%)	No Fungus	FWC	FWI	Row Total
15-29	14 (63.6%)	04 (25%)	03 (25%)	21
30-59	05 (22.7%)	06 (37.5%)	04 (33.3%)	15
>60	03 (13.6%)	06 (37.5%)	05 (41.7%)	14
Column Total	22 (44%)	16 (32%)	12 (24%)	50

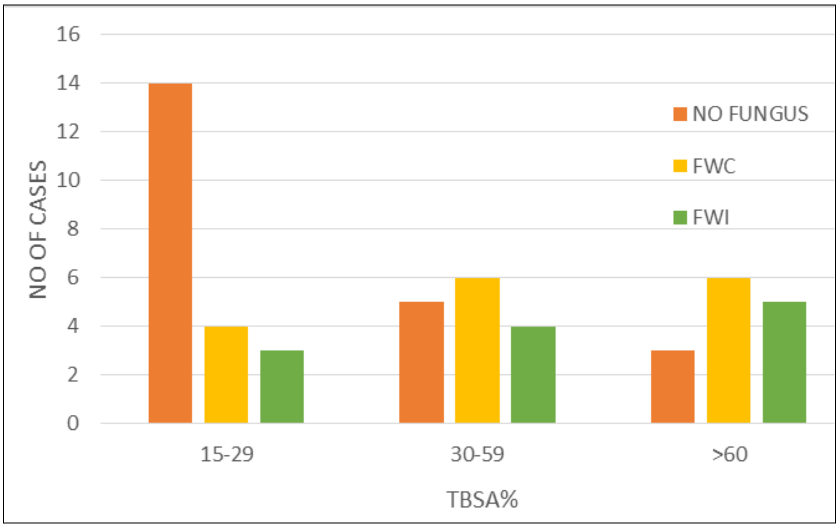

Chart 5: Showing number of patients in 3 fungal categories in three TBSA groups

Of the total 50 patients, 22 patients (44%) did not show any fungus on tissue histopathology, fungal wound colonization (FWC) seen in 16 patients (32%), and 12 patients (24%) showed fungal wound infection (FWI). Low-TBS patients predominated in the no fungus category (63.6%), high-TBS patients predominated in the FWI category (41.7%), and FWC patients showed no obvious pattern of predominance with respect to TBS group.

There were 20 deaths prior to discharge, for an overall raw mortality rate of 40%. Because FWC had no detectable independent association with mortality, for subsequent analyses, a 2-level categorical variable (FWI category) was also recorded as FWI-Yes or FWI-No (FWI-No including both no fungus patients and FWC patients).

Table 7: Mortality comparisons of FWI-Yes versus FWI-No separately in the 3 TBS groups.

TBS Group (n)	Pooled FWI-No/Yes	FWI-no	FWI-yes
15-29 % (21)	17	15	02
Survivors non-survivors	04 (19%)	03(16.7%)	01(33.3%)
30-59 % (15)	08	07	01
Survivors non-survivors	07(46.7%)	04(36.4%)	03 (75%)
>60 % (14)	06	04	02
Survivors non-survivors	08 (57.1%)	05(55.5%)	03(60%)

FWI-NO indicates the pool of no-fungus patients and FWC patient

Chi-Square Test and P value was calculated for the three TBSA group and was found as follows:

TBSA (15-29%) X^2 = .002785, p value = 0.9579

(30-59%) X^2 = 1.759, p value = 0.1847

(>60%) X^2= .02593, p value = 0.872

Chi- Square & P values were statistically non-significant in the three TBSA group but the percentage mortality calculated in the three groups was significant. This may be explained by small sample size of the study.

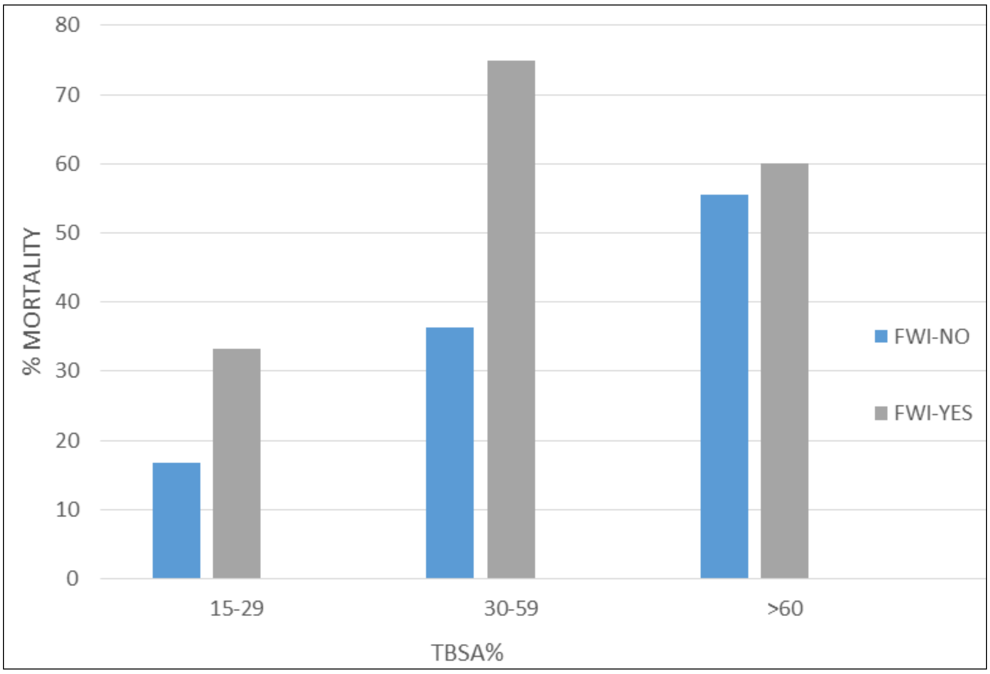

Chart 6: Observed mortality in each fungal-status category within each burn-size group.

Percentage mortality in the fungal category FWI-NO increased with increase in TBSA%. The effect of the FWI-YES interaction with TBS group 30% to 60% on mortality was significantly greater than that with TBS group 15-29% and greater than that with TBS group >60%.It appears that FWI-YES influences mortality more in the TBS 30% to 60% range than in the TBS ranges lower or higher than this, when the contributions of other variables are taken into consideration.

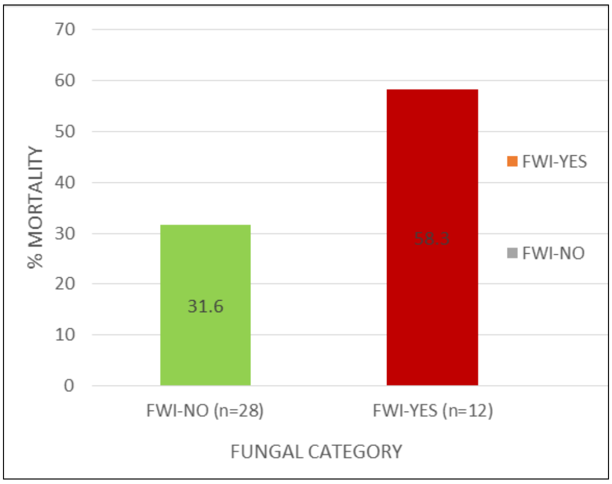

Chart 7: Showing relation between fungal category & % of mortality

Total number of patients in category FWI-NO was 38 which included 22 patients with no fungal elements & 16 patients with fungal wound colonizations (FWC).

Mortality in FWI-NO category was 31.6% while of the 12 patients in category FWI-YES mortality was 58.3%.

Thus there was higher observed mortality with deeper fungal involvement. FWC, fungal wound colonization; FWI, fungal wound infection (invasion). Each category has significantly different percentage of mortality from each of the others.

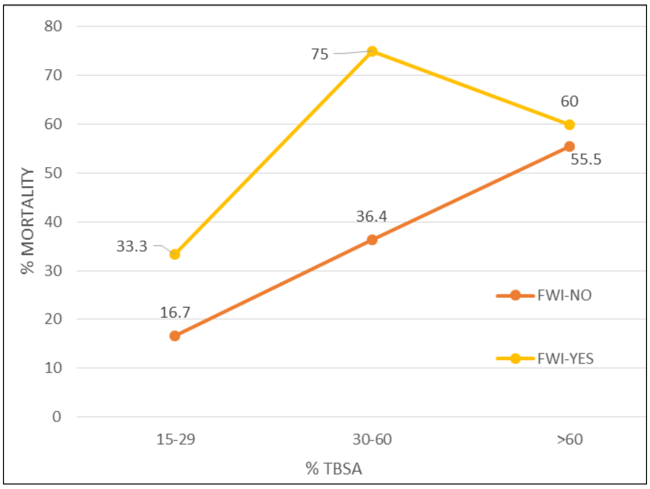

Chart 8: Showing relationship between % mortality in two fungal categories within 3 TBSA group

Observed mortality in relation to total burn size (TBS, percentage body surface area TBSA %) and fungal wound infection (FWI). FWI-No includes FWC and no fungus. TBS groups are represented in the following way: the first (left-most) symbol for FWI-Yes and for FWI-No represents TBS 15-29%, the second symbol TBS is 30%–60%, and the third (right-most) symbol TBS >60% For the second (middle) point in each curve, mortality is different between FWI-Yes and FWI-No, although not significantly different (FWI-Yes vs. FWI-No) at the first points or at the third points.

Among the 28 patients with a primary fungal categorization as FWC or FWI, fungal wound involvement (specimen report as either FWI or FWC) was detected on median post-burn day (PBD) 16 (IQR 9–24). Specifically, among the 16

FWC patients, FWC was first detected on median PBD 19 (IQR 11–27). Among the 12 FWI patients, FWI was first detected on median PBD 12.5 (IQR 9–23). Among these 12 FWI patients, the 07 non-survivors had a median lag of 8 days (IQR 2–20) from first detection of FWI to death.

Out of 16 FWC patients 1st detection of fungus colony was found on median PBD 19 while in 12 FWI patients it was 12.5 so it was clear that chance of getting fungal positivity was earlier in FWI category.

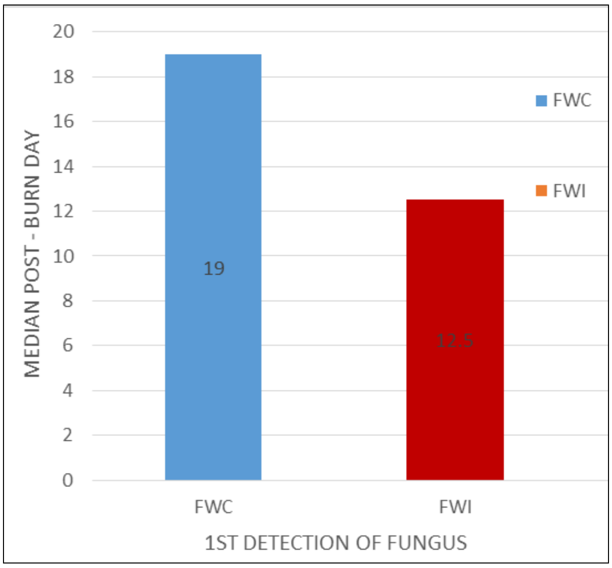

Chart 9: Showing relation between median post burn day & 1st detection of fungus in two fungal categories

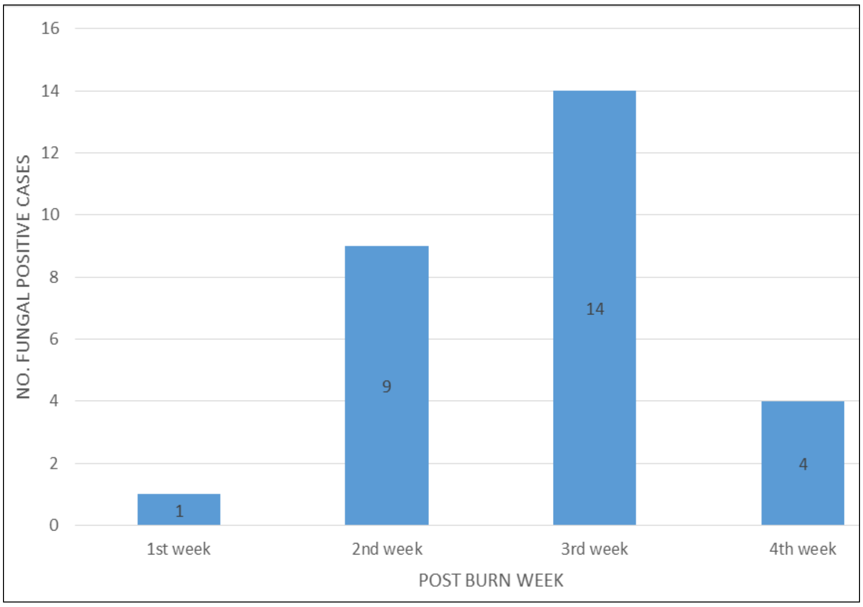

Chart 10: Showing relation between post burn-week & number of positive cases detected

Out of 56% (28) fungal positive cases 50 % cases were detected in 3rd post burn week (14 cases), followed by 2nd week 32% (09 cases), then 4th week 14% and 3.5% in 1st week so chance of getting fungal positivity was maximum in 3rd week & least in 1st week.

Table 8: Fungal Morphology Identified Histopathologically in Sections of Burn Wound Tissue*

Descriptive Fungal Morphologic Class	FWC Patients (n =16)	FWI Patients (n=12)	FWC and FWI Patients Pooled (n=28)
Yeast-like morphology: presence of budding yeasts or rounded yeast-like structure (C. albicans & non albicans Candida)	10(62.5%)	07(58.3%)	17(60%)
Aspergillus-like morphology: presence of parallel-walled, branching, septate hyphae	03 (18.8%)	03 (25%)	06 (21.4%)
Mucor-like morphology (zygomycosis/mucormycosis): presence of wide, ribbon-like, rarely septate hyphae	01 (6.2%)	01 (8.3%)	02 (7%)
Any combination	02 (12.5%)	01 (8.3%)	03 (10.7%)

*The numbers indicate the number of patients each having the given descriptive fungal morphologic class in at least 1 tissue specimen

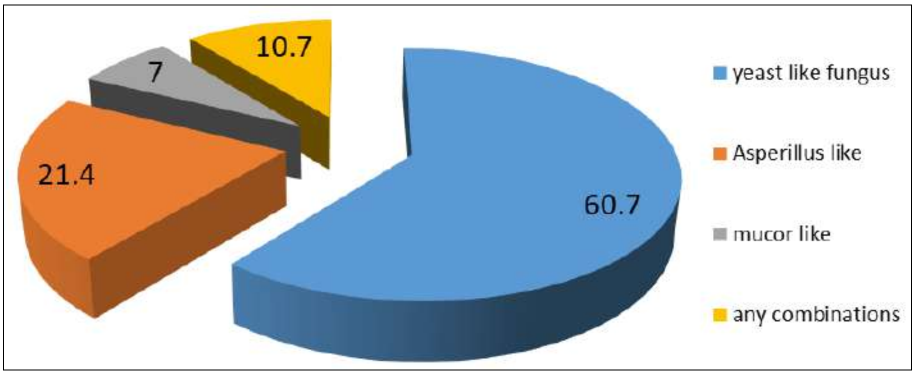

Chart 11: Showing % of various fungal morphologies among total positive cases

Among the 28 patients in the FWC and FWI categories pooled, Candida fungi were seen in the greatest fraction of patients (60.7%), Mucor-like in the smallest fraction (7%), and Aspergillus-like in an intermediate fraction (21.4%).

Table 9: type of fungal morphology detected in 3 TBSA (%) group

TBSA Group (n= number of positive cases in each group)	Fungal Morphology			
	Yeast like	*Aspergillus* like	*Mucor* like	Any combination
15-29 % (n=07)	05	01	0	01
30-59 % (n=10)	05	02	01	02
>60% (n=11)	07	03	01	0
Total (n=28)	17	06	02	03

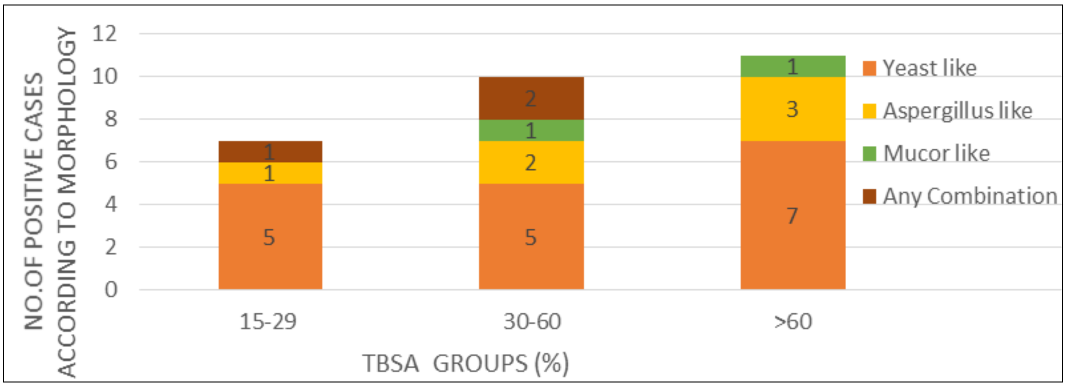

Chart 12: Showing No. of positive cases according to morphology in 3 TBSA groups:

Among the total positive cases (28) Yeast like morphology found in all three TBSA groups with almost equal frequency however as the percentage of TBSA increased frequency of other fungal morphologies like Aspergillus & Mucor also increased.

Discussion

Burn wound provides a suitable substrate for fungal colonization, the reported incidences being around 20% [4]. In this study we found 56% of fungal positivity in total 50 cases. [Table 1] The near eradication of invasive gram-negative burn wound infection following the introduction of effective topical antimicrobial agents in 1964 highlighted, in subsequent years, the importance of fungal infections both of the burn wound and of open, previously excised wounds [8].

In this study stringent infection-control practices were in place. Full-thickness burns were excised by 7–10 days post burn. Patients were treated topically with mafenide acetate (morning) alternating with silver sulfadiazine (evening).Time interval of collecting burn wound samples was at 7th, 14th, 21st days and ≥28 day. Specimens for fungal culture in burns: for demonstration of FWI, tissue biopsy (living tissue including dermis) is done from under the eschar (0.5 g wt.) multiple sites (at least three sites) and multiple times (at least three times).Patients were examined daily for signs of infection. Protein and calorie needs were supplied enterally as soon as possible after burn.

Samples taken were analysed, out of total 50 patients 28 cases were positive for fungal elements, total negative cases were 22. GMS stain and 10% KOH stain (Smear test) were positive in 25 patients and showed 89% sensitivity and 81% specificity while culture was positive in 23 cases & showed sensitivity of 82% & specificity approximately 90%.Thus smear tests showed acceptable sensitivity and specificity comparable to culture test. [Table 2]

Growth of fungal colonies is slow & take up to 3 weeks. The limitations associated with classic culture techniques for the diagnosis of invasive fungal infections have lead to the emergence of many non-culture based methods including deoxyribose nucleic acid (DNA)-based enzyme linked immunosorbent assay and polymerase chain reaction [14].

Literature reports that frequency of fungal colonization increases steadily during hospital stay peaking at third and fourth weeks [15]. In our study colonization with fungi was more commonly seen in second and third week.

In this study total 50 cases were further divided in 3 groups as per the total body surface area of burn as 15-29%, 30-59% and 60% or more. 56% of total cases were found to be positive for fungal elements of which 33.33% were in 15-29% TBSA group, 66.7% were in 30-59% TBSA group and 78.6% were in 60% or above TBSA group. This showed a clear increase in fungal positive cases with increase of total body surface involvement. [Table 3]

This study included 19 male and 33 female patients (total 50 cases). Total number of male patients tested positive for fungal elements were 11(57.9%) and total number of female patients positive for fungal elements were 17(54.8%).This showed that incidence of fungal positivity was approximately similar in both sexes. P value was 0.7823 (non-significant). Thus no detectable differences in fungal positivity in relation to sex of the patients. [Table 4]

Of the total 56% of infected cases 33.3% were in the age group of 18-29 years, 54% cases in age group 30-39 yrs, 58.3% cases in age group 40-49 yrs, 63.6% cases were in age group 50-59 yrs and 71.4% cases were in age group 60 yrs or more. Thus showing a clear trend of increasing fungal positivity with increase in age. [Table 5 & chart 4] Thus we can conclude that keeping other factors constant chance of infection was least in young patients & risk increased with age.

Each patient's fungal-status category was defined according to the deepest level of fungal involvement observed during the hospital course: no fungus (22 patients), fungal wound colonization (FWC, 16 patients), or fungal wound infection (FWI, 12 patients). Low-TBS patients predominated in the no fungus category (63.6%), high-TBS patients predominated in the FWI category (41.7%), and FWC patients showed no obvious pattern of predominance with respect to TBS group. [Table 6 & chart 5]

Burn patients are known to harbour various species of Candida and Candida albicans is always considered as the most frequent pathogenic species causing nosocomial fungal infections in burn patients. Aspergillus has been the next common fungus infecting burn wound [4]. Similar results were found in this study also, among the 28 patients in the FWC and FWI categories pooled, Candida fungi were seen in the greatest fraction of patients (60.7%), Mucor-like in the smallest fraction (7%), and Aspergillus-like in an intermediate fraction (21.4%).There were 20 deaths prior to discharge, for an overall raw mortality rate of 40%. Because FWC had no detectable independent association with mortality, for subsequent analyses, a 2-level categorical variable (FWI category) was also recorded as FWI-Yes or FWI-No (FWI-No including both no fungus patients and FWC patients).Total number of patients in category FWI-NO was 38 which included 22 patients with no fungal elements & 16 patients with fungal wound colonizations (FWC). Mortality in FWI-NO category was 31.6% while of the 12 patients in category FWI-YES mortality was 58.3%.Thus there was higher observed mortality with deeper fungal involvement. Each category has significantly different mortality from each of the others.

Logistic regression was used to detect significant independent associations. FWI was associated with higher TBS. Mortality was associated with TBS, FWI, and age etc. Unlike FWI, FWC was not independently related to mortality, the greater observed mortality in FWC being explained by other variables such as TBS percentage of mortality in the fungal category FWI-NO increased with increase in TBSA%. The effect of the FWI-YES interaction with TBS group 30% to 60% on mortality was significantly greater than that with TBS group 15-29% and greater than that with TBS group >60%.It appears that FWI-YES influences mortality more in the TBS 30% to 60% range than in the TBS ranges lower or higher than this, when the contributions of other variables are taken into consideration.

Because of lack of a demonstrable relationship of FWC to mortality it was mainly of interest to find contributors to the probability of FWI. The dependent variable (FWI) was coded 0 = no (i.e., comprising FWC and no fungus) or 1 = yes.

Logistic regression yielded the following equation for predicted probability of FWI:

$$P\ (\text{invasion}) = 1/(1 + 1/\, e^{k})$$

Age, and sex were rejected as independent contributors to the probability (P) of invasion. Thus, the main contributor to the likelihood of FWI was TBS, with a highly significant association. When fungal-status category (3-level variable: no fungus, FWC, FWI) was added as an independent variable, there was no significant association of FWC with mortality but there was a strong association of FWI, after excluding patients with FWI, regression for mortality rejected FWC and sex.

This TBS-FWI interaction suggests that special attention should be given to the aggressive prevention and early diagnosis of these infections especially in the TBS range of 30% to 60%, including investigation of early prophylactic or empiric treatment of fungal invasion. With the advent of newer diagnostic strategies such as serology and molecular techniques and newer antifungal therapies with less toxicity than standard treatments like intravenous amphotericin B, the importance of accurate prediction models of fungal burn wounds is paramount.

It is not evident from this study why some patients with large burns are at increased risk for FWI and/or FWC. Whether fungal infection itself contributes causally to mortality, or just represents a marker for other contributors, has not yet been definitively assessed in these patients. The relationship between fungal infection and the anatomic cause of death in burn patients remains to be determined.

Conclusion

Despite major advances in the care of burned patients, infectious complications remain an important cause of morbidity and death. The incidence of fungal infection for burn victims is increasing dramatically during recent years. Fungal infection can induce local or systemic inflammatory response and cause serious substantial damage to the patient.

To conclude, this study showed that fungal infection influenced mortality and morbidity of burn patients. Also mortality due to fungal infection in these patients was significantly associated with TBSA% and age of patient. However no relation was found with respect to sex of patient. So serious strategies need to be employed to prevent and control fungal infections. As in the prevention of other infections, practical measures such as air filtration, regular hand washing and avoidance of potted plants and flowers needs to be adopted to avoid exposing patients to fungi.

References

1. Church D, Elsayed S, Reid O, Winston B, Lindsay R. Burn wound infections. Clin Microbiol Rev 2006;19:403-34.
2. Goyal NK, Gore MA, Goyal RS. Fungal colonisation in burn wounds: An Indian scenario. Indian J Surg 2010;72:49-52.
3. Horvath EE, Murray CK, Vaghan GM, Chung KK, Hospenthal DR, Wade CE *et al.* Fungal wound infection (not colonization) is independently associated with mortality in burn patients. Ann Surg 2007;245:978-85
4. Mousa HA. Fungal infection of burn wound in patients with open and occlusive treatment methods. East Mediterr Health J 1999;5:333-6.
5. Tsoutsos D, Tsati E, Metaxotos N, Keramidas E, Rodopoulou S, Ioannovich J. Extensive burn injury complicated by mucormycosis: A case report. Ann Burns Fire Disasters 2001;16:1-2.
6. Gupta N, Hague A, Lattif AA, Narayan RP, Mukhopadhyay G, Prasad R. Epidemiology and molecular typing of Candida isolates from burn patients. Mycopathologia 2005;158:397-405.
7. Murray C, Loo F, Hospenthal D, Cancio L, Jones J, Kim S *et al.* Incidence of fungal infections and related mortality following severe burns. Burns 2008;34:1108-12.
8. Becker WK, Cioffi WG, McManus AT, Kim SH, McManus WF, Mason AD, *et al.* Fungal burn wound infection: A 10 year experience. Arch Surg 1991;126:44-8.
9. Ballard J, Edelman L, Saffle J, Sheridan R, Kagan R, Bracco D *et al.* Multicentre Trials Group. American Burn Association. J Burn Care Res 2008;29:213-21.
10. Mousa HA. Aerobic anaerobic and fungal burn wound infections. J Hosp Infect 1997;37:317-23.
11. Schofield CM, Murray CK, Horvath EE, Cancio LC, Kim SH, Wolf SE *et al.* Correlation of culture with histopathology in fungal burn wound colonization and infection. Burns 2007;33:341-6.
12. Cochran A. Systemic Candida infection in burn patients: A case control study of management patterns and outcomes. Surg Infect (Larchmt) 2002;3:367-74.
13. Ryan CM, Schoenfeld DA, Thorpe WP *et al.* Objective estimates of the probability of death from burn injuries. New Engl. J Med 1998;338:362-366.
14. White Lewis P, Archer Alice E, Barnes Rosemary A. Comparison of Non-Culture-based methods for detection of Systemic Fungal Infections, with emphasis on Invasive Candida infections. J Clin Microbio 2005;43(5):2181-87.
15. Jefferson Lessa Saores de Macedo, Joao Barberino Santos Bacterial and Fungal coloninisation of Burn wounds. Mem Inst Oswaldo Cruz. Rio de Janerio 2005;100(5):535-539.