Aquatic yeasts: diversity, characteristics and potential health implications

Mzimkhulu Ephraim Monapathi, Carlos Cornelius Bezuidenhout and Owen Howard James Rhode

ABSTRACT

There has been a rising interest in the levels, diversity and potential impacts of yeasts in aquatic environments. Some of the species isolated from such niches are known pathogens or have pathogenic and antifungal resistance features. This deems it necessary to understand the characteristics and potential health implications of such environmental yeasts species. Studies on these subjects are limited. Most studies on aquatic yeasts have linked them to water pollution. However, the current gold standards to determine microbial pollution of water use bacteria as the main indicator organisms. Including yeasts in water quality standards may provide a different dimension on the quality of water when determining its fit-for-use properties. Pathogenic yeasts cause superficial infections or life-threatening infections, especially in immunocompromised people. Some of the yeast species isolated in recent studies were resistant to commonly used antifungal agents of clinical and veterinary relevance. With the high prevalence rate of HIV in sub-Saharan Africa, particularly in South Africa, antifungal resistance is a public concern as it poses serious medical and economic challenges. Most available studies are concerned with clinical environments only. There is, thus, a need to review the literature that also focuses on aquatic environments.

Key words | aquatic yeasts, diversity, health implications, microbial pollution, resistance, water quality

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INTRODUCTION

Yeasts are eukaryotic microorganisms classified in the kingdom fungi and are divided into two phylogenetic groups, i.e. ascomycetes and basidiomycetes. Yeasts commonly occur in water, animals, plants, soil and insects (Montes de Oca *et al.* 2016). Cases where yeasts were identified as the primary agent that caused infections increased, which, in turn, increased interest in the specific species and characteristics of that particular yeast. Interest was further fuelled by the advent of human immunodeficiency virus (HIV) co-infectious or opportunistic infections by some yeasts species infecting immunocompromised individuals (Moges *et al.* 2016; Mnge *et al.* 2017). Most of these patients that are compromised are those in therapeutic technology including organ transplants and anticancer therapies or have certain disease conditions such as malignancy and HIV (Pincus *et al.* 2007; Richardson & Lass-Florl 2008). The latter presents a global challenge, especially in South Africa with its high HIV epidemic of 37.9 million and a further 7.1 million people that are currently living with HIV (UNAIDS 2019).

Initially, the identification of yeast was based on its morphological and physiological traits (van Uden & Ahearn 1963; Woollett & Hendrik 1970; Hagler & Medonca-Hagler 1981;

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Sláviková *et al.* 1992; Rosa *et al.* 1995; Dynowska 1997; Sláviková & Vadkertiová 1997; Bogusławska-Was & Dabrowski 2001). However, identifications made using this approach is laborious, inconclusive and often inaccurate (Kurtzman & Robnett 1998). Various studies showed that molecular analyses are more reliable when identifying yeasts to species level (Brandão *et al.* 2010, 2011, 2017; Brilhante *et al.* 2016; Novak Babič *et al.* 2016; Monapathi *et al.* 2017, 2018; Pires *et al.* 2017; Moubasher *et al.* 2018; Maciel *et al.* 2019). Recent studies conducted in different environments furthermore applied next generation sequencing (NGS) methods to determine yeasts community structures and dynamics (Aguilar *et al.* 2016; Okuno *et al.* 2016; Romão *et al.* 2017).

Although yeasts constitute the aquatic environments microbial community, their biodiversity and distribution have been ignored (Yurkov & Pozo 2017). The present study explores the occurrence of yeasts in natural water resources with emphasis on freshwater systems. A structured review was conducted to determine the extent of current knowledge of yeasts in freshwater systems using the literature relevant to the characteristics, diversity and health implications of aquatic yeasts. The following databases were used during this research: EBSCOhost, Google scholar, Sabinet and Science Direct. The literature that included one or more keywords, such as yeasts, identification, uses, aquatic environments, microbial pollution, yeast infections, antifungal resistance and resistance mechanisms, were used as references.

YEAST DIVERSITY IN AQUATIC ENVIRONMENTS

Compared with other environments such as soils and indoors, the presence of yeasts in aquatic environments has received little attention. Furthermore, the occurrence of yeasts in water as compared with other microorganisms such as bacteria and protozoans has not been largely studied (Pereira *et al.* 2010). With limited studies on aquatic yeasts, most of them are concentrating on polluted water (Nagahama 2006). Few yeast species exclusively associated with aquatic environments (Libkind *et al.* 2017). The section below addresses the diversity of yeasts in different aquatic environments.

Freshwater

The diversity and ecology of yeasts in freshwater environments (temperate and tropical rivers, lakes and lagoons) has been reviewed in a study by Libkind *et al.* (2017). The review conforms to the present review with respect to yeast identification. Identification of yeasts was primarily based on morphological and physiological characteristics. However, the identification was strenuous and in many cases, inconclusive (Kurtzman & Robnett 1998). As stipulated in Table 1, most of the conducted studies before 2001 relied on morphology and physiological tests for identification. The use of more reliable molecular data in yeasts identification followed in most studies thereafter. From a review by Libkind *et al.* (2017) and studies summarized in the current study (Table 1), yeast isolates associated with tropical and temperate lakes, rivers and lagoons comprise species of *Candida*, *Clavispora*, *Cyberlindnera*, *Cryptococcus*, *Debaryomyces*, *Hanseniaspora*, *Kluyveromyces*, *Metschnikowia*, *Meyerozyma*, *Pichia*, *Rhodotorula*, *Saccharomyces*, *Torulaspora*, *Trichosporon* and *Yarrowia*. Studies on yeasts in tropical rivers and lakes have been linked to freshwater pollution. Tropical ecosystems are surrounded by forests and located near urban areas. Rich yeasts species reflect inputs from terrestrial sources such as soil and plant debris and anthropogenic activities (Medeiros *et al.* 2008; Brandão *et al.* 2011; Libkind *et al.* 2017). Furthermore, some of the yeast species isolated from these freshwater environments have been implicated as opportunistic pathogens (Medeiros *et al.* 2008, 2012; Brandão *et al.* 2011; Van Wyk *et al.* 2012; Monapathi *et al.* 2017, 2018).

Drinking water

Surface water and groundwater are primary sources of drinking water (Katsanou & Karapanagioti 2017). Regular detection of emerging opportunistic yeast pathogens in taps suggests that it might be a vector for human infections (Novak Babič *et al.* 2017). From studies conducted (Table 1), the following yeast genera have been isolated from water distribution systems and tap water: *Candida*, *Clavispora*, *Cryptococcus*, *Debaromyces*, *Meyerozyma*, *Pichia*, *Rhodotorula*, *Trichosporon* and *Yarrowia*. Yamaguchi *et al.* (2007) isolated the following *Candida* species, namely *C. albicans*,

Table 1 | Some of the aquatic environment studies conducted on yeasts (√ = done; nd = not done)

Authors	Background to study	Resource type	Country	Mode of identification	Asco/ Basidiomycota	Antimicrobial activity	Resistance mechanisms	Virulence tests
Freshwater environments								
van Uden & Ahearn (1963)	Diversity	Surface and deep water	USA	Morphology and physiological tests	Both	nd	nd	nd
Woollett & Hendrik (1970)	Pollution	Lakes and rivers	USA	Morphology and physiological tests	Both	nd	nd	nd
Hagler & Medonca-Hagler (1981)	Pollution	Estuarine waters	Brazil	Morphology and physiological tests	Both	nd	nd	nd
Sláviková *et al.* (1992)	Diversity	Artificial fresh lakes		Morphology and physiological tests	Both	nd	nd	nd
Rosa *et al.* (1995)	Pollution	Lake	Brazil	Morphology and physiological tests	Both	nd	nd	nd
Sláviková & Vadkertiová (1997)	Pollution	River	Slovakia	Morphology and physiological tests	Both	nd	nd	nd
Dynowska (1997)	Pollution	River	Poland	Physiological tests	Both	nd	nd	nd
Bogusławska-Was & Dabrowski (2001)	Pollution	Lagoon	Poland	Morphology and physiological tests	Both	nd	nd	nd
Gadanho & Sampaio (2004)	Diversity	River	Portugal	Sanger sequencing	Both	nd	nd	nd
Medeiros *et al.* (2008)	Diversity	Natural lakes and rivers	Brazil	Physiological tests and Sanger sequencing	Both	√	nd	nd
Brandão *et al.* (2010)	Diversity	Lakes	Lakes	Physiological and Sanger sequencing	Ascomycota	√	nd	nd
Biedunkiewicz & Baranowska (2011)	Diversity	Lake	Poland	Morphology and physiological tests	Ascomycota	nd	nd	nd
Brandão *et al.* (2011)	Diversity	Lakes	Brazil	Morphology, physiological tests and molecular tests	Both	nd	nd	nd
Medeiros *et al.* (2012)	Diversity	Lakes	Brazil	Molecular techniques	Both	nd	nd	nd
Van Wyk *et al.* (2012)	Diversity	Rivers	South Africa	Morphology and physiological tests	Both	nd	nd	nd
Biedunkiewicz *et al.* (2013)	Diversity	Lakes	Poland	Morphology and physiological tests	Ascomycota	nd	nd	nd
Silva-Bedoya *et al.* (2014)	Diversity	Artificial lakes	Colombia	Morphology and molecular tests	Both	nd	nd	nd
Aguilar *et al.* (2016)	Diversity	Surface water, tailing ponds and sediments	Canada	Molecular techniques	Both	nd	nd	nd

(*continued*)

Table 1 | continued

Authors	Background to study	Resource type	Country	Mode of identification	Asco/ Basidiomycota	Antimicrobial activity	Resistance mechanisms	Virulence tests
Brilhante *et al.* (2016)	Resistant mechanisms	Lake	Brazil	Morphology and physiological tests	Both	√	√	nd
Brandão *et al.* (2017)	Diversity	Lake	Brazil	Morphology, physiological tests and molecular tests	Both	nd	nd	nd
Monapathi *et al.* (2017)	Diversity	Rivers	South Africa	Physiological tests and molecular tests	Ascomycota	√	nd	nd
Monapathi *et al.* (2018)	Resistant mechanisms	Rivers	South Africa	Physiological tests and molecular tests	Ascomycota	√	√	nd
Moubasher *et al.* (2018)	Diversity	Mud from hypersaline and freshwater bodies	Egypt	Physiological tests and molecular techniques	Both	nd	nd	nd
Drinking water environments								
Yamaguchi *et al.* (2007)	Diversity	Bottled and tap water	Brazil	Physiological and molecular tests	Ascomycota	nd	nd	nd
Kanzler *et al.* (2008)	Diversity	Wells, water tanks, tap water and groundwater	Austria	Morphology and molecular techniques	Both	nd	nd	nd
Ayanbimpe *et al.* (2012)	Diversity	Taps, wells, boreholes and streams	Nigeria	Morphology and physiological tests	Both	nd	nd	nd
Biedunkiewicz *et al.* (2014)	Diversity	Bottled and tap water	Poland	Morphology and physiological tests	Both	nd	nd	nd
Novak Babič *et al.* (2016)	Diversity	Tap and groundwater	Slovenia	Physiological and molecular tests	Both	nd	nd	nd
Zupančič *et al.* (2016)	Diversity	Dishwashers	Slovenia	Molecular techniques	Both	nd	nd	nd
Wastewater environments								
Yang *et al.* (2011)	Diversity	Activated sludge	China	Morphology and molecular techniques	Both	nd	nd	nd
Liébana *et al.* (2015)	Diversity	Activated sludge	Spain	Morphology and molecular techniques	Both	nd	nd	nd
Karimi & Hassanshahian (2016)	Diversity	Soil and wastewater	Iran	Molecular techniques	Ascomycota	nd	nd	nd
Rajendran *et al.* (2016)	Diversity	Sewage water and sludge	Taiwan	Morphology and molecular techniques	Ascomycota	nd	nd	nd
Mahgoub *et al.* (2016)	Diversity	Activated sludge	Egypt	Morphology and molecular techniques	Ascomycota	nd	nd	nd
Pires *et al.* (2017)	Diversity	Wastewater	Brazil	Morphology and molecular techniques	Both	nd	nd	nd

Assress *et al.* (2019)	Diversity	Wastewater	South Africa	Molecular techniques	Both	nd	nd	nd
Groundwater environments								
Kanzler *et al.* (2008)	Diversity	Wells, water tanks, tap water and groundwater	Austria	Morphology and molecular techniques	Both	nd	nd	nd
						nd	nd	nd
Pereira *et al.* (2009)	Diversity	Groundwater, surface and spring water	Portugal	Morphology and physiological tests	Both	nd	nd	nd
Pereira *et al.* (2010)	Diversity	Groundwater, surface and springs	Portugal	Molecular techniques	Both	nd	nd	nd
Branda *et al.* (2010)	Diversity	Superficial and deep sediments, ice cores and meltwaters	Italy	Molecular techniques	Both	nd	nd	nd
Samah *et al.* (2014)	Diversity	Groundwater wells	Egypt	Morphology and physiological tests	Ascomycota	nd	nd	nd
Novak Babič *et al.* (2016)	Diversity	Tap and groundwater	Slovenia	Physiological and molecular tests	Both	nd	nd	nd
Marine environments								
Rédou *et al.* (2015)	Diversity	Deep subseafloor sediment	New Zealand	Molecular techniques	Both	nd	nd	nd
Chang *et al.* (2015)	Diversity	Sea surface microlayer and underlying water	Taiwan	Molecular techniques	Both	nd	nd	nd
Zuza-Alves *et al.* (2016)	Pathogenesis	Beaches	Brazil	Physiological tests	Ascomycota	√	nd	√
Francis *et al.* (2016)	Diversity	Seaweeds	New Zealand	Molecular techniques	Both	nd	nd	nd
Abreu *et al.* (2016)	Diversity	Beach sands	Portugal	Physiological tests		nd	nd	nd
Zaky *et al.* (2016)	Diversity	Seashore	UK, Egypt and USA	Morphology, physiological and molecular techniques	Ascomycota	nd	nd	nd
Romão *et al.* (2017)	Diversity	Beach sands	Portugal	Molecular techniques	Both	nd	nd	nd
Maciel *et al.* (2019)	Antifungal susceptibility	Sand and seawater	Brazil	Morphology, physiological and molecular techniques	Both	√	nd	√

C. glabrata and *C. parapsilosis* from bottled mineral and tap water from municipal supplies. In a study conducted by Ayanbimpe *et al.* (2012), yeasts species such as *Candida tropicalis*, *Yarrowia lipolytica* and *Rhodotorula* sp. were isolated from tap water. Novak Babič *et al.* (2016) and Zupančič *et al.* (2016) isolated ubiquitous opportunistic pathogenic yeasts *Candida parapsilosis* and *Rhodotula mucilaginosa* from tap water and hot aerosols from dishwashers.

Groundwater

Freshwater from groundwater represents the raw water that is used to produce drinking tap water (Libkind *et al.* 2017). The diversity of yeasts in groundwater is comparable to that of surface water (Novak Babič *et al.* 2016) and comprise of genera *Candida*, *Clavispora*, *Cryptococcus*, *Geotrichum*, *Pichia*, *Rhodotorula*, *Saccharomyces*, *Trichosporon* and *Yarrowia* (Kanzler *et al.* 2008; Pereira *et al.* 2009, 2010; Brandão *et al.* 2010; Ayanbimpe *et al.* 2012; Samah *et al.* 2014; Novak Babič *et al.* 2016; Libkind *et al.* 2017). However, groundwater is dominated by black yeasts (Kanzler *et al.* 2008; Novak Babič *et al.* 2016). With groundwater systems as drinking water and freshwater resources, it could be expected and it is not surprising to observe similar genera in these water systems.

Marine

Marine environments are treated by pollution from municipal sewage/wastewater and industrial discharges, surface and agricultural run-off and domestic effluent. This is a public health risk to coastal residents and tourists in direct contact with the water (Maciel *et al.* 2019). Yeasts have been studied from marine environments, including oceans, marine sediments, seawater, seaweeds and digestive tracts of marine organisms (Zaky *et al.* 2014). Some yeast species isolated from marine environments are opportunistic pathogens (Maciel *et al.* 2019). The following yeast genera have been isolated from the studies stipulated in Table 1: *Bullera*, *Candida*, *Clavispora*, *Cryptococcus*, *Debaromyces*, *Hanseniaspora*, *Kluveronmyces*, *Meyerozyma*, *Metschnikowia*, *Pichia*, *Rhodotula*, *Saccharomyces*, *Yarrowia* and *Wickerhamomyces*. Yeasts in marine environments are vital in the food web (Zaky *et al.* 2014). They might be sources of food for some marine invertebrates and zooplanktons (Nagahama 2006). Moreover, marine yeasts are important for their application in the production of biofuel, enzyme production, single-cell protein, single cell oil and nanoparticles (Zaky *et al.* 2014; Sarkar & Rao 2016).

Wastewater

Microorganisms (including pathogenic) are required for treatment processes in waste water treatment plants (WWTPs) (Kowalski *et al.* 2017). Yeast species belonging to the genera *Candida*, *Cryptococcus*, *Debaryomyces*, *Pichia*, *Rhodotorula*, *Torulaspora*, *Trichosporon*, *Saccharomyces*, *Yarrowia* and *Wickerhamonyces* (Yang *et al.* 2011; Liébana *et al.* 2015; Karimi & Hassanshahian 2016; Mahgoub *et al.* 2016; Rajendran *et al.* 2016; Pires *et al.* 2017; Assress *et al.* 2019) have been isolated from WWTPs. Some yeast species have the potential to act as a biological treatment in the WWTP (Pires *et al.* 2017). They can treat high concentrations of organic wastewater, heavy metal ion wastewater and domestic sewage (Wang *et al.* 2018). Their importance in wastewater treatment stems from their ability to degrade phenol compounds (Karimi & Hassanshahian 2016).

SURVIVAL OF YEASTS IN FRESHWATER ENVIRONMENTS

Existing environmental conditions maintain the survival of yeasts in the ecosystem. Most yeasts are mesophilic and grow best at temperatures between 20 and 30 °C (Deak 2006). Human pathogens grow well at 37 °C, the normal internal temperature of the human body (Gabaldón & Carreté 2016). Yeasts species that grow at this particular temperature may have pathogenic potential as opportunistic species for humans. Yeasts prefer a slightly acidic medium with optimum pH between 4.5 and 5.5 (Deak 2006). Furthermore, yeasts can grow aerobically on particular carbon compounds such as alcohols, organic acids and amino acids as their sole energy source (Rodrigues *et al.* 2006). Deak (2006) stipulated that increased dissolved oxygen and dissolved organic matter in aquatic environments favour yeast growth. Yeasts can also utilize a wide range

of nitrogen compounds as nitrogen sources. Some nitrogen-containing compounds such as amino acids and ammonia can also be used by yeasts as carbon sources (Messenguy *et al.* 2006).

YEASTS-POLLUTION MONITORING TOOL

Recent microbial water pollution has been determined by standard faecal indicator bacteria (SFIB) such as *Escherichia coli* and intestinal enterococci (Kirschner *et al.* 2017). However, some studies have demonstrated that yeast counts can be potential microbial monitoring tools. From studies conducted by Van Wyk *et al.* (2012) and Monapathi *et al.* (2017) in North West Rivers, South Africa, yeast levels ranged up to 8,680 and 2,573 CFU/l, respectively. In a study conducted by Medeiros *et al.* (2012) in the Doce River basin in Brazil, the highest yeasts count was 4,660 CFU/l. A study done in Brazil at Lago Rico River reported on 721.6 CFU/l yeast counts (Brandão *et al.* 2017). Total yeast counts up to 1,720 CFU/l in water and 4,085 CFU/l in sands were enumerated in a study by Maciel *et al.* (2019). Aquatic environments in the aforementioned studies were associated with anthropogenic activities, eutrophication and high influx of domestic and industrial waste. A rapid response of yeasts to organic contamination makes yeasts important indicators of nutrient enrichment since these convert easily accessible carbon sources into energy for reproduction (Brandão *et al.* 2010). Yeasts could potentially be informative water quality indicators. They can be utilized as complements and/or alternatives to faecal indicator bacteria.

OPPORTUNISTIC PATHOGENIC YEASTS

Some of the yeasts species mentioned in the section 'Yeast diversity in aquatic environments' are opportunistic pathogens and may cause mild to severe infections in humans. Most invasive yeast infections are frequently caused by pathogens from the genera *Candida* and *Cryptococcus* (Bajpai *et al.* 2019). Candidiasis is one of the common opportunistic infections caused by *Candida* species. *C. albicans* is the most prevalent causal species (Friedman & Schwartz 2019). The following non-*Candida albicans* species are also to cause candidiasis: *C. glabrata*, *C. parapsilosis*, *C. tropicalis*, *C. krusei* and *C. auris* (Kullberg & Arendrup 2015; Zupančič *et al.* 2016; Friedman & Schwartz 2019). Human cryptococcal infections are primarily caused by *Cryptococcus neformans* and *C. gattii* (Mada *et al.* 2017). Cryptococcosis is one of the leading causes of mortality in adults living with HIV in sub-Saharan Africa (Hurtado *et al.* 2019).

Rare non-*Candida* and non-*Cryptococcus* species are also associated with yeast infections. *Trichosporon* species (*Trichosporon asahii*, *T. faecale*) cause invasive trichosporonosis in patients with haematological malignancies and other medical conditions associated with immunocompromised people (Castano & Mada 2018; Maciel *et al.* 2019; Ruosta *et al.* 2019). Opportunistic pathogenic *Rhodotorula* species (*R. mucillaginosa*, *R. glutinis* and *R. minuta*) cause infections with high mortality rates in haematologic patients particularly on central venous catheters (Potenza *et al.* 2018). The following uncommon clinical yeast species have also been reported as opportunistic pathogens: *Clavispora lusitania*, *Cyberlindnera fabianii*, *Debaryomyces hansenii*, *Kluyveromyces marxianus*, *Meyerozyma guilliermondii*, *Pichia kudriavzevii*, *Saccharomyces cerevisiae*, *Torulaspora delbruecki* and *Yarrowia lipolytica* (Chitasombat *et al.* 2012; Al-Sweih *et al.* 2018; Ruosta *et al.* 2019). The above-mentioned pathogenic yeast species have been isolated from freshwater water environments (Medeiros *et al.* 2008, 2012; Brandão *et al.* 2010, 2011, 2017; Van Wyk *et al.* 2012; Monapathi *et al.* 2017; Moubasher *et al.* 2018; Maciel *et al.* 2019). There is a lack of studies that link these isolates/strains from the environment to those from clinical settings.

Virulence factors in pathogenic yeasts

The expression of virulence factors in pathogenic/opportunistic pathogenic yeasts enable them to cause diseases (Polvi *et al.* 2015). Detailed knowledge about these factors in yeasts is limited. Some of the virulent traits in pathogenic yeasts are high-temperature growth, adaptation to pH, overexpression of melanin, nutrient limitation, morphological transition, secretion of extracellular enzymes, induction of capsule formation and formation of biofilms (Polvi *et al.* 2015). Virulence factors have been detected in

some studies in pathogenic environmental yeasts (Zuza-Alves *et al.* 2016; Maciel *et al.* 2019). Virulence factors allow pathogenic yeast species to invade hosts, to resist their immune system defence mechanisms and to cause infections, especially in immunocompromised people (Abulreesh *et al.* 2019).

Antifungal resistance in pathogenic yeasts

Antifungal drugs are available to treat yeasts infectious (Perfect 2017). There has been a concerted effort to monitor and report on resistance development among clinical yeasts isolates to commonly used antifungal agents. Antifungal susceptibility studies have been conducted on pathogenic environmental yeasts (Medeiros *et al.* 2008; Brandão *et al.* 2010; Brilhante *et al.* 2016; Monapathi *et al.* 2017, 2018; Maciel *et al.* 2019) and antimicrobial resistance has been observed. Resistance to antifungal agents develops from continuous exposure of yeasts to antifungal agents (Morschhäuser 2016). Prolonged contact of pathogenic yeasts in water to antifungal agents could result from sub-therapeutic levels of antifungal agents that constantly land into aquatic environments (Singer *et al.* 2016; Meade *et al.* 2017). This is linked to prevailing therapy regimes (infection control or prophylactic treatment), disposal routes, waste (wastewater) treatment options and agricultural run-off. The presence of antifungal agents in any environment affects the diversity and selection of antifungal resistant pathogens/opportunistic pathogens (Cowen *et al.* 2015).

PUBLIC HEALTH CONCERN OF FINDING PATHOGENIC YEASTS IN ENVIRONMENTAL WATER

The occurrence of opportunistic yeast species in environmental water suggests a potential risk to direct water users. This public health threat is worsened by poor susceptibility to commonly used antifungal drugs (Maciel *et al.* 2019). People at peril are communities that use water for domestic and agricultural purposes as well as activities where direct exposure is common such as recreation and religious cleansing or baptism (Zenani & Mistri 2005). Direct contact with water polluted with pathogenic yeasts could cause diseases/infections in healthy and immunocompromised individuals (Monapathi *et al.* 2017; Maciel *et al.* 2019). This is a public and health concern and needs more research to highlight this aspect but also to generate sufficient data to evaluate if policy changes are required for including yeasts in water quality guidelines.

POSSIBLE ROUTES OF YEAST INFECTIONS: AQUATIC INTERVENTION

Some of the yeast species in water resources are pathogenic and infectious diseases may be transmitted through contaminated water (Ayanbimpe *et al.* 2012). Figure 1 shows possible routes of yeast infections *via* water resources. Drinking water is the direct route of yeasts to humans (DEFRA 2011). Drinking water can be a reservoir for opportunistic pathogenic yeasts, which can cause infections in immunosuppressed patients (Kanzler *et al.* 2008). Yeasts species of *Candida*, *Cryptococcus*, *Debaryomyces*, *Saccharomyces* and *Trichosporon* have been detected from gut microbiota in human (Hallen-Adams & Suhr 2017). Microorganisms in the gut constitute human sewage microbiome. These are from different human body sources, including skin, respiratory tract, oral cavity, gastrointestinal tract and urogenital tract. The sewage is taken to the WWTPs for treatment (Cai *et al.* 2014). These are the same WWTPs that are known to harbour pathogenic yeasts (Chu *et al.* 2018). Subsequently, treated and/or untreated wastewater will end up in surface water (Edokpayi *et al.* 2017).

Drinking water from surface and groundwater resources is purified through various processes and disinfected before it is distributed to consumers. If water is inefficiently treated, yeasts from the aforementioned resources could end up in drinking water (DEFRA 2011). Yeasts in drinking water distribution systems are known to act as pathogens (Oliveira *et al.* 2016). Their occurrence in drinking water can pose a health threat to consumers with direct daily contact such as drinking and showering (Novak Babič *et al.* 2016). The possible pathway of yeast infections from drinking to surface water is confirmed by the presence of similar genera of species in the gut, WWTPs and surface water. Furthermore, studies by Göttlich *et al.* (2002) and Oliveira *et al.* (2016) suggest groundwater as a yeast vehicle to drinking water. Plants

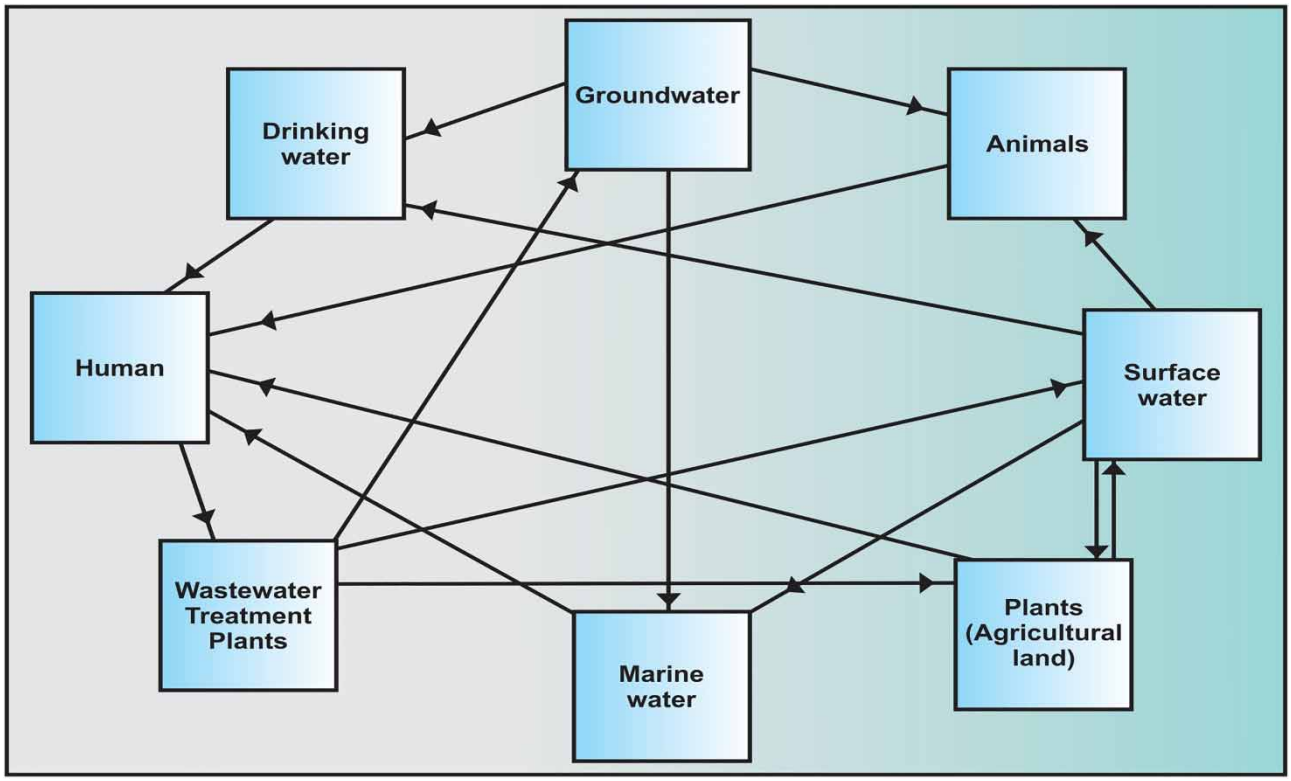

Figure 1 | Possible routes of yeast infections *via* water transmission.

may be the other route of yeast infections in humans. Faeces of animals and humans used as fertilizers in agriculture contain pathogenic bacteria and yeasts. The use of fertilizers could contaminate the soil and field crops, and ultimately infect consumers (Scheinemann *et al.* 2015; Al-Sadi 2017; Lamastra *et al.* 2018).

The human population exploits a large number of aquatic animal species for food (Ogden 2017). Some of these animals require surface and marine water for survival. If the water is contaminated with pathogenic yeasts, human beings are likely to be infected through consumption of these animals. There have been some reports on marine water contamination from oil spills, pharmaceuticals and personal care products and microplastics (Arpin-Pont *et al.* 2016; Brennecke *et al.* 2016). These reports are bothersome as marine environments are used for recreational activities such as swimming, fishing, surfing and boating (Sumaila & Cisneros-Montemayor 2010; Beaumont *et al.* 2019). From another public health view, in direct contact with the water, this association could serve as an additional route of pathogenic yeasts to humans.

MICROBIOLOGICAL RISK ASSESSMENTS

Microbiological risk assessment (MRA) is an estimate of the possibility of illness from a pathogen in a given population (Rocourt *et al.* 2003). It is vital in risk management and communication thereof to minimize negative impacts on human health (Brown & McClure 2006). MRA assists in policy development, public health decision-making and establishment of microbial pathogen regulations and research planning (Sherif *et al.* 2009). Most of the pathogenic yeasts isolated until now have been from clinical samples where known infections occurred (Shokohi *et al.* 2018; Consortium OPATHY & Gabaldón 2019; Friedman & Schwartz 2019). Finding similar species in environmental water is thus cumbersome. For aquatic yeasts, contact transmission is

normally the route of infection (Eames *et al.* 2009). In determining MRA in aquatic pathogenic yeasts, a qualitative exposure assessment would be ideal.

There are direct and indirect possible contact ways between yeasts and humans through aquatic pathways (Figure 1). Surface and groundwater are drinking water resources. Furthermore, they are also used in agricultural, industrial and/or domestic sectors (Wada *et al.* 2014; Katsanou & Karapanagioti 2017; Libkind *et al.* 2017). Drinking water or consuming plants and/or animals contaminated with pathogenic yeasts may also be an important direct exposure to humans. According to a study by Hageskal *et al.* (2009), drinking contaminated water has not caused acute diseases in healthy individuals. However, there is a risk of superficial or localized infections in these healthy individuals and more severe and invasive infection in immunocompromised persons. As mentioned in the previous section on marine environments, recreational activities also expose humans to possibly contaminated water.

A quantitative risk characterization would assist in determining the severity of known and potential adverse health effects (Rocourt *et al.* 2003). From clinical tests, for microorganisms to cause an infection, the number of colony-forming units (CFU)/ml in the bloodstream should be defined. In bloodstream infection, *Candida* CFU/ml in the first 50% positive blood culture had <1 CFU/ml of circulating organisms (Pfeiffer *et al.* 2011). For candidemia, classified as high-grade and low-grade candidemia, 25 CFU or more per 10 ml and 10 CFU or fewer per 10 ml of blood, respectively, were defined (Telenti *et al.* 1991). According to Perlin & Wiederhold (2017), a low initial concentration (often <10 CFU/ml) of the pathogen within the collected specimen can grow to cause an infection. This suggests that low levels of yeasts in direct exposure to humans could cause an infection. Similar quantitative risk data for environmental exposures are not available, and there is a necessity to generate such information.

CONCLUSION

The number of peer-reviewed articles about yeast diversity in water has increased and some have originated in South Africa. The present review largely focused on freshwater environments. Most of the studies on yeasts in aquatic environments address water pollution aspects. Yet, bacterial indicator species are mainly the microbes that are used in water quality assessments. Declining water quality is a global concern, and in these systems, the chemical and physical conditions are such that yeast species could survive. Some of these are known as pathogenic or opportunistic pathogens. Future studies are needed to generate data to determine whether it is necessary to include yeasts in water quality guidelines. This may be necessary if one considers the large sections of populations in developing countries that are immunocompromised, particularly those living with HIV. Studies on health implications have mostly been addressed on pathogenic clinical isolates. This creates a gap in research as similar isolates have been isolated from aquatic environments. The same resistance patterns to antifungal agents and resistance mechanisms associated with clinical isolates were also found to exist among environmental isolates. Molecular methods to study antifungal resistance mechanisms should be extended to environmental isolates. Direct exposure to polluted water is a health threat. Studies in the clinical settings have shown that to cause an infection, yeast level as low 1 CFU/ml is sufficient. Similar data for environmental water levels are needed. More studies are required in South Africa and globally to address the possible implications of antifungal resistant pathogenic yeasts in water.

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