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Original Research Paper

Community Medicine

CRITICALLY & NON CRITICALLY ILL PATIENTS' INVESTIGATION BASED SCRUTINY TO COMPARE TRENDS OF CANDIDURIA IN COVID & NON COVID ERA: AN ANALYTICAL STUDY.

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ABSTRACT

BACKGROUND: To reduce delays in diagnosis & treatment in order to prevent severe morbidity & mortality from certain opportunistic infections like fungal co infections, awareness about them is required. Actually these pathogens take advantage of an opportunity that can stem from various factors (not normally available).

OBJECTIVES: To study the pattern about frequency distribution of candiduria in critically &non critically ill patients of Covid & Non Covid era in a tertiary medical care setting. To explore any association between anticipated predisposing factors & occurrence of candiduria.

METHODOLOGY: A cross sectional analytical study was undertaken based on non probability convenience sampling to compare investigation reports of critically & non critically ill candiduria patients in a tertiary care hospital. This comparison study was conducted to observe difference in pattern of distribution of candiduria patients in Covid-19 & Non Covid-19 era.

CONCLUSION: It was seen that candiduria patients increased in Covid-19 era with altered male is to female ratio. These were mainly associated with co morbidities like Diabetes Mellitus etc & age group > 50 yrs. Candida non albicans species were reported more in Covid-19 era in comparison to Non Covid timings. To avoid opportunistic infection by commensals, re stratification & scaling up of infection control practices are required in all medical set ups.

KEYWORDS : Candiduria, Covid-19, Critically ill, Infection Control, Bhopal.

INTRODUCTION:

People with severe COVID-19, such as those in an intensive care unit (ICU), are particularly vulnerable to fungal infections. These fungal co infections are spotlighted with increasing frequency and can be associated with severe illness and death.

Candiduria is defined as the presence of candida species in the urine. Candiduria could be asymptomatic and rare in relatively healthy patients, but is more common in hospitalized patients and especially those in intensive care units (ICU). Research based evidences proved that the incidence rate of candiduria is as high as 1.61% in hospitalized patients and 22.89% in ICU patients. Risk factors for candiduria are diabetes, urinary catheter, female gender, antibiotics, major abdominal surgeries and ICU admissions. It is research proven now that presence of candiduria is an archetypal pointer of serious underlying conditions & the mortality rate in candiduria ICU patients is about 3 times higher than those without candiduria. Other than being a marker for seriously ill patients that need particular attentions, candiduria is also an independent risk factor for invasive candidiasis (IC). The Infectious Diseases Association of America (IDSA) guidelines (2016 version) emphasized the importance of treatment for candiduria patients under high-risk candidiasis conditions. A molecular analogousness between candida strains isolated from candidemia and concomitant candiduria indicated that hematogenous dissemination possibly existed in ICU candiduria patients.[1-8]

The presence of fungus in urine or funguria is a common finding at a tertiary care hospital. Candiduria is observed in 16-22 per cent of hospitalized patients. The common risk factors for funguria are female sex, extremes of age, intensive care unit (ICU) admission, urinary catheterization, diabetes mellitus, and broad-spectrum antibiotic therapy. Candida albicans is the most common fungal aetiological agent, but because of resistance to antifungals etc, non-albicans candida species accounted for > 50 per cent of urinary candida isolates in certain studies.[9]

As COVID-19 is an emerging infectious disease & there is scarcity of literature on this topic, more & more research work is needed to cover all aspects of this malady including associated candiduria.

AIM: To study the pattern about frequency distribution of candiduria in critically &non critically ill patients of Covid & Non Covid era in a tertiary medical care settings of Bhopal city.

OBJECTIVES: To explore any association between anticipated predisposing factors & occurrence of candiduria.

METHODS:

Study Centre: JK Hospital & Research Centre, LNCT University.

Study duration: Comparison of 3 specific months' data (season, geography & setting wise matching) for the year 2019 & 2020 (1 August to 1 November).

Study design: A cross sectional analytical study.

Study Area: Critical and other care units of JK Hospital & RC. Bhopal

Study Subject: Investigation reports of critically ill patients (with candiduria) admitted in hospital during above mentioned period. Non critical patients with candiduria were also included in this study.

INCLUSION CRITERIA: Patients from all age groups were included. All study subjects whose records were properly maintained with date-wise investigation reports & provisional diagnosis were included.

EXCLUSION CRITERIA: All patients whose investigation records were poorly maintained and whose MRD files were incomplete were excluded from study.

Sample Size: All the IPD patients admitted in given study period.

Sampling: Non probability convenience sampling.

Tools and Technique:

Study Tool: MRD files of those study subjects who have qualified the inclusion criteria.

Technique: Microbiological culture & susceptibility data regarding status of candiduria in critically ill/non critical admitted patients for 3 consecutive months (August, September & October) of 2019 (Non Covid era) & 2020 (Covid era) was collected, compared & analysed as per aim and

objectives of the study. KOH mount & Germ tube test were done to identify fungus type.

Data Collection and Analysis: Data was retrospectively collected from MRD files of study subjects for both the years to facilitate comparison purposes. Analysis was done by comparing both the data after assessing normal distribution.

Statistical Analysis Plan: Incidences (monthly basis) of candiduria in 2 consecutive years were observed for comparison purposes to assess Covid-19 association.

RESULTS:

In 2020 Covid era study duration, out of total 22 candiduria positive patients, 2 candida non albicans cases were isolated in the month of August. 5 candida non albicans were reported in samples of September month. In October, 14 candida non albicans were reported along with one candida albicans case. All these were isolated from urine culture & sensitivity samples of 21 critically ill patients & 1 Non critical patient. 17 patients were from medical ICU, 2 from cardiac critical unit, 2 from casualty & 1 from Covid general ward. Amongst these 6 females & 16 males group, 3 were in 40s age group, 7 in 50s age group, 9 in 60s age group & 3 were in their 70s.

In contrast to above data, in 2019 Non Covid study duration, out of total 12 candiduria positive patients, 3 candida non albicans cases were isolated in the month of August along with 1 candida albicans case. 4 candida non albicans were reported in September month with 2 candida albicans cases. In October, 2 candida albicans cases were reported. All these were isolated from urine culture & sensitivity samples of 7 critically ill patients & 5 non critical patients. 6 patients were from medical ICU, 1 from casualty & remaining from general wards. Amongst these 6 females & 6 males group, 4 were in 20s age group, 1 in 30s age group, 3 in 50s age group, 3 were in their 60s & 1 in 70s.

DISCUSSION:

In our study, as opposed to year 2019, in Covid-19 pandemic timings, number of diagnosed candiduria IPD patients were more & that too were candida non albicans majorly. With that caveat, we tried to consider why the candiduria rates may increase with Covid -19 pandemic.

One study suggested that because of hyper inflammation, there could be disruption of respiratory mucosal membranes to facilitate commensal candida to invade deeper tissues, but still there are evidences that COVID-19 in itself is not directly associated with the increased invasive candida disease rates. Classic clinical risk factors (eg, central lines, antibiotics, steroids), sepsis-induced gut microbiota translocation, changed composition of micro biota-promoting commensal/ colonizing candida, altered infection control practices are the other factors during the pandemic, which could have predisposed for increased invasive candida disease. [10,11,12]

In another study it was reported that managing, multiple complex patients of Covid-19, while wearing extensive personal protective equipment may have influenced infection prevention and control practices. Maintaining a pre–COVID-19 standard of oral care in critical care patients is difficult due to COVID-19 infection control concerns. Subsequent increased oropharyngeal candida colonization combined with invasive ventilatory support may have enhanced invasive candida disease.

It was a common finding of many studies that candida albicans was the predominant (79.4%) species isolated irrespective of COVID-19 status. Rodriguez and colleagues given a report which confirmed significant invasive candida disease in COVID-19 patients caused by predominantly non-albicans species, including candida auris. It could be due to probability of geographical variation. In this comparative study it was found that in last 5 years span, only one patient in Wales had C. auris isolated, so its absence during pandemic from Wales cohorts is not unexpected and is opposite to what is seen in Colombia, where C. auris is endemic in certain regions, leading to healthcare transmission and outbreaks. As C. auris has been predominately identified as a healthcare-associated infection, this prospective is suggestive of the facts that the increase is related to a change in practice associated with the pandemic and the impact of potentially unnecessary use of azoles in driving the emergence of resistant species. Mortality rate in the Colombian study was higher than Wales, but there's a need for inquiry if this is associated with a delay in appropriate antifungal therapy, particularly in cases of non-albicans candidemia. [13,14]

A growing public health threat in the US, C auris can cause life-threatening and difficult-to-treat infections in hospitalized patients. Florida State of USA is tracking C auris cases since 2017 to limit their communicability. There additional screening found that 52% of 67 COVID-19 patients in the dedicated unit were colonized with the yeast. [15]

Then it becomes a matter of concern, joint CDC-Florida Department of Health investigation has taken cognizance of the incidence & found that health care workers of dedicated Covid-19 unit wore 2 layers of gowns and gloves during COVID-19 patient care, which the CDC does not recommend. Their base layer—including eye protection, a cloth gown, N95 respirator, gloves, a bouffant cap, and shoe covers—stayed on during their entire shift. They donned a second disposable gown and gloves before entering each patient room and then doffed them on exit. Health care workers cleaned their base-layer gloves with alcohol-based hand sanitizer during doffing and washed their hands when they left the unit. [15]

Probable causes deducted were contamination of base layers during donning and doffing, using shared mobile computers (not disinfected frequently), and thirdly when accessing medical supplies in open bins kept in hallways. After taking corrective & preventive actions like the hospital removed supplies from the hallways, enhanced cleaning and disinfection of shared equipment, and ended double layers of personal protective equipment, authorities detected no further C auris cases. [15]

So there are strong chances that because of panic of pandemic, infection control practices might have been jeopardized in terms of true patients' care. Hospital infection control practices were shrunken to just donning-doffing of the PPEs & hand sanitization only in that dreadful haunting period. For months, hospitals were continuously flooding with Covid-19 positive cases with paucity of beds. Health care systems were working exhaustingly without a pause for months. Nonstop inflow of bed occupancy kept the intensive & extensive disinfection measures like fogging etc. at bay. None of the beds/rooms were empty to carry out full washing & fogging etc at that time.

Still none of the evidences are meeting the highest standard of accuracy for exact pathogenesis of these co-infections is there, there are several immunological mechanisms that can facilitate the development of fungal diseases. SARS-CoV-2 infection leads to the release of danger-associated molecular patterns. Consecutive activation of innate pattern recognition pathways may cause hyper inflammation during the antiviral immune response, leading to lung tissue damage and causing disruption of mucous membranes, thus contributing to an environment that allows for fungal infections. While most microbiological detection of candida spp. as commensals does not have pathological relevance, transition into invasive candidiasis during critical illness has a reported lethality rate of up to 70% and is considered a relevant complication in COVID-19 patients. Details regarding the susceptibility of these patients to candida infection and characteristics of an impaired immune response have not been described yet. [16-21]

Woehrle T in 2008 reported that extensive contamination of the hospital environment has been detected in hospitals experiencing outbreaks of C. auris infection, warranting adherence to strict hospital infection prevention practices, such as enhanced cleaning of rooms with chlorine-based disinfectants at high concentrations (0.5%) for highly resistant pathogens such as C. auris. Critically ill COVID-19 patients with C. auris infection tend to have concurrent conditions (e.g., diabetes mellitus, chronic kidney disease) and risk factors (e.g., need for mechanical ventilation, receipt of steroids). To reduce complications, admission times in overburdened hospitals, and death rates among COVID-19 patients, identifying and treating C. auris infections is vital.[22]

A recent report that investigated changes in the fecal fungal microbiomes of COVID-19 patients has shown increasing prevalence of opportunistic fungal pathogens such as C. albicans, C. auris, and Aspergillus flavus.[23] This finding is a milepost clincher to pinpoint transfiguration in invasive candida albicans & non albicans diseases.

Another important finding of He Z study was the fact that multisite colonization was common in candiduria patients. Up to 70.83% of candiduria patients had *candida* positive cultures in sputum. They speculated that the incidence of multisite colonization and invasive candidiasis may be higher than is generally thought. Several risk assessment tools including colonization index (CI), corrected colonization index (CCI) and candida score (CS) etc are used in hospital settings to screen out as early as possible to revert the track of anticipated catastrophe.[24]

Akin certain above studies, our study findings are also pointing towards similar environmental conditions & baseline situations.[10,11,12,13,14,22,23]

Before Covid-19 era in our hospital in the year 2019, all types (age-group wise, morbidity-profile wise, status wise) of patients were getting admitted. At that time (post monsoon season) candida albicans & candida non albicans co infections were noted mostly in immune-compromised ICU patients with co-morbidities, but they were fewer in comparison to Covid-19 era, when only & only Covid positive patients got admitted (hospital was designated as a dedicated Covid-19 centre by the authorities). During pandemic time maximum candida positive patients were from ICUs with co-morbidities (chiefly Diabetes Mellitus type-2) and age group majorly more than 50 years. Also it was noted that number of candida non albicans infections in Covid-19 era outnumbered candida albicans one. Male is to female ratio for funguria was found altered. Use of immunomudulatory/ immunosuppressant drugs along with altered infection control practices could be a strong reason.

One of the limitations of the study was that data related to associated conditions was not uniform. Another limitation was that follow up of study subjects for the response to the treatment and outcome was not done in a structured manner. Third limitation is that drug susceptibility profiles were not tracked for all candiduria patients. So overall, it's a simple very basic study to contribute any database.

CONCLUSION:

In pandemics, it is a warping reality that capriciously disciplined systems & transpiring health practices heralded a breach in ongoing hospital infection control practices. Perilous climb of morbidity rates & creaky public healthcare mechanisms are making infection rates harder to abate. Opportunistic infections busy the immune system, leaving other problems in human body unaddressed. So it's time to make quantified information available through epidemiological steps to reiterate with assertiveness about future infection control policies for any anticipated pandemic. Early screening for underlying fungal infections is desired by utilizing appropriate indices/scores etc. Early culture & drug susceptibility testing is an essential component in any fungal infection to accurately diagnose the specific etiological agent & to start precise anti-fungal therapy on time. Surveillance & monitoring of emerging/re-emerging infections is to be done with ultra-caution to get the nub of problem for spearheading positive changes.

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