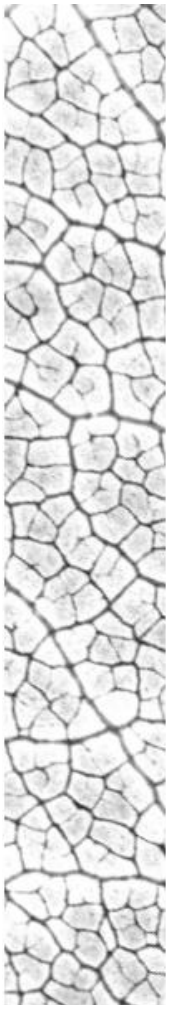

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Opportunistic mycoses among hepatitis patients in Iraq

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Abstract
Opportunistic mycoses are the human fungal infections associated with immunocompromised patients. Due to wide world incidences of Hepatitis infections, Opportunistic mycoses became more prevalence among patients with Hepatitis A virus (HAV) , Hepatitis B virus (HBV) and Hepatitis C virus (HCV) in Iraq. The current study focused on detection of *Candida* species as an opportunistic mycoses causative agents among HAV, HBV and HCV patients admitted to Misan Hospitals in Iraq. A swab samples from oral cavity were taken from patients with HAV, HBV and HCV during 1st Jan 2018 – 31 December 2018. The present study revealed that Sub- districts residents recorded higher number of viral infections (53) compared with urban residents (37). From total of 90 samples infected with Hepatitis viruses (HAV 40 , HBV 40 , and 10 with HCV) ,11 (27.5%) samples were infected with opportunistic mycoses among HAV patients , 19 (47.5%) from HBV patients and 7(70%) from HCV patients, whereas Control Group revealed 14 infections only with *Candida* species from total of 90 samples (15.5%). The study recorded different fungal species from oral cavity included: *Candida albicans* (32), *C.krusei* (2), *C.dubliniensis*(1), *C.tropicalis* (1) ,*and Fusarium verticillioides* (1).

Keywords: hepatitis, opportunistic, mycoses, Iraq

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INTRODUCTION

Hepatitis is one of the infectious diseases caused by viruses leads to damage of liver cells, and resulting in mild or moderate Jaundice cases or develop to acute morbidity incidences in addition to chronic liver cirrhosis or sometimes to liver cancer. Hepatitis A virus (infectious hepatitis) causes mild liver disease and may develop to severe illness, the virus transmits by water or contaminated food and by contact persons. The risk of HAV is low comparison with HBV and HCV, patients may recover completely and get acquired immunity for a long time. Although HBV ('homologous serum jaundice') is with higher risk than HAV, the most dangerous and deadly type is Hepatitis C virus (HCV) which cause liver cirrhosis, carcinoma, acute hepatic failure, coma and death (Negro 2014, Höfken 2013, Kurnatowski and Kurnatowska 2010, Nagao and Sata 2010, Lemon et al. 2018).

Currently, Hepatitis B virus (HBV) and Hepatitis C virus (HCV) considered the high chronic diseases that affect human health during the last decades in the world. Many Hepatitis viruses transmitted mainly through blood or blood products infected with the viruses, 80% of infected patients recorded chronic hepatitis cases, 25% developed liver cirrhosis, and then liver cancer (Coffin et al. 2012).

Most Hepatitis parasitic viruses when occupy human host cell it opens different tracks to weakened the human immunity defenses which lead to penetration of immunity barriers and cause cell damage. HBV is the causative agent of chronic hepatitis B (CHB) disease which transmitted by different tracks such as perinatal, sexual exposure, percutaneous, and by close contacts particularly among infants in hyperendemic regions. Sometimes Hepatitis C leads to serious liver cases during transmitted by contaminated blood processes. Many organizations and medical agents proposed a global strategy for controlling and elimination hepatitis C as a community health risk factor by 2030 (Terrault et al. 2018).

The vast majority of patients with HCV and HBV referred as people from developing countries, and viral hepatitis has become one of the leading causes of death in mentioned countries according to many surveys and studies, although the number of deaths from liver cancer due to hepatitis disease increased during the last decades in the world(McMahon 2010, AASLD-IDSA Hepatitis C Guidance Panel 2020, Höfken, 2013).

The infection by HBV and HCV leads to decline of human immunity system powerful which encourage

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opportunistic microorganisms such as fungi to be active and switch from nonpathogenic yeast to a pathogenic mold, that fight human organs and increasing chances of acute fungal infections. Millions of people that infected with the HCV and HBV develops morbidity cases by opportunistic mycoses, and thousands of them suffer from complications of cirrhosis or liver cancer associated with *Candida* infections (Paya 2001).

Although *Candida* is one of important genera of fungi that survive in different parts of human body as commensals microorganisms and safely controlled by healthy body, *Candida* cause a variety of diseases such as chronic candidiasis, vaginitis, meningitis, and endocarditis (Ergun et al. 2010) . The *Candida* genus characterized by having two fungal forms, spherical shape as yeast and filamentous as pseudohyphae, so it is called dimorphic fungus, that play an important role in healthy people as commensal microorganism with no risk factors, in addition to its ability to transform and switch from nonpathogenic form as a yeast into pathogenic form as pseudohyphae (Bhat et al. 2013, Williams and Lewis, 2000).

The presence of *Candida* in skin, mouth and gastrointesitinal system as nonpathogenic agents indicates a balance factor with other essential microorganisms, that keep the human body under the control of body barriers and host innate immune system (Höfken 2013, Williams and Lewis 2000). *Candida* is the most common genus of opportunistic fungi that infect patients with weakened immune system particularly Hepatitis patients. Candidiasis, the disease caused by *Candida*, occurred by the fungal species *Candida albicans*. The most preferable colonization zone and ecological niche for *Candida albicans* is human mucous membrane. *Candida albicans* strongly appears as opportunistic microorganism in case of people with weakened immunity specially Hepatitis patients that were recorded high rates particularly during liver transplant surgery (McMahon 2010, Kumar et al. 2006, Nagao et al. 2012, Naglik et al. 2008, Naglik et al. 2003).

Species belong to non- *albicans Candida* (NAC) cause outbreaks in addition to resistance against antifungal drugs due to the thick cell wall of fungi which has level of resistance to direct lysis, and has ability to cause higher mortality cases particularly with Immunocompromised patients. The most inducer agents facilitates opportunistic mycoses to be more active are using immunosuppressive treatments drugs, sustain the role of neutropenia, and open a track to pathogenic microorganisms during long-term therapy by antibiotics (Singh et al. 2020, Gow et al. 2013, Vila and Sultan 2020, Jabra-Rizk et al. 2016).

One of the processes in which mycoses activated the infection is the dysfunction of immunity system tools such as lymphocytes, and production of immunoglobulin A, which facilitate the attachment of the causative agent cell to the host cell surface via mucous and skin.

MATERIALS AND METHODS

Sample collection

From 1st January 2018 to 31st December 2018, 90 swab samples were received from Hepatitis patients admitted to Misan Hospitals in Iraq. Also 90 samples from control group with healthy people, matched for age and locations area. Samples were transferred to microbiology laboratory at Amarah Technical Institute.

Fungal identification:

A) Culture method

Identification of *Candida* species cultured on fungal media was identified according to morphological characteristics and physiological criteria. The present study used method of germ-tube test for diagnosis and classification of fungal species which inducing hyphal growths to form germ tubes in a culture with horse serum incubated for four hours at 37°C, which shows heavy growth of *Candida albicans* with defined germ tubes of *C.dubliniensis* (Raju and Rajappa 2011). Chrome agar method is a simple procedure to identify *Candida* species was used in present study, during incubation culture colonies at 35°C for 48 hrs. Color morphology appears different *Candida* species as presumptive identification using light microscope.

B) Molecular method

PCR process used to identify genetic molecular ID for *Candida* species followed by genetic analysis of fungal species using (RFLPs) with electrophoresis gel according to Williams and Lewis (2020), for determination of genetic ID to each species using pure culture of *Candida* colonies previously cultured on SDA.

RESULTS

Table 1. Prevalence of Hepatitis viruses associated with patients according to resident location

Type of Hepatitis	No. of infected patients in sub-districts area	No. of infected patients in Urban area
Hepatitis A	25	15
Hepatitis B	22	18
Hepatitis C	06	4
Total	53	37

Table 2. Oral cavity samples with *Candida* species among HAV , HBV and HCV patients

Sample no, of HAV patients	Sample no, of HBV patients	Sample no. of HCV patients	*Candida albicans*	*C. dubliniensis*	*C. krusei*	*C. tropicalis*	*Fusarium verticillioides*
1, 4	2, 3, 5	9	+++++	+	-	-	-
11, 13	12	15	+++	-	+	-	-
27	25, 26	28	+++	-	-	+	-
33	35, 37	-	+	-	+	-	-
41	43, 45	48	+++	-	-	-	+
54	52, 58	57	++	-	-	-	-
63	62, 64, 65	-	++++	-	-	-	-
74	75, 77	78	+++	-	-	-	-
86	84, 88	89	++	-	-	-	-

Table 3. Prevalence of Candida species among Hepatitis patients according to resident location

Oral cavity pathogens	No. of infected patients in sub-districts area	No. of infected patients in Urban area	Total no. of pathogens (%) n=90
Candida albicans	18	8	26 (28.8%)
C.dubliniensis	1	0	1 (1.1%)
C.krusei	1	1	2(2.2%)
C.tropicalis	1	0	1(1.1%)
Fusarium verticillioides	0	1	1(1.1%)

Table 4. Prevalence of Candida species associated with Control Group by resident areas

Enteric pathogen	No. of Candida species associated with non-Hepatitis patients in sub-district area	No. of on *Candida* associated with non-Hepatitis patients in urban area	Total no. of pathogens (%) n=90
Candida albicans	7	4	11 (12.2%)
C.dubliniensis	1	0	1 (1.1%)
C.krusei	1	0	1(1.1%)
C.tropicalis	1	0	1 (1.1%)
Fusarium verticillioides	0	0	0 (0%)

DISCUSSION

Table 1 revealed total of 90 infections with Hepatitis viruses, divided into 53 infections in sub-district area belongs to 25 HAV, 22 HBV and 06 HCV patients, whereas 37 infections in urban area (Bhat et al. 2013, Nagao et al. 2012, Nagao and Sato 2010) among HAV, HBV and HCV patients respectively. The patients originated from sub-district area recorded higher infections cases with Hepatitis B and Hepatitis C virus in comparison with patients from urban areas, this may be due to non-hygienic facilitates in rural community.

According to **Table 2**, *Candida* species associated with HAV, HBV and HCV patients belongs to: *Candida albicans, C.tropicalis, C.dubliniensis, C.krusei,* and *Fusarium vertcillioides*. 11 samples (27.5%) were infected with opportunistic mycoses among HAV patients, 19 (47.5%) among HBV patients and 7 samples (70%) among HCV patients.

As shown in **Table 3**, *Candida* species associated with HAV, HBV and HCV patients revealed 21 infections from rural area and 10 from urban area whereas **Table 4** shows 10 infections with *Candida* and non-*Candida* species in sub-district area and 4 infections in urban area among Control Group, this increasing of fungal infections associated with Hepatitis patients comparison to Control Group may due to poor hygienic facilities in rural areas. Oral cavity mucous membrane is the weak ecological niche that hospitalize the *Candida* yeast fungus and increase the virulence of mycosis pathogenicity specially those patients originated from rural areas suffering from decline of community health services.

CONCLUSION

Candidiasis is a disease caused by dimorphic causative agent *Candida* , which looking for opportunity to be more virulence factor among patients with a weak immunity barriers such as severe illness incidences like Hepatitis patients, so infection with Hepatitis viruses leads to decline the powerful of immune defenses and open a pathways for opportunistic mycoses to be more active particularly among HBV and HCV patients.

CONFLICT OF INTEREST

I declare no conflict interest related with this paper.

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