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Review

Mucormycosis following burn injuries: A systematic review

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ABSTRACT

Introduction: Mucormycosis is an opportunistic fungal infection with a high mortality rate. Though typically associated with diabetes and other conditions that affect innate immune function, infections can also be precipitated by conditions such as trauma and burns. Burn patients are particularly susceptible to fungal infections due to the immune dysfunction that often accompany their wounds. Indeed case series have described mucormycosis to occur in patients with burn injuries, however the factors contributing to mortality have not been well described. Thus, the purpose of our review was to identify factors contributing to morbidity and mortality in burn patients with Mucormycosis.

Methods: A systematic review of the literature of mucormycosis infection in burn injury patients was performed on Pubmed and Google Scholar using the keywords: Mucor, Mucorales, Mucormycosis, Mucormycotina, Zygomycosis and burn or thermal injury. Clinical trials, observational studies, case reports, and case reviews were included if they provided information regarding mortality in adult and pediatric burn patients diagnosed with mucormycosis, review articles, non-English articles, and articles without patient information were excluded. No time limit was placed on our review. Individual patient data was stratified based on mortality. Statistical analysis was performed to investigate the relationship between patient risk factors and mortality, and the Oxford Level of Evidence was used to evaluate study quality.

Results: 46 articles were included in our final review, encompassing 114 patients. On average, survivors had a total body surface area (TBSA)% of 46 (SD 19.8) while non-

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survivors had a TBSA of 65% (SD 16.4), and this difference was significant ($p < .001$). Patients with disseminated mucormycosis experienced an 80% mortality rate compared to 36% mortality rate in patients with localized disease ($p < .001$). We found no statistically significant difference in mean age ($p > .05$), diabetes ($p > .05$), mean delay in diagnosis ($p > .05$), time to antifungal therapy ($p > .05$), or type of therapy used ($p > .05$) between survivors and non-survivors. Our review was limited by the lack of prospective, controlled trials; thus, our review primarily consists of case reports.

Conclusion: Disseminated infections and higher TBSA both increased the risk of mortality in burn patients with mucormycosis, while diabetes did not increase mortality risk. The severity of the initial injury and infection locations must be taken into consideration to inform patient prognosis.

Contents

1. Introduction

Mucormycosis is an opportunistic infection caused by fungi of the subphylum Mucormycotina, order Mucorales. These infections have been classically associated with immunocompromised states, such as diabetes, altered iron homeostasis, neutropenia, and corticosteroid use [1–3].

The incidence of Mucormycosis infections has been rising globally, with an estimated prevalence of 910,000 cases annually and mortality rates up to 80% [4]. Infections are more common in Low and Middle Income Countries such as India and China and are often seen in patients suffering from traumatic disruption of the protective skin barrier [4]. This is particularly true for burn patients, who are susceptible to fungal infections as their injuries often include large disruptions of the physical skin barrier with simultaneous immune system dysfunction and the use of broad-spectrum antibiotics [5]. Mucorales are ubiquitously found in soil and other organic matter, and the effects of burn injury on skin integrity and immune response can predispose patients to fungal infections that present differently when compared to other critically ill patients [6]. These fungal infections can be challenging to manage as they often invade into deep tissues, making them difficult to identify while inhibiting adequate penetration of antifungals [1,4,7]. Though some case reports of mucormycosis in burn patients are in the literature, the factors contributing to morbidity and mortality in these patients has not yet been identified. Therefore, the aim of this study was to conduct a systematic review and meta-analysis of all reported cases of mucormycosis in burn patients to identify the risk factors contributing to morbidity and mortality.

2. Methods

This systematic review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA) [8].

2.1. *Eligibility criteria*

Peer-reviewed articles in English providing information about mortality in burn patients diagnosed with Mucormycosis were included in our review. No time limit was placed on articles and the last search was performed on July 1, 2020. Articles were included if they provided information regarding mortality in burn patients with Mucormycosis. Review articles, non-English articles, articles lacking patient information, and those that did not involve burn patients were

excluded. Due to rarity of cases and scarcity of reports, case reports and case series with fewer than 10 patients were included for analysis. Oxford Level of Evidence was used to evaluate study quality.

2.2. Information sources

A systematic review was performed utilizing PubMed and Google Scholar databases. No ethics approval was required as all information was gathered from public databases.

2.3. Study selection

Three unblinded reviewers (PG, ML, JD) independently performed eligibility assessments with no disagreements between reviewers. Search terms included: Mucor, Mucorales, Mucormycosis, Mucormycotina, or Zygomycosis and burn or thermal injury. The following MeSH terms were used: mucor, Mucormycosis, Zygomycosis, burn, and thermal injury. After screening abstracts and removing articles that did not meet inclusion criteria, a total of 46 papers were included in our analysis.

2.4. Data items/summary measures

Variables of interest included number of patients, age, biologic sex, percent of total burn surface area burned (TBSA), full-thickness burn area, burn sites, presence of inhalation injury, coinfections, coexisting non-thermal injury, comorbidities, mortality, day of diagnosis, delay in initiation of antifungal therapy, type of antifungal therapy used, infection site, antimicrobial and surgical treatments performed, and length of stay. Differences in TBSA, diabetes, and day of diagnosis was compared between survivors and non-survivors.

2.5. Statistical analysis

Information was organized into Microsoft Excel (Microsoft Corp., Redmond, Wash.). Two-tailed *t*-tests were conducted using Microsoft Excel for nominal variables, two-proportion z-tests were performed for categorical variables, and significance was defined as p-value less than 0.05.

Univariate and multivariate analysis was performed on 114 of patients utilizing logistic regression on SPSS, Version 26 (SPSS, Inc., Chicago, IL, USA). Univariate analysis was performed for TBSA, Disseminated Disease, Age, Sex, Mucor infection, time from injury to diagnosis, and Combination Therapy. To test for confounding, a backwards step-wise variable selection method was used on these variables to determine which would be included in the multivariate logistic regression model. TBSA and Disseminated Disease were added as variables in the multivariate models. Two multivariate models were generated; one with TBSA as a continuous variable, and one with TBSA as a categorical variable with cutpoint value of > 50%. To determine a clinically relevant cut-point for TBSA, the receiver operator characteristics (ROC) curve was created and assessed for the point of maximum sensitivity and specificity for mortality. Only patients with complete data for both TBSA and Disseminated Disease (53) were included in the multivariate model.

Table 1 – Demographic and injury variables in burn patients with Mucormycosis infection.

Demographic information	%
Patients included in analysis	114
Sex (n = 76)	
Male	76
Female	24
Mean Age (years, SD) (n = 86)	37 ± 14.7
Patients with diabetes (n = 49)	16
Burn location (n = 59)	
Head and neck	34
Upper extremity	78
Lower extremity	39
Trunk	51
Inhalation injury (n = 25)	52
Mean TBSA% (n = 86)	55 ± 20.3

3. Results

When duplicate articles were removed, 101 abstracts were screened, and 88 remained for full text review. Our final analysis included 46 studies constituting a total of 114 patients (Table 6) [6,9–53]. The mean age was 37.3 years (SD 14.7), 76% (n = 58) were male (Table 1). Of patients with a recorded past medical history, 16% (n = 8) had diabetes, which was the only consistently reported comorbidity. The mean TBSA was 55% (SD 20.3) and 13/25 patients (52%) investigated had evidence of inhalation injury. The majority experienced upper extremity burns (78%), followed by the trunk (51%), lower extremity (39%), and head and neck (34%) (Fig. 1).

On average patients were diagnosed with mucormycosis on hospital day 22 (SD 17.2), and 48.2% of patients had reported antibiotic administration prior to the development of mucormycosis. The most common site of infection was the upper extremity (46%) followed by the trunk (44%), lower extremity (31%), and face and head (21%), with 36/63 patients (57%) experiencing infections in multiple sites (Table 2). The most commonly identified species were in the *Mucor* genus (44%, n = 50). Within the *Mucor* genus, *Mucor circinelloides* comprised 18% (n = 21) of the identified species, and other unspecified *Mucor spp*. comprised 25% (n = 29). *Lichtheimia* (formerly *Absidia*) *spp* were the second most commonly isolated species and comprised 19% (n = 22) of all species isolated. Other species were isolated with lower frequency including *Rhizopus spp*. accounting for 6% (n = 7), and unspecified species in the Mucorales order comprising 20% of the total (n = 23). While most (84%, n = 96) experienced infections to burned skin, five (4%) patients also experienced rhino-orbital fungal infections, four (4%) patients had cerebral or meningeal involvement, and three (3%) patients had pulmonary involvement.

The most common form of management was a combination of medical and surgical management (n = 48/82, 59%), while 30/82 (37%) of patients received either antifungal or surgical management alone (Table 3). Overall, antifungal

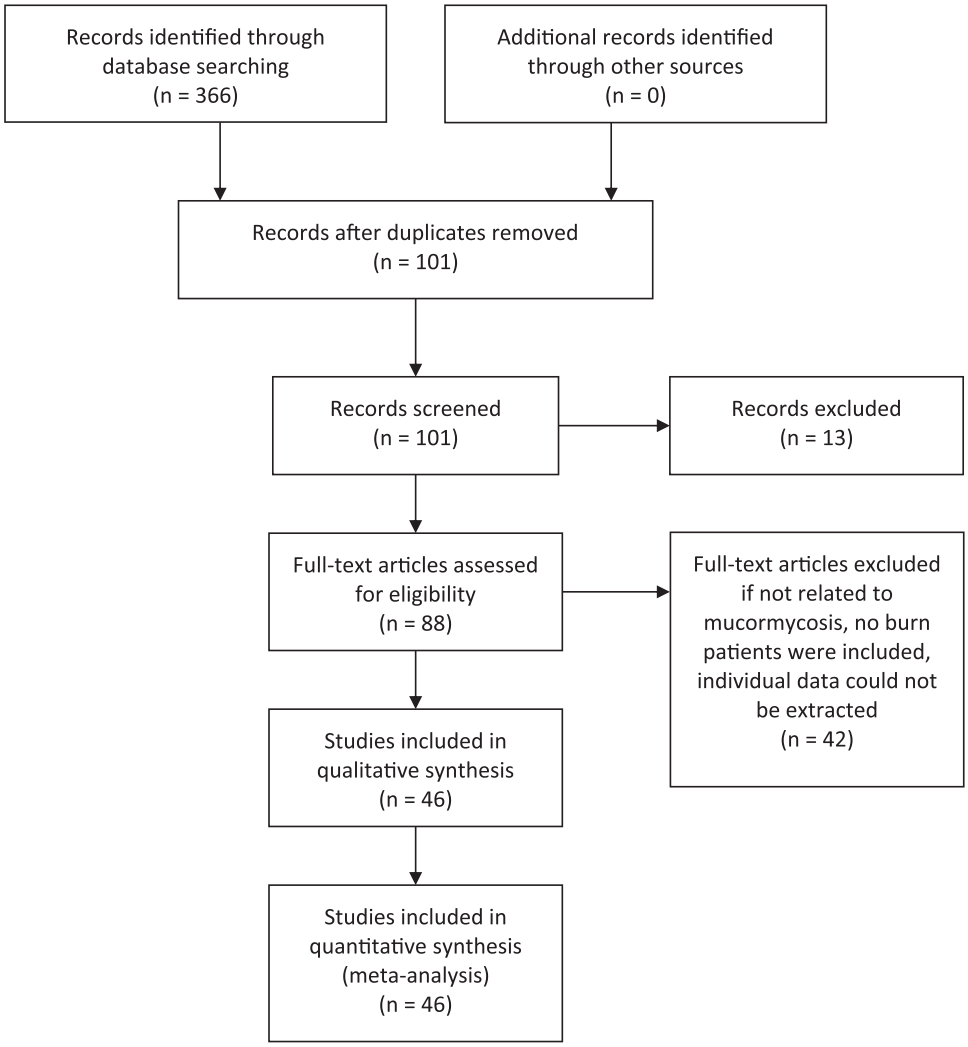

Fig. 1 – PRISMA diagram of search results.

therapy was given to 67% (n = 65/96) of patients; Amphotericin B was the most common antifungal used and was given to 63% (n = 60/96) of patients. Information regarding specific formulations of amphotericin B was inconsistently reported; 24% (n = 23/96) of patients received an unspecified amphotericin B formulation, 37% (35/96) received liposomal amphotericin B, one patient received amphotericin B deoxycholate, and one patient received amphotericin B lipid complex. Of patients with documented surgical intervention, debridement was performed on 88% (n = 63/72), 36% (n = 26/72) underwent skin grafting, and 50% (n = 36/72) underwent amputation. Upper extremity amputation was performed in 22/72 (31%) patients, and 9/72 (13%) patients received lower extremity amputations. Eye enucleations were undertaken in three (4%) patients, two (3%) patients underwent ear amputations, one (1%) patient had a mandibular resection, and one (1%) patient underwent masseter resection. Overall mortality was 54% (n = 61/114), with reports specifically attributing death to invasive fungal infection in 15% (n = 17/114) of patients.

We found no statistically significant difference in mean age ($p > .05$), history of diabetes ($p > .05$), mean delay in diagnosis ($p > .05$), time to initiation of antifungal therapy ($p > .05$), whether patients received antifungal therapy ($p > .05$) or whether patients received combination surgical and antifungal therapy ($p > .05$) between survivors and non-survivors (Table 4). On average, survivors had a TBSA% of 46 (SD 19.8) while non-survivors had a TBSA of 65% (SD 16.4), and this difference was significant ($p < .001$). Patients with Mucormycosis in ≥2 locations experienced an 80% mortality rate compared to 36% mortality rate in patients with localized disease ($p < .001$).

Univariate analysis demonstrated that TBSA%, TBSA > 50%, and infections in ≥2 locations were all significantly associated with mortality (TBSA: odds ratio (OR) = 1.05, confidence interval (CI) = 1.02 – 1.08, p = .001; TBSA > 50%: OR = 9.67, CI = 3.47 – 26.90, $p < .001$; Infection in 2 ≥ locations: OR = 7.00, CI = 2.24 – 21.92, p = .001). Age, gender, time from injury to diagnosis, combination therapy, and infection with *Mucor spp.* were not

Table 2 – Characteristics of infection location and species.

Infection characteristics		%
Fungal species (n = 114)		
	Mucor spp.	44
	Mucor circinelloides	18
	Other *Mucor spp.*	25
	Lichtheimia spp.	11
	Saksenea spp.	4
	Rhizopus spp.	6
	Rhizomucor spp.	3
	Apophysomyces spp.	4
	Unspecified Mucorales order	20
Infection Location (n = 78)		
	Head/Neck	21
	Upper Extremity	46
	Trunk	44
	Lower Extremity	31
	Infection ≥ 2 Locations*	57

* Only 63 patients had detailed enough information to determine number of infection sites.

significantly associated with mortality and were not confounders for the effects of TBSA and number of infections on mortality. TBSA, TBSA > 50%, and infection in 2 ≥ locations remained significantly associated with mortality on multivariate analysis (TBSA: adjusted OR = 1.04, CI = 1.01 – 1.08, p = .026; TBSA > 50%: adjusted OR = 6.06, CI = 1.57 – 23.44, 0.009; Infection in 2 ≥ locations: OR = 7.92, CI = 1.95 –32.10, p = .004).

4. Discussion

Mortality rates following Mucormycosis infections in the burn patients ranged from 29% to 67% depending on TBSA, infection locations, and fungal species. Therefore, it is important to maintain a high index of suspicion to quickly identify and initiate therapy for mucormycosis infection in burn patients with non-healing wounds.

The results of this systematic review confirmed findings in previous reports that infections manifested in rhino-orbital-cerebral, pulmonary, cutaneous, gastrointestinal, renal, and disseminated locations, which led to complications such as sepsis, amputation, and death [4,54]. Patients with infections in two or more locations had poorer outcomes than

Table 3 – Management and outcomes of Mucormycosis in burn patients.

Management and outcomes			%
Surgical Management (alone, in combination, and in combination with medical management, n = 72)			
	Debridement		88
	Amputation		50
		Upper Extremity	31
		Lower Extremity	13
		Eye Enucleation	4
		Ear	3
	Skin Graft		36
Antifungal Therapy (alone, in combination, and in combination with surgery, n = 65)			
	Amphotericin B		92
	Voriconazole		17
	Posaconazole		9
	Isavuconazole		5
Complications (n = 114)			
	Rhino-orbital infection		4
	Mucor Meningitis		4
	Vascular Invasion		2
	Pulmonary Mycosis		3
Overall Mortality (n = 114)			54
Mortality Rate by Species (Total Number infected by species)			
	Mucor spp. (50)		60
	Lichtheimia (formerly *Absidia*) *spp.* (22)		32
	Sakenea spp. (5)		40
	Apophysomyces spp. (4)		50
	Rhizomucor spp. (3)		67
	Rhizopus spp. (7)		29
	Unspecified Mucorales Order (23)		70
Mortality Attributable to Mucormycosis* (n = 114)			15

* Mortality was considered attributable to Mucormycosis if article specifically cited Mucormycosis as cause of death or if Mucormycosis was primary cause of infection resulting in mortality.

Table 4 – Characteristics of survivors vs. non-survivors.

Variable (n)	Survivor	Non-Survivor	P-value
Mean Age in Years (86)	37 ± 15	37 ± 15	0.95
Mean Delay in Diagnosis, Days (62)	24.8 ± 20.5	18.9 ± 10.4	0.14
Mean Time to Antifungal, Days (32)	12.2 ± 9.4	17.5 ± 13.8	0.18
% Received Antifungals (96)	59.2	76.6	0.07
% Combination Therapy (82)	50	66.7	0.13
% with Diabetes (49)	13.8	20	0.56
Mean TBSA (86)	46 ± 19.8	65 ± 16.4	**< 0.001**
% with Infection ≥2 Locations (63)	36.4	80.0	**< 0.001**

those with local infections, and those with larger TBSA had significantly higher rates of mortality after mucormycosis (p = .00 and p = .00, respectively); these correlations persisted even when adjusting for potential confounders. This is consistent with previous observations that higher surface area burned is correlated with higher rates of infections [55]. While TBSA has been shown to be an independent predictor of mortality after burn injury, here we have demonstrated that TBSA > 50% offers the greatest prognostic value for predicting mortality in burn patients with mucormycosis and that infection in 2 or more locations is a stronger predictor of mortality than TBSA > 50% (OR = 7.92, CI = 1.95–32.10, p < .01 and OR = 6.06, CI = 1.57 – 23.44, p < .01 respectively) [56]. As both large burns and mucormycosis are shown to significantly contribute to mortality, we hope that sharing our findings can raise awareness about the incidence and clinical course of fungal infections in burn patients so that proper steps can be taken to identify these infections early and increase patient survival.

The presentation of mucormycosis is varied and can present a challenge to clinicians [7]. Clinicians should maintain a high index of suspicion for clinical signs and patient risk factors. In burn patients mucormycosis typically presents as cutaneous infection. Common findings include necrotic plaques and nodules, sometimes with growing mold. When non-healing burn wounds are identified, a biopsy with pathologic analysis and staining should be performed [54]. Microscopic analysis typically reveals nonseptate hyphae with a width of 6–25 μm and wide-angle branching of 90 degrees [7]. Tissue histopathology may also reveal inflammation and evidence of angioinvasion and infarction. Serological or molecular diagnostic tests are emerging methods that demonstrate promise but suffer from a lack of standardization and licensing for the diagnosis of mucormycosis [7,54,57].

The management of Mucormycosis is based on a personalized, multimodal approach that accounts for multiple patient factors such as site of infection, antifungal properties, and patient comorbidities [58]. While Amphotericin B has historically been the antifungal of choice, it is no longer a first-line option to most experts due to its toxicity liabilities [59–61]. Instead, first-line therapy for mucormycosis is generally accepted to be a lipid formulation of amphotericin B, typically dosed at 5 mg/kg/d for non-CNS disease, with escalation to 5–10 mg/kg/d if the brain is involved [59–61]. The role of isavuconazole remains unclear as first-line therapy, as its approval for the treatment of mucormycosis in the US was based on a small, historically controlled case series, most of the patients of which had been pre-treated with amphotericin formulations. Posaconazole is reserved for salvage therapy and is not a first-line therapeutic option. The role of topical amphotericin or other antifungals is unclear as virtually no data are available to evaluate efficacy.

The angioinvasive nature of mucormycosis pathogenesis results in vessel thrombosis and tissue necrosis, which can impede antifungal drug delivery to the site of infection [3]. Thus, in addition to antifungals, patients often undergo surgical intervention, traditionally consisting of excision of necrotic and infected tissue [7,58].

Previous reviews of mucormycosis infections have reported that the most common organism were *Rhizopus* species, in contrast to our findings [54,62]. Surprisingly, the most commonly identified fungal species causing mucormycosis in this review was *Mucor circinelloides*, followed by other *Mucor spp*., which accounted for nearly half of all cases. Consistent

Table 5 – Univariate and multivariate logistic regression analysis for mortality.

Variable (n)	Univariate		Multivariate, TBSA continuous (53)		Multivariate TBSA, categorical (53)	
	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)[1]	p-value	Adjusted OR (95% CI)[2]	p-value
TBSA % (86)	1.05 (1.02 – 1.08)	**0.001**	1.04 (1.01 – 1.08)	**0.026**		
TBSA > 50% (86)	9.67 (3.47 – 26.90)	**< 0.001**			6.06 (1.57 – 23.44)	**0.009**
2 ≥ infection locations (63)	7.00 (2.24 – 21.92)	**0.001**	6.80 (1.77 – 26.04)	**0.005**	7.92 (1.96 –32.10)	**0.004**
Age (86)	1.00 (0.97 –1.03)	0.95				
Gender (76)	0.95 (0.33 –2.75)	0.92				
Mucor spp. (114)	1.60 (0.76 –3.38)	0.22				
Time from injury to diagnosis (days) (62)	0.98 (0.94 –1.01)	0.19				
Combination Therapy (82)	2.00 (0.82–4.88)	0.13				

Table 6 – Summary of study characteristics with Oxford level of evidence.

Reference	Study Type [Oxford Level of Evidence]	Number of burn patients with Mucormycosis Infection	Mean TBSA (%)	Species Causing Mucormycosis	Mortality Rate (%)
Samaddar et al. (2019)	Case report [5]	1		Apophysomyces variabilis	0
Thielen et al. (2019)	Case report [5]	1	47	Lichtheimia corymbifera	0
Frealle et al. (2018)	Case series [4]	7	49	Lichtheimia corymbifera	29
Bhatt et al. (2018)	Case report [5]	1		Unspecified species within Mucorales order	0
Garcia-Hermoso et al. (2018)	Prospective observational study [5]	10		Mucor circinelloides	80
Stanistreet & Bell (2017)	Case report [5]	1	20	Mucor spp.	100
Galvez Alvaro et al. (2017)	Case report and review of literature [4]	1	47	Mucor spp.	0
Ayaz & Moein (2017)	Case report [5]	1	4.5	Mucor spp.	0
Legrand et al. (2016)	Prospective observational study with retrospective data analysis [3]	10	61	Mucor circinelloides, other Mucor spp., Lichtheimia corymbifera	60
Kyriopoulos et al. (2015)	Case reports [4]	4	37.5	Rhizomucor, Rhizopus	50
Akers et al. (2015)	Case report [5]	1	20	Saksenaea vasiformis	0
Church et al. (2015)	Case report [5]	1	56	Mucor spp.	100
Schaal et al. (2015)	Retrospective review [4]	9	51.7	Mucor circinelloides, other Mucor spp., Lichtheimia corymbifera, Rhizomucor, Rhizopus	22
Ressaire et al. (2015)	Letter to the Editor [5]	3		Mucor circinelloides	100
Mitchell et al. (2014)	Retrospective review [3]	12	64.4 (n = 8)	Mucor spp., other unspecified species within Mucorales order	92
Moon & Jithendran (2014)	Case report [5]	1		Absidia	0
Atty et al. (2014)	Case report (Clinicopathological challenge) [5]	1	92	Mucor spp.	100
Austin et al. (2014)	Case report [5]	1		Apophysomyces variabilis	100
Katz et al. (2014)	Retrospective review [3]	3	55	Mucor spp., Absidia	33
Kaur et al. (2014)	Case report [5]	1	60	Lichtheimia corymbifera	0
Li et al. (2012)	Case report [5]	1	80	Unspecified species within Mucorales order	1
dela Cruz et al. (2012)	Case report [5]	1	90	Apophysomyces variabilis	100
Hospenthal et al. (2011)	Case report [5]	1	56	Saksenaea vasiformis	100
Struck et al. (2010)	Case report [5]	1	54	Rhizopus	100
Antonetti et al. (2009)	Case report [5]	1	96	Mucor spp.	0

(continued on next page)

Table 6 – (*continued*)

Reference	Study Type [Oxford Level of Evidence]	Number of burn patients with Mucormycosis Infection	Mean TBSA (%)	Species Causing Mucormycosis	Mortality Rate (%)
Lipovy et al. (2009)	Case report [5]	1	82	Absidia	100
Piazza et al. (2009)	Case report [5]	1	45	Mucor spp.	0
Ledgard et al. (2008)	Case report and review of literature [4]	1	60	Unspecified species within Mucorales order	0
Constantinides et al. (2008)	Case report and review of literature [4]	0	45	Absidia	0
Christiaens et al. (2005)	Letter to the Editor [4]	5		Absidia	60
Vega et al. (2001)	Case report and review of literature [4]	1	65	Saksenaea vasiformis	0
Tsoutsos et al. (2001)	Case report [5]	1	50	Mucor spp.	100
Stern & Kagan (1999)	Case report and review of literature [4]	1	29	Unspecified species within Mucorales order	100
Tang & Wang (1998)	Case report [5]	1	85	Rhizopus	0
Zabel (1997)	Retrospective review [4]	1	35	Mucor spp.	0
Lidor & Nunley (1997)	Image in Clinical Medicine (with case description) [5]	1		Rhizopus	0
Kraut et al. (1993)	Case report [5]	1	67	Mucor spp.	100
Cocanour et al. (1992)	Retrospective review [4]	2	65.5	Mucor spp.	50
Cooter et al. (1990)	Case report [4]	1	25	Apophysomyces variabilis	0
Goldschmied-Reouven et al. (1989)	Case report [5]	1	65	Saksenaea vasiformis	0
Padhye et al. (1988)	Case report and review of literature [4]	1		Saksenaea vasiformis	100
Chuntrasakul & Chantarakul (1983)	Case report [5]	2	60	Mucor spp,	50
Salisbury et al. (1974)	Retrospective review [3]	12	53.2	Mucor spp., unspecified species within Mucorales order	42
Foley et al. (1968)	Case report [5]	1	65	Mucor spp.	0
Rabin et al. (1961)	Case report [5]	2	54.5	Unspecified species within Mucorales order	100
Baker (1956)	Case series [4]	1	75	Mucor spp.	100

with previous reports, infections with organisms in the *Mucor* genus were associated with higher mortality rates than other species within the Mucorales order (60% mortality rate), though significance level was not determined in our review due to lack of sufficient information to adequately compare mortality rates for all species. Further research is required to better understand the factors influencing why the mortality rate was higher in patients infected with *Mucor spp*., and why burn patients are more likely to be infected with *Mucor spp*.

Previous reports of mucormycosis infection in non-burn patients have identified that the most common manifestation of mucormycosis is rhino-orbital-cerebral mucormycosis (ROCM), which is often seen in immunocompromised patients such as those with diabetes [54]. In our study however, most (84%, n = 96) mucormycosis infections presented as

skin infections, while only 6% (n = 7) of patients had ROCM. Additionally, we found no statistically significant difference in mortality between those with and without diabetes (p = .56). This is consistent with studies of non-burn patients with Mucormycosis that have demonstrated that diabetes is not associated with increase mortality rates [63,64].

The primary limitation of these data are the lack of prospective, controlled investigations. To date, only 1 randomized controlled trial of therapy for mucormycosis has ever been conducted [63,65]. The data from that trial demonstrated that active malignancy and neutropenia were associated with increased risk of death, but selection of antifungal therapy, presence of diabetes, or even transplant status were not, similar to the findings in the current study. Other limitations include a lack of individual patient level data and lack of standardization in reporting data, such as comorbidities. Additionally, only a few articles in this review included information on patient comorbidities which can ultimately effect on patient outcomes [56]. Limited data combined with lack of standardization between reports have demonstrated a deficiency in the literature. If more data were collected through prospective studies or mandated reporting to the National Burn Repository, robust studies that identify significant predictors of outcomes in mucormycosis infections could be possible. Future investigations regarding early recognition of mucormycosis in burn patients is also of benefit in order to reduce their mortality.

5. Conclusion

Mucormycosis infection in burn patients is associated with a high mortality rate. Additionally, this systematic review suggests TBSA is significantly inversely correlated with survival, while pre-existing diabetes does not seem to affect mortality. However, these findings are limited by the paucity of literature and lack of standardization in reporting. Maintaining a high index of suspicion for possible mucormycosis infection, specifically in nonhealing wounds following burn injury, is critical to early diagnosis and timely management. Standardization in case reporting must be improved and further studies are of benefit to identify pertinent risk factors such as patient comorbidities and antibiotic use that may help predict the development and morbidity and mortality associated with mucormycosis infection in burn patients.

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CRediT authorship contribution statement

Design and conception of study was performed by JD, PG, KJC, EM, MJL, CHP, HAY, TJG. Study materials were provided by HAY and TJG. Data acquisition, analysis and interpretation were performed by JD, EM, PG, MJL, BS, TJG. All authors contributed to manuscript writing, and the final manuscript was approved by all authors.

Declaration of Competing Interest

None.

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