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Systematic Review

Gastric Mucormycosis: A Systematic Review with Metadata

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Abstract

Introduction

Gastric mucormycosis is a highly lethal condition with nonspecific signs that have become increasingly underrecognized in the last decade. The current study aims to systematically review gastric mucormycosis, highlighting its presenting symptoms, risk factors, various management approaches, and their outcomes.

Methods

Scopus, PubMed, Web of Science, and Google Scholar were systematically searched for papers on gastric mucormycosis published up to June 1, 2024. The current study included papers documenting cases of gastric mucormycosis across all ages and genders, detailing diagnostic modalities and management approaches.

Results

A total of 106 studies were selected, including 115 patients, of whom 80 (69.4%) were male. The average age of the patients was 47.91 ± 17.01 years. The main presenting symptom was abdominal pain in 58 (50.4%) patients, followed by vomiting, fever, and melaena in 28 (24.3%), 25 (21.7%), and 18 (15.6%) patients, respectively. No identifiable risk factor was present in 33 (28.7%) patients. However, a history of organ transplantation, diabetes mellitus, or hematologic malignancy was reported in 26 (22.6%), 25 (21.7%), and 10 (8.7%) patients, respectively. The conservative management approach exhibited the highest survival rate among the various strategies, with 39 (66.1%) patients surviving, which was statistically significant (P-value <0.001).

Conclusion

Conservative management demonstrates higher survival rates than combined surgical and conservative approaches. However, this finding could be attributed to a more extensive disease in those requiring surgery. Therefore, an individualized assessment of each patient should be made on a case-by-case basis.

1. Introduction

Gastric mucormycosis, though rare, is a highly lethal fungal infection caused by the infiltration of Mucorales, a filamentous fungus [1]. The most prevalent species include Rhizopus, Mucor, Rhizomucor, and Lichtheimia [2]. These fungi exhibit broad, aseptate or sparsely septate, ribbon-like hyphae when observed under a light microscope. These organisms' spores are widespread in the environment, particularly in the soil and decaying organic material. The primary modes of infection typically involve inhalation of fungal spores or penetration through compromised skin barriers. The most frequent manifestation of invasive mucormycosis is rhino-orbital-cerebral involvement. However, there has been a rise in gastrointestinal mucormycosis cases over the past two to three decades. This type of involvement occurs in 7–13% of invasive mucormycosis cases. Among these, gastric involvement accounts for 58% of the cases, while the remaining 42% affect the small and large intestines [3,4].

Gastric mucormycosis can lead to significant mortality rates, reaching up to 54% in immunocompromised individuals [1]. In immunocompromised patients or patients undergoing hematological and allogeneic stem cell transplantation, mucormycosis has emerged as the third most prevalent invasive mycosis, following candidiasis and aspergillosis in order of significance [5,6]. The primary treatment approach for gastric mucormycosis involves conservative management with antifungal agents like lipid formulations of amphotericin B, posaconazole, or newer triazoles [7]. Combining medical therapy with early surgical resection may enhance treatment outcomes in cases of severe diseases with tissue necrosis or delayed presentation [8].

The current study aims to systematically review the symptoms and risk factors of gastric mucormycosis, focusing on different management and diagnostic modalities to provide insight into appropriate management techniques. The reliability of the references has been assessed thoroughly [9].

2. Methods

2.1. Study design

The current systematic review, with metadata, followed the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

2.2. Literature search

A comprehensive systematic search was performed across Scopus, PubMed, Web of Science, and Google Scholar databases to identify papers published up to June 1, 2024. The search employed the following keywords: “Stomach OR cardia OR fundus OR body OR antrum OR pylorus OR gastric OR abdomen OR abdominal OR gastrointestinal AND mucormycosis OR mucoromycetes OR zygomycosis OR zygomycete”. The search was limited to studies conducted in the English language and involving human participants.

2.3. Eligibility

The present systematic review and metadata incorporated studies meeting the following stringent eligibility criteria: 1) documented cases of mucormycosis occurring in the stomach or its anatomical regions, 2) comprehensive medical records and sufficient follow-up data for assessing short-term or long-term outcome, 3) inclusion of patients across all age groups and genders, and 4) studies detailing diagnostic modalities specific to gastric mucormycosis. Exclusion criteria encompassed studies utilizing animal models, those without explicit diagnostic and management modalities for the condition, and studies classified as reviews or commentaries lacking original data. Furthermore, studies published in predatory journals or those lacking peer review were excluded from being included.

2.4. Study Selection Process

Initially, two independent researchers screened titles and abstracts from the identified studies, followed by a thorough full-text evaluation using the predefined inclusion and exclusion criteria. Subsequently, studies that met the eligibility criteria were selected for inclusion. When discrepancies arose between the researchers, a third author intervened to facilitate resolution through deliberation and consensus-based discussions.

2.5. Data items

Data extraction was performed utilizing Microsoft Office Excel. Two authors independently gathered information, including study title, Study’s first author name, study design, country of the study, number of participants or reported cases, publication date, study design type, age (in years), gender, presenting symptoms, risk factors, different diagnostic modalities, treatment or management, as well as outcomes.

2.6. Data analysis and synthesis

The extracted data were analyzed using the Statistical Package for Social Sciences (SPSS) 26.0 software for quantitative synthesis. Summary tables displaying pertinent variables were generated. Categorical data in the tables were summarized using frequency and percentage, while quantitative data were represented using mean and standard deviation. Chi-square tests were used to analyze categorical variables, whereas ANOVA was used to compare means for quantitative variables. Statistical significance was set at a significance level of 0.05, with a p-value of 0.05 or less indicating significant findings.

3. Results

3.1. Study selection

Initially, a systematic search across the specified databases yielded 346 studies. After excluding 13 duplicate studies, seven non-English studies, two closed access studies, and 37 studies that could not be retrieved, 287 studies remained for initial screening based on their titles and abstracts. Of these, 123 studies were excluded at this stage, leaving 164 for full-text assessment. Upon further review, five studies involving non-human models, ten review articles, 11 letters to the editor or commentaries, and seven pre-print studies were excluded. Subsequently, 131 studies were assessed for eligibility, with 25

studies being excluded due to publication in predatory journals. Ultimately, 106 studies [1-3,8,10-111] were selected for inclusion in the current analysis (Figure 1).

3.2. Characteristics of the studies

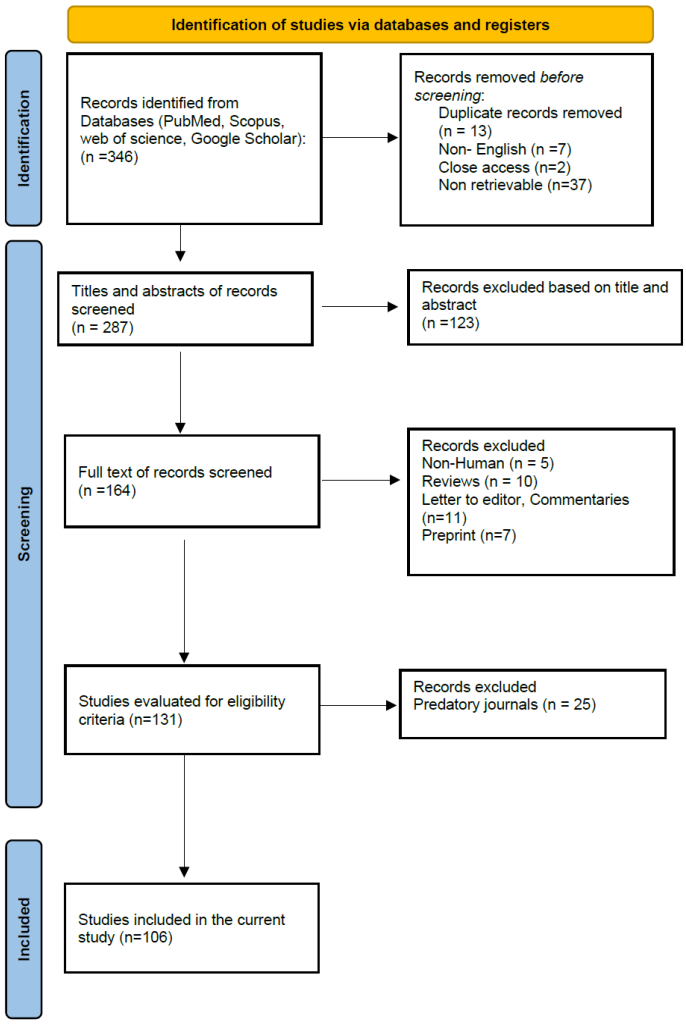

Figure 1. Study selection PRISMA flow chart.

Of the included studies, there were 105 (99.1%) case reports, while the remaining one (0.9%) was a case series. The United States of America contributed 34 (29.3%) studies, followed by India with 26 (22.4%) studies, and Korea with 8 (6.9%) studies (Table 1).

3.3. Patient characteristics

In the current study, 115 (100%) patients were included, with 80 (69.4%) being male. The average age of the patients was 47.91 ± 17.01 years. A total of 80 cases (51.6%) were diagnosed with gastric mucormycosis in the scientific literature after 2010, while the earliest patient dated back to the 1960s.

3.4. Main findings

The main presenting symptom of patients was abdominal pain in 58 (50.4%) patients, followed by vomiting, fever, and melaena in 28 (24.3%), 25 (21.7%), and 18 (15.6%) patients, respectively. No identifiable risk factor was present in 33 (28.7%) patients. However, a history of organ transplantation, diabetes mellitus, or hematologic malignancy was reported in 26 (22.6%), 25 (21.7%), and 10 (8.7%) patients, respectively (Table 2).

In 55 (47.8%) cases, CT scans were performed, and their findings are summarized in (Table 3). Esophagogastroduodenoscopy was performed in 83 (72.1%) patients, with most of the cases revealing gastric ulceration with necrosis and grayish-green exudates (Table 3). Histopathological examination was diagnostic in 112 (97.4%) cases, which showed broad, non-septate, branching fungal hyphae. The other three (2.6%) cases were diagnosed through culture. A conservative treatment strategy involving antifungal medications was chosen for 57 (49.6%) patients, while a combined conservative and surgical approach was implemented

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Table 1. Demographic and clinical characteristics of the included patients.

Author	Study design	Country	Number of participants	Publication date	Age	Gender		Presenting Symptoms	Risk factors
						Male	Female		
Naqvi et al. [1]	*	USA	1	2020	55	0	1	Abdominal pain, Nausea	Diabetes Mellitus
Uchida et al. [2]	*	Japan	1	2019	82	0	1	Melaena, Abdominal pain	None
Bhowmik et al. [3]	*	India	1	2023	48	1	0	NA	Trauma
Khanna et al. [8]	*	India	1	2023	43	1	0	Vomiting, Melaena	Viral infections
Abreu at al. [10]	*	Brazil	1	2018	23	0	1	Fever, Abdominal distention, Vomiting	None
Aerts et al. [11]	*	Belgium	1	2023	37	1	0	Abdominal pain, Fever	Hematological malignancy
Al-Rikabi et al. [12]	*	Saudi Arabia	1	2000	55	1	0	Abdominal pain	Diabetes Mellitus
Albtoosh et al. [13]	*	Jordan	1	2023	46	1	0	Abdominal pain, Melaena	None
Aldahash et al. [14]	*	Saudi Arabia	1	2023	54	1	0	Vomiting	Diabetes Mellitus
Alfano et al. [15]	*	Italy	1	2018	42	0	1	Melaena, Abdominal pain	OT
Berne et al. [16]	*	USA	1	2009	55	1	0	Abdominal pain, Fever	None
Bhaskar et al. [17]	*	India	1	2022	22	0	1	Abdominal pain, Fever	None
Bini et al. [18]	*	North Africa	1	2014	26	0	1	Abdominal pain, Fever	Diabetes Mellitus
Buckholz et al. [19]	*	USA	1	2020	63	1	0	NA	Hematological malignancy
Chang et al. [20]	*	Republic of Korea	1	2012	46	0	1	Abdominal pain, Fever	OT
Chaudhari et al. [21]	*	India	1	2024	50	1	0	NA	None
Cherney et al. [22]	*	USA	1	1999	69	1	0	Abdominal pain, Abdominal distention	None
Chhaya et al. [23]	*	England	1	2011	53	1	0	NA	None
Chow et al. [24]	*	USA	1	2017	34	1	0	NA	Trauma
Chugh et al. [25]	*	USA	1	2017	36	1	0	Tachycardia	Viral infection
Chung et al. [26]	*	Korea	1	2008	58	1	0	Fever, Abdominal pain	None

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Dannheimer et al. [27]	*	Germany	1	1974	46	1	0	Abdominal pain	Diabetes Mellitus
Deja et al. [28]	*	Germany	1	2006	48	1	0	NA	Trauma
Devlin et al. [29]	*	USA	1	2007	32	1	0	Abdominal pain	None
Dora et al. [30]	*	USA	1	2018	57	1	0	Vomiting, Melaena	None
Douglas et al. [31]	*	USA	1	1997	53	1	0	Abdominal pain, Nausea	OT
Dutta et al. [32]	*	India	1	2012	64	0	1	Abdominal distention	None
Enani et al. [33]	*	Saudi Arabia	1	2014	54	1	0	Abdominal distention, Melaena	Diabetes Mellitus
Feng et al. [34]	*	Taiwan	1	2010	57	1	0	Abdominal pain, Fever	H. Pylori
Gani et al. [35]	*	USA	1	2019	79	1	0	Swallowing problem	Diabetes Mellitus, OT
Garcia et al. [36]	*	Spain	1	2006	73	0	1	Fever	None
Gaut et al. [37]	*	USA	1	2017	48	0	1	Abdominal pain, Abdominal distension	Diabetes Mellitus, OT, Viral infections
Guddati et al. [38]	*	USA	1	2019	42	1	0	Vomiting	None
Hachem et al. [39]	*	Lebanon	1	2016	67	1	0	Fever, Abdominal pain, swallowing problem	Hematological malignancy
Hameed et al. [40]	*	India	1	2020	22	0	1	Abdominal pain, Abdominal distention	None
Hattori et al. [41]	*	Japan	1	2021	66	1	0	NA	Hematological malignancy, Diabetes Mellitus
Huai Ho et al. [42]	*	Taiwan	1	2007	58	0	1	Abdominal pain	Alcoholic
Huang et al. [43]	*	China	2	2021	24.5	1	1	Vomiting, Abdominal pain	None, Trauma
Ibrahim et al. [44]	*	USA	1	2020	39	0	1	NA	Hematological malignancy, OT
Irtan et al. [45]	*	France	1	2013	4	0	1	Vomiting	OT
Islam et al. [46]	*	South Africa	1	2009		1	0	Abdominal pain, Abdominal distention, Vomiting	Viral infections
Janakiram et al. [47]	*	USA	1	2021	32	1	0	NA	Alcoholic
John et al. [48]	*	South Africa	1	1960	50	1	0	Abdominal pain	None

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Samet et al. [49]	*	USA	1	2008	79	1	0	NA	None
Jung et al. [50]	*	Korea	1	2007	43	1	0	Abdominal pain	Diabetes Mellitus
Jung et al. [51]	*	Korea	1	2020	41	0	1	Melaena	None
Junior et al. [52]	*	Brazil	1	2020	86	1	0	Fever, Melaena	Viral infection
Kahn et al. [53]	*	South Africa	1	1963	17	1	0	Vomiting	Diabetes Mellitus
Kaiser et al. [54]	*	Switzerland	1	2014	62	0	1	NA	OT
Katta et al. [55]	*	USA	1	2013	60	1	0	Abdominal pain	Viral infection
Keum et al. [56]	*	USA	1	2022	62	1	0	Abdominal pain	Hematological malignancy
Khsiba et al. [57]	*	Tunisia	2	2022	60	0	1	Fever, Vomiting	Diabetes Mellitus
Kim et al. [58]	*	Korea	1	2018	55	1	0	Abdominal pain, Vomiting	OT
Kim et al. [59]	*	USA	1	2022	66	1	0	NA	OT
Kim et al. [60]	*	USA	1	2023	57	1	0	Abdominal pain, Fever, Vomiting	Diabetes Mellitus, OT
Knoop et al. [61]	*	Belgium	2	1998	43.5	2	0	Fever, Abdominal pain	OT
Kulkarni et al. [62]	*	India	1	2014	50	1	0	Abdominal pain, Fever, Abdominal distention, Vomiting, Nausea	Diabetes Mellitus, Alcoholic
Lalwani et al. [63]	*	India	1	2012	32	1	0	Vomiting	Alcoholic
Lankarani et al. [64]	*	USA	1	2019	54	0	1	Abdominal pain, Vomiting, Nausea, Melaena	None
Lee et al. [65]	*	Korea	1	2014	55	1	0	Abdominal pain	Alcoholic
Machicado et al. [66]	*	USA	1	2013	48	1	0	Melaena	Trauma
Malakar et al. [67]	*	India	1	2023	82	1	0	Vomiting, Melaena	Viral infection
Malek et al. [68]	*	USA	1	2019	54	0	1	Abdominal pain, Fever	Diabetes Mellitus
Malik et al. [69]	*	USA	1	2018	48	1	0	Melaena	None
Mathur et al. [70]	*	India	1	2013	0.011	1	0	Abdominal distention	None

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Metussin et al. [71]	*	Brunei	1	2017	42	1	0	Vomiting	Diabetes Mellitus
Mittal et al. [72]	*	India	1	2016	85	1	0	Abdominal pain, Abdominal distention, Vomiting	None
Muthuswamy et al. [73]	*	USA	1	2012	52	1	0	NA	None
Nandwani et al. [74]	*	India	1	2015	45	1	0	Fever, Abdominal pain	OT
Nasa et al. [75]	*	India	1	2017	31	1	0	Abdominal pain, Fever, Melaena	None
Nasta et al. [76]	*	India	1	2015	50	1	0	Abdominal pain	Diabetes Mellitus
Noor et al. [77]	*	Pakistan	1	2022	21	1	0	Fever	Viral infections
Oliveira et al. [78]	*	Brazil	1	2002	17	0	1	Abdominal pain	Diabetes Mellitus
Park et al. [79]	*	Korea	1	2002	56	1	0	Abdominal pain, Fever, Melaena	Viral infection, Alcoholic
Paydar et al. [80]	*	Iran	1	2010	36	1	0	Fever, Vomiting, Abdominal pain	Diabetes Mellitus
Pickeral et al. [81]	*	USA	1	2000	66	1	0	Abdominal pain, Vomiting, Nausea	None
Platt et al. [82]	*	USA	1	2019	33	0	1	Abdominal pain, Vomiting, Nausea	Viral infection
Poma et al. [83]	**	Spain	5	2004	50	1	4	Vomiting, Abdominal pain	OT (5), Alcoholic (1), Trauma (1)
Prasad et al. [84]	*	India	1	2005	42	1	0	Abdominal pain	OT, alcoholic
Pruthvi et al. [85]	*	India	1	2010	76	1	0	Fever	None
Rathi et al. [86]	*	India	1	2023	42	1	0	Abdominal pain, Fever	Alcoholic
Ravi et al. [87]	*	India	1	2016	65	0	1	Abdominal pain	Diabetes Mellitus
Rivas et al. [88]	*	Scotland	1	2020	40	1	0	Vomiting, Nausea	None
Rotundo et al. [89]	*	USA	1	2019	24	1	0	None	Trauma
Sachan et al. [90]	*	India	2	2022	38	1	1	Melaena	Diabetes Mellitus, None
Safwan et al. [91]	*	India	1	2022	45	1	0	Abdominal pain	OT
Schulman et al. [92]	*	South Africa	1	1979	23	1	0	Vomiting, Abdominal pain	None

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Shahapure et al. [93]	*	India	1	2002	35	1	0	Abdominal pain	Alcoholic
Sharaan et al. [94]	*	USA	1	2019	28	1	0	Abdominal pain	Alcoholic
Sharma et al. [95]	*	India	2	2020	59.5	0	2	Abdominal pain, Fever, Melaena	Diabetes Mellitus, OT
Lyo et al. [96]	*	USA	1	2017	36	1	0	Vomiting, Melaena	Alcoholic
Shenoi et al. [97]	*	USA	1	2010	14	1	0	Abdominal pain, Fever	None
Singh et al. [98]	*	USA	1	1995	28	1	0	None	OT
Small et al. [99]	*	USA	1	2010	60	1	0	Abdominal pain	None
Song et al. [100]	*	Korea	1	2006	60	1	0	Abdominal pain	Hematological malignancy
Suhaildeen et al. [101]	*	India	1	2016	52	0	1	Abdominal pain	Diabetes Mellitus
Sun Ha et al. [102]	*	Korea	1	2015	31	1	0	Abdominal pain, Fever	None
Suzuki et al. [103]	*	Japan	1	2009	60	1	0	None	Hematological malignancy, Diabetes Mellitus
Tathe et al. [104]	*	India	1	2016	56	1	0	Abdominal pain, abdominal distension, Vomiting	Alcoholic
Termos et al. [105]	*	Kuwait	1	2018	52	0	1	None	Diabetes Mellitus, alcoholic, OT
Tinmouth et al. [106]	*	USA	1	2001	57	1	0	Abdominal pain, Abdominal distension	OT
Velázquez et al. [107]	*	Spain	1	2017	53	0	1	None	None
Vera et al. [108]	*	England	1	2002	45	1	0	None	OT, Alcoholic
Wien et al. [109]	*	USA	1	2020	74	1	0	None	Hematological malignancy
Winkler et al. [110]	*	Austria	1	1996	37	0	1	Melaena	OT
Yusuf et al. [111]	*	Canada	1	2019	51	1	0	None	Hematological malignancy

Abbreviations: *: Case report, **: Case series, OT: Organ Transplantation

Table 2. Frequency of patient characteristics.

Variables	Frequency/ Mean	Percentage/ Standard deviation
Age (Years)	47.91	17.01
Gender		
Male	80	69.6
Female	35	30.4
Presenting symptoms		
Abdominal Pain	58	50.4
Vomiting	28	24.3
Fever	25	21.7
Melaena	18	15.6
Abdominal distension	12	10.4
Nausea	7	6.1
Swallowing problem	2	1.7
Tachycardia	1	0.8
Risk factors		
None	33	28.7
Organ transplantation	26	22.6
Diabetes mellitus	25	21.7
Alcoholic	15	13
Hematological malignancy	10	8.7
Viral infections	10	8.7
Trauma	7	6.1
Helicobacter pylori	1	0.8
Not mentioned	3	2.6
Management		
Conservative	57	49.6
Surgery + Conservative	34	29.5
Surgery	11	9.6
None	13	11.3
Outcome		
Alive	59	51.3
Dead	52	45.2
Not mentioned	4	3.5

in 34 (29.5%) patients. Surgical intervention alone was undertaken in 11 (9.6%) individuals. Of the reported cases, 52 (45.2%) resulted in mortality. The conservative management approach exhibited the highest survival rate among the various strategies, with 39 (66.1%) patients surviving, which was statistically significant (P-value <0.001). Surgery, whether performed alone or in conjunction with conservative methods, showed lower survival rates of 2 (3.4%) and 17 (28.8%) patients, respectively (Table 4).

4. Discussion

Mucormycosis is colloquially referred to as "black fungus" in certain countries, a term derived from the necrosis and black exudate observed when it affects various anatomical sites. The scientific literature has extensively documented its orofacial manifestations. Additionally, the general population recognizes the urgency of seeking medical attention when such ominous signs appear in the orofacial area. However, there are significant knowledge gaps regarding gastric mucormycosis. Unlike orofacial cases, gastric mucormycosis may not manifest obvious external signs. Even clinicians face the challenges of identifying such cases, often diagnosed postmortem [3][112]. Furthermore, Bhowmik et al. mentioned that there has been a rise in the incidence of gastric mucormycosis in the past few decades. The current systematic review further supports this, as nearly half (80 patients) of all the cases were reported after 2010. This can be attributed to advances in diagnostic modalities, coupled with an increasing number of high-risk patients due to the concurrent rise in diabetes mellitus and organ transplantation in the past decade [3].

The specific mechanism by which mucormycosis affects the gastrointestinal tract remains elusive for most patients; however, ingestion of fungal spores is widely recognized as the primary route, which can be found in fermented milk, porridges, dried bread products, and alcoholic beverages made from maize contaminated with the fungus. One notable finding in this investigation is that 15 (13%) patients were alcoholic, raising the possibility that the alcoholic beverage they were consuming was contaminated; however, this cannot be confirmed without actual evidence of Mucorales in the alcoholic beverages they were consuming. This was not included in any of the gastric mucormycosis case reports [1]. Another recognized route of spread involves penetrating trauma, which can introduce fungal spores from the environment into the gastrointestinal tract. For example, Chow et al. reported a case of a 34-year-old patient who sustained eight gunshot wounds to the abdomen, with gastric mucormycosis diagnosed on the 29th postoperative day [24]. Overall, seven (6.1%) patients had a recent history of trauma preceding their diagnosis in this systematic review. This transmission may occur through direct environmental contact during abdominal penetrating trauma, as mentioned earlier, or potentially via dissemination from another injured site through the bloodstream. While less probable, transmission through contaminated surgical instruments used in these trauma cases is also conceivable. The present study's risk factors for gastric mucormycosis aligned with those observed in the sino-orbital region. These included organ transplantation, diabetes mellitus, and hematological malignancies, all of which are commonly recognized as predisposing factors. Another interesting route was reported by Maravi-Poma et al., where the spread of this condition was attributed to the handling of medication among critically ill individuals dependent on tube feeding, where contaminated wooden tongue depressors and applicators were utilized for crushing and blending medications [83].

One of the challenges posed by gastric mucormycosis lies in its diagnosis due to the obscure anatomical location and nonspecific presenting symptoms. Most patients primarily experience abdominal pain, with vomiting and fever also commonly reported. The presence of melaena alongside abdominal pain may prompt physicians to perform an endoscopy, often revealing an unexpected grayish-blackish ulceration in the majority of cases [113]. Endoscopy with histopathological examination is crucial for diagnosing gastric mucormycosis, as imaging alone is insufficient. The CT results might show no findings and miss the possible diagnosis of gastric mucormycosis, or they might reveal gastric wall thickening, ulceration, and other nonspecific abnormalities in the gastric wall which are not unique to mucormycosis. Nonetheless, these strategies could potentially aid in excluding disseminated disease and addressing specific complications. Therefore, direct histopathological examination of tissue specimens, which shows broad, non-septate, branching fungal hyphae, is essential to confirm the presence of mucormycosis [114].

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Table 3. Summary of Studies regarding different diagnostic modalities with management Outcomes.

Author	Study design	Publication date	CT scan finding	Endoscopic finding	Histopathological finding	Treatment or Management	Outcome
Naqvi et al. [1]	*	2020	Transmural thickening of the stomach and the peri-gastric	ulcerated lesion in the gastric fundus with the exudative material	Invading fungal hyphae	Conservative	Alive
Uchida et al. [2]	*	2019	No abnormalities	Peptic ulcers at the pylorus	Non-septate hyphae branching at wide angles	Conservative	Dead
Bhowmik et al. [3]	*	2023	NA	Green exudates surrounding the lesions.	Broad, aseptate, and foldable fungal hyphae.	None	Dead
Khanna et al. [8]	*	2023	NA	large deep necrotic ulcer	Fungal hyphae	Conservative	Alive
Abreu at al. [10]	*	2018	Gastric distension, parietal thickening, heterogeneous impregnation	Smooth, brownish, thickened stomach	Zygomycotic hyphae	Conservative + Surgery	Alive
Aerts et al. [11]	*	2023	Splenic thrombosis, infarction, stomach perforation	NA	Ribbon-like hyphae	Surgery	Dead
Al-Rikabi et al. [12]	*	2000	Thickening of the stomach wall, small hypodense area	Large ulcer, friable mucosa with thickened gastric antrum	broad and non-septate hyphae with minimal branching	Surgery	Dead
Albtoosh et al. [13]	*	2023	Negative for the lesions	Large Cratered ulcer, visible vessel, nodular and hyperemic mucosa.	Aseptate fungal hyphae	Conservative	Alive
Aldahash et al. [14]	*	2023	Pleural effusions and colon mucosal edema.	large ulcer with a clipped visible vessel	Pauci-septate ribbon-like hyphae with right angle branching.	Conservative	Dead
Alfano et al. [15]	*	2018	NA	Non-bleeding gastric ulcers surrounded by hyperemic mucosa	septations, broad and irregular width hyphae	Conservative	Alive
Berne et al. [16]	*	2009	no clear abscesses or fluid collections.	NA	invasive fungal elements	Conservative + Surgery	Dead
Bhaskar et al. [17]	*	2022	Peripancreatic collections compressing the posterior wall of the stomach.	Large ulcerated area involving the lesser curvature of the stomach.	Broad-based aseptate fungal hyphae.	Conservative + Surgery	Dead
Bhowmik et al. [3]	*	2023	NA	Green exudates surrounding the lesions.	Broad, aseptate, and foldable fungal hyphae.	None	Dead
Bini et al. [18]	*	2014	Full-thickness oedema of the stomach along with lung, kidney and paranasal sinus involvement.	Gastric necrosis	Mucormycosis	Conservative + Surgery	Alive
Buckholz et al. [19]	*	2020	Air in the stomach wall, short gastric veins.	Erythematous stomach, covered in large majority by a thick, black eschar and necrotic debris.	NA	Conservative + Surgery	Dead
Chang et al. [20]	*	2012	disappeared normal mucosal enhancement and thinned wall in stomach greater curvature of cardia.	Portal hypertensive gastropathy and duodenal ulcer scar.	Mucormycosis	Conservative	Alive
Chaudhari et al. [21]	*	2024	NA	Proliferative lesion in the gastric fundus with greenish exudate.	Aseptate hyphae	None	Dead
Cherney et al. [22]	*	1999	Air in the gastric wall	Adherent, thick, green exudate with areas of necrosis.	Broad based, non-septate hyphae branching at right angles.	None	Not mentioned

Chhaya et al. [23]	*	2011	NA	Multiple large superficial plaque-like ulcers in the upper and mid stomach.	Broad, irregular, non-septate, branching hyphae.	Conservative	Alive
Chow et al. [24]	*	2017	Enteric contrast within the left pleural space with an apparent open communication between the stomach and pleura.	Patch of necrosis in the posterior of the stomach along with linear erosions.	Broad, non-pigmented, non-septate hyphae with right angle branching.	None	Not mentioned
Chugh et al. [25]	*	2017	NA	Necrotic Ulcer with Surrounding Exudate.	Broad, Irregular, non-septate Hyphae with Right-Angled Branching.	Conservative	Alive
Chung et al. [26]	*	2008	ileus	Ulcer with a greenish coating at the greater curvature of the mid-body of the stomach	Right-angled, pauci-septate, and ribbon-like hyphae	Conservative	Alive
Dannheimer et al. [27]	*	1974	NA	NA	Non-septate hyphae and branching at obtuse angles.	None	Dead
Deja et al. [28]	*	2006	NA	Necrotized and ulcerated gastric mucosa encompassing the stomach	broad, un-septate hyphae	Conservative	Alive
Devlin et al. [29]	*	2007	Pneumoperitoneum	Hemorrhage and necrosis with an associated area of white fibrinous material.	broad-based, non-septate hyphae with right-angle branching	Conservative	Dead
Dora et al. [30]	*	2018	Diffuse peri-colonic inflammation most pronounced at the rectosigmoid colon.	Multiple ulcerated lesions of the gastric mucosa.	fungal hyphae favoring mucormycosis.	Conservative	Alive
Douglas et al. [31]	*	1997	NA	Circumferential green, necrotic-appearing gastric ulcer at the juncture of the stomach	non septate fungal hyphae, with right-angle branching.	Surgery + Conservative	Alive
Dutta et al. [32]	*	2012	NA	Multiple erosive ulcers in the fundus and body of stomach.	broad, thin-walled, and pleomorphic fungal hyphae	Conservative	Alive
Enani et al. [33]	*	2014	Free air in the abdomen posterior to the fundus of the stomach	An ulcer over the ampullary fold	branching non-septate fungal hyphae with an extensive necrosis.	Surgery	Dead
Feng et al. [34]	*	2010	A collection of intramural gas over the greater curvature of the gastric body.	Well-defined giant round ulcer with brown-greenish exudate.	Non-septate hyphal elements with right angle branching.	Conservative	Alive
Gani et al. [35]	*	2019	NA	Gastric lesion which causes severe gastritis.	Fungal elements in a background of necrotic and acute inflammatory exudate.	Conservative	Alive
Garcia et al. [36]	*	2006	NA	Giant ulcer with Yellowish and hemorrhagic exudates	Broad and irregularly branched non-septate fungal hyphae	None	Dead
Gaut et al. [37]	*	2017	Right lower quadrant collection of fluid, extraluminal gas adjacent.	NA	Branching fungal hyphae	Conservative	Alive
Guddati et al. [38]	*	2019	NA	Multiple ulcers in the body with fresh blood in the stomach.	broad aseptate fungus with variable angle branching	Conservative	Alive
Hachem et al. [39]	*	2016	Bilateral interstitial and centrilobular nodular disease in favor of an infectious etiology.	Gastric ulcer at the greater curvature of the stomach.	Irregular, Broad, and aseptate hyphae.	Conservative	Alive

Hameed et al. [40]	*	2020	NA	NA	Large, non-septate hyphae with 90-degree angle hyphal branching.	Surgery + Conservative	Dead
Hattori et al. [41]	*	2021	Cystic mass with a diameter of 4.5 cm on the stomach	NA	Fungal hyphae in the arteries and veins of the ulcer base	Conservative	Dead
Huai Ho et al. [42]	*	2007	NA	mass in the gastric antrum, posterior wall of gastric body	broad, non-septate hyphae with branches occurring at right angles.	Conservative	Alive
Huang et al. [43]	*	2021	NA	Heavy bleeding	Mucormycosis	Surgery	Alive
	*	2021	NA	Large blood clot in the gastric cavity	Mucormycosis	Surgery	Alive
Ibrahim et al. [44]	*	2020	Pneumoperitoneum, gastric pneumatosis, stomach edema	Non-bleeding crated ulcer	Ribbon-like fungal hyphae	Surgery	Dead
Irtan et al. [45]	*	2013	NA	NA	Large non-septate hyphae	Conservative	Alive
Islam et al. [46]	*	2009	NA	NA	Branching, non-septate hyphae	Surgery	Dead
Janakiram et al. [47]	*	2021	NA	gastric fundal ulcer	Gastric mucormycosis	Conservative	Alive
John et al. [48]	*	1960	NA	NA	Broad, non-septate hyphae	None	Dead
Samet et al. [49]	*	2008	Irregular thickening of the gastric folds in a mottled type appearance.	NA	NA	Conservative	Dead
Jung et al. [50]	*	2007	Gastric wall thickening with a collection of dirty air bubbles.	NA	Broad-based, non-septate, right angular branched fungal hyphae	Surgery + Conservative	Dead
Jung et al. [51]	*	2020	NA	Large number of ulcerations with bloody discharge.	Non-septate fungal hyphae	Conservative	Alive
Junior et al. [52]	*	2020	Ground-glass opacity with consolidative abnormalities	A giant ulcer in the stomach parts	Broad, irregular, non-septate hyphae	None	Alive
Kahn et al. [53]	*	1963	NA	NA	Broad non-septate hyphae	None	Dead
Kaiser et al. [54]	*	2014	NA	Tumor infiltration	Ribbon-like hyphae with irregular septation and right-angle branching	Conservative	Dead
Katta et al. [55]	*	2013	NA	Gigantic ulcer	broad non-septate fungal hyphal with 90-degree-angle branching	Conservative	Alive
Keum et al. [56]	*	2022	Multiple lymphadenopathies above and below the diaphragm with gastric wall thickening	Non-bleeding deep ulcers	Mucorales	Conservative	Not mentioned
Khsiba et al. [57]	*	2022	NA	Gastric ulcer with bleeding stigmata	Large, irregular, and non-septate hyphae.	None	Dead
	*	2022	NA	Ulcerated fundic mucosa with grayish exudate	Broad zygomycetes hyphae branching at right angle.	Conservative +Surgery	Dead
Kim et al. [58]	*	2018	Diffuse gastric wall thickening	Grey necrotic debris surrounded by erythematous erosive mucosa	Broad-based, non-septate, right angle branched fungal hyphae	Conservative	Alive

Kim et al. [59]	*	2022	NA	significant clot in his stomach and an ulcerated fungating lesion	Morphologic features consistent with mucormycosis	Conservative	Dead
Kim et al. [60]	*	2023	Gastric pneumatosis	necrotic-appearing mucosa of the stomach	Mucormycosis	Conservative	Dead
Knoop et al. [61]	*	1998	Bilateral pleurisy but no parenchymal infiltrate	NA	Broad, un-septate fungal hyphae	Surgery + Conservative	Dead
	*	1998	Noncavitary nodular lesions	NA	Fungal hyphae	Surgery + Conservative	Alive
Kulkarni et al. [62]	*	2014	NA	NA	Branched obtuse angled fungal hyphae	Surgery	Dead
Lalwani et al. [63]	*	2012	NA	NA	Broad aseptate hyaline fungal hyphae	Surgery + Conservative	Dead
Lankarani et al. [64]	*	2019	Intramural gastric abscess with gas in the Portal Venous System	Intramural (subepithelial) heterogenous density containing mass versus debris		Conservative	Alive
Lee et al. [65]	*	2014	Pneumoperitoneum and hemoperitoneum		Non-septate fungal hyphae	Surgery + Conservative	Alive
Machicado et al. [66]	*	2013	NA	Large exudative ulceration in the gastric body	Broad aseptate fungal hyphae with right angle branching	Conservative	Alive
Malakar et al. [67]	*	2023	NA	Large gastric ulcer	Broad aseptate fungal hyphae	Conservative	Alive
Malek et al. [68]	*	2019	Fluid collection, free intra-abdominal air consistent with gastric perforation	NA	Broad, irregularly branched, rarely septate hyphae	Surgery + Conservative	Alive
Malik et al. [69]	*	2018	NA	large ulcer in the proximal stomach	Fungal aseptate hyphae morphologically consistent with mucormycosis	Conservative	Dead
Mathur et al. [70]	*	2013	NA	NA	Broad branching fungal hyphae	Conservative	Alive
Metussin et al. [71]	*	2017	NA	Large ulcer with raised edges on the greater curve of stomach	Branching hyphae of the mucormycosis	Conservative	Dead
Mittal et al. [72]	*	2016	Gastrocolic fistula	large ulcer on the gastric wall, covered with necrotic slough.	NA	Conservative	Dead
Muthuswamy et al. [73]	*	2012	NA	large necrotic-appearing ulcer along the greater curvature	Broad, thin-walled hyphae	Conservative	Dead
Nandwani et al. [74]	*	2015	NA	NA	Broad non-septate mucor hyphae	Surgery + Conservative	Dead
Nasa et al. [75]	*	2017	Presence of free peritoneal air and perforation in the stomach wall	Multiple esophageal and gastric ulcerations	Angio invasive mucormycoses	Conservative	Dead
Nasta et al. [76]	*	2015	Perforation of fundus with extravasation	NA	Septate hyphae branching at right angles	Surgery	Dead
Noor et al. [77]	*	2022	NA	NA	Broad aseptate fungal hyphae	Surgery + Conservative	Alive
Oliveira et al. [78]	*	2002	NA	Ulcerated lesion covered by yellowish exudate	Gastric lesion, showing hyphae characterized as Mucor	Conservative	Dead

Park et al. [79]	*	2002	Coarseness of the liver surface, mild splenomegaly, and irregular thickening of the gastric wall	Giant, circumferential ulcer extending from fundus to mid body of the stomach.	hyphae and necrotic debris.	Surgery + Conservative	Alive
Paydar et al. [80]	*	2010	NA	Ulcerated lesion involving the proximal part of the greater curvature of the stomach	Broad, aseptate with acute angle branching hyphae	Surgery + Conservative	Alive
Pickeral et al. [81]	*	2000	Leaking abdominal aortic aneurysm	Ulcer of the gastric cardia with irregular edges	Broad, ribbon-like, non-septate hyphae	Conservative	Dead
Platt et al. [82]	*	2019	Gastric pneumatosis	Ulcer in the gastric cardia	Broad, sparsely septate fungal hyphae	Surgery + Conservative	Dead
	**	2004	NA	Gastric lesions, with ulcerations and necrosis, with greenish exudates	Non-septate fungal hyphae	Surgery + Conservative	Alive
	**	2004	NA	Gastric lesions, with ulcerations and necrosis, with greenish exudates	Non-septate fungal hyphae	Surgery + Conservative	Alive
Poma et al. [83]	**	2004	NA	Gastric lesions, with ulcerations and necrosis, with greenish exudates	Non-septate fungal hyphae	Surgery + Conservative	Dead
	**	2004	NA	Gastric lesions, with ulcerations and necrosis, with greenish exudates	Non-septate fungal hyphae	Conservative	Dead
	**	2004	NA	Gastric lesions, with ulcerations and necrosis, with greenish exudates	Non-septate fungal hyphae	Conservative	Dead
Prasad et al. [84]	*	2005	NA	Sloughed-out area in the body of the stomach	Non-septate fungal hyphae	Surgery + Conservative	Alive
Pruthvi et al. [85]	*	2010	NA	Large ulcerative lesion on the high lesser curve of the stomach	Aseptate, broad, right-angled branching hyphae	Conservative	Alive
Rathi et al. [86]	*	2023	Significant thinning with concealed perforation from the anteroinferior stomach wall	Inflamed gastric mucosa with an ulcer	Mucormycosis and gangrenous necrosis	Surgery	Dead
Ravi et al. [87]	*	2016	Multiple perforated gastric ulcers, perforated diaphragm and liver abscess	NA	Wide-branching fungal hyphae	Surgery + Conservative	Dead
Rivas et al. [88]	*	2020	Perforation and bowel ischemia	A gastric fundus ulcer with irregular borders	Large, non-septate right angle branching hyphae	Surgery	Dead
Rotundo et al. [89]	*	2019	Significant intramural emphysema within the stomach	Severe gastritis with mucosal sloughing and transmural necrosis	Fungal hyphae	Surgery + Conservative	Dead
Sachan et al. [90]	*	2022	NA	Ulcerated mucosa in esophagus and black colored polypoid	Fungal aseptate hyphae	Conservative	Alive
	*	2022	NA	Friable black colored coating on stomach mucosa with no bleed	fungal aseptate hyphae	Conservative	Alive
Safwan et al. [91]	*	2022	NA	Ulcerations with thick adherent mucus in the stomach	Non-septate fungal hyphae invading the gastric mucosa	Surgery + Conservative	Dead
Schulman et al. [92]	*	1979	NA	NA	Non-septate hypha	Conservative	Alive
Shahapure et al. [93]	*	2002	NA	Ulcerated plaque-like lesion in the stomach.	Mucormycosis of the stomach	Surgery + Conservative	Alive
Sharaan et al. [94]	*	2019	Pneumoperitoneum	Extensive ulceration with transmural necrosis	Obtuse-angled aseptate hyphae with angioinvasion	Surgery + Conservative	Alive

Sharma et al. [95]	*	2020	Emphysematous gastritis with localized perforation	large sloughed out gastric ulcer	Fungal hyphae	Surgery + Conservative	Alive
	*	2020	Emphysematous gastritis with localized perforation	large sloughed out gastric ulcer	Fungal hyphae	Surgery + Conservative	Alive
Lyo et al. [96]	*	2017	NA	Necrotic ulcer which occupied nearly 40% of the body of the stomach	Microorganism was consistent with mucormycosis.	Conservative	Alive
Shenoi et al. [97]	*	2010	Diffuse free fluid with loculated collections in the right-lower quadrant	Multiple serpiginous, purplish, nodular submucosal lesions of the gastric wall	Large, irregular, branching hyphae	Conservative	Alive
Singh et al. [98]	*	1995	NA	Grayish-black exudate	Broad, sparsely septate fungal hyphae	Surgery + Conservative	Dead
Small et al. [99]	*	2010	Thickening of the wall of the gastric body	Large ulcer was encountered in stomach	Fungal organisms consistent with mucormycosis	Conservative	Alive
Song et al. [100]	*	2006	Massive collection of intramural gas and hematoma	NA	Fungal hyphae with irregular widths and right-angle branching	Surgery + Conservative	Alive
Suhaildeen et al. [101]	*	2016	Irregular wall thickening involving stomach	NA	Thick un-septate fungal hyphae suggestive of mucormycosis	Surgery + Conservative	Alive
Sun Ha et al. [102]	*	2015	A large pneumoperitoneum and perforation of the proximal jejunum	NA	Broad, irregular and non-septate fungal hyphae	Surgery + Conservative	Dead
Suzuki et al. [103]	*	2009	Pneumonia in the upper-left pulmonary lobe	NA	Broad, rarely septate hyphae	None	Dead
Tathe et al. [104]	*	2016	NA	Large ulcer along greater curvature of stomach	Broad, ribbon-like fungal hyphae with right angled branching	Conservative	Alive
Termos et al. [105]	*	2018	Free air and a large amount of free fluid in the abdominal cavity	Loss of esophagus viability	Large, non-septate hyphae with 90-degree angle hyphal branching	Surgery + Conservative	Alive
Tinmouth et al. [106]	*	2001	Splenic abscess	Elevated ulcer at the margins and black, necrotic centers.	Fungal hyphae	Surgery + Conservative	Dead
Velázquez et al. [107]	*	2017	NA	large circumferential ulcer extending from the esophagogastric junction to the upper stomach.	broad and non-septate hyphae with vascular invasion and thrombosis	None	Dead
Vera et al. [108]	*	2002	NA	Anastomotic stricture, which was not technically amenable for stenting.	Broad irregular fungal hyphae characteristic of zygomycosis	Surgery + Conservative	Alive
Wien et al. [109]	*	2020	NA	A large fungating, necrotic, ulcerated, non-bleeding mass	large 90-degree branching fungal hyphae	Conservative	Alive
Winkler et al. [110]	*	1996	NA	A large ulcer covered by a greyish exudate	Non-septate, rectangular, branching hyphae	Conservative	Alive
Yusuf et al. [111]	*	2019	NA	Diffuse abnormal greyish thickening from the gastric cardia to mid-antrum	Broad fungal hyphae consistent with Mucormycosis	Conservative	Not mentioned

Abbreviations: *Case report, ** Case series

Table 4. Comparison of Patient Outcomes by Management Approaches, Age, and Gender

Variable		Outcome			P- value
		Alive	Dead	Not mentioned	
Management N (%)	Surgery	2 (3.4%)	9 (17.3%)	0 (0%)	<0.001
	Conservative	39 (66.1%)	16 (30.8%)	2 (50%)	
	Surgery + Conservative	17 (28.8%)	17 (32.7%)	0 (0%)	
	None	1 (1.7%)	10 (19.2%)	2 (50%)	
Age (Mean ± SD)		47 ± 18.06	48.49 ± 16.23	54.00 ± 15.25	0.054
Gender N (%)	Male	37 (62.7%)	39 (75%)	4 (100%)	0.151
	Female	22 (37.3%)	13 (25%)	0 (0%)	

The theorized pathophysiology of gastric mucormycosis infection focuses on impaired phagocytosis, compromised chemotaxis, and faulty intracellular breakdown of Mucorales. Mucormycosis progresses with angioinvasion as a prominent feature, leading to vascular thrombosis and tissue necrosis. This mechanism is thought to facilitate hematogenous spread to other organs. During Mucorales' invasion of host cells, the method of hyphal growth relies on acquiring host iron. It is suggested that gastric bleeding from the newly formed invasion of the fungus or perhaps from prior peptic ulcers could serve as a source of iron for this purpose [1,2,13]

There are currently no guidelines specific to managing gastric mucormycosis in the scientific literature, resulting in different approaches to its management. In the current study, conservative management with antifungals had significantly higher survival rates than combined surgical and conservative approaches or surgical approaches alone. This result could be due to selection bias because patients requiring surgical intervention likely have more extensive disease or complications that warrant such invasive treatment. In contrast, those managed conservatively with antifungals alone may represent cases with milder disease or better overall health, potentially skewing survival rates favorably towards the conservative approach. This scenario introduces a confounding factor where the severity of the disease influences both the choice of treatment and the observed outcomes. Despite this study reporting a mortality rate of approximately 50% for gastric mucormycosis, the true mortality rate could potentially be significantly higher, given the number of patients who die without a diagnosis or due to the underreporting of such cases in the literature. It's noteworthy that gender and age did not influence the outcomes of the patients in the present study.

5. Conclusion

Conservative management has demonstrated significantly higher survival rates compared to a combined approach with surgery. However, this finding could be attributed to more extensive disease in those requiring surgery. Therefore, an individualized assessment of each patient, including the necessity of surgery and antifungal therapy, should be made on a case-by-case basis.

Declarations

Conflicts of interest: The author(s) have no conflicts of interest to disclose.

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