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A Clinicomycological Study of Meningitis among HIV Seropositive Patients in a Tertiary Care Hospital, Odisha

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1. Introduction

- Cryptococcal meningitis caused by *Cryptococcus neoformans* an opportunistic infection in HIV seropositive patients. [1] It is one of the presenting manifestation of AIDS. [2]
- This encapsulated yeast is found in soil contaminated with bird droppings particularly from pigeons & chickens, usually inhaled through lungs and remain dormant for many years. Reactivation which occur primarily among immunosuppressed individuals such as people living with human immunodeficiency virus/acquired immunodeficiency syndrome (PLHA), leads to infection and most of which is meningitis. [3]
- It is most common lethal fungal infection in patients with AIDS worldwide. [4 - 6]CM is a significant cause of morbidity and mortality among PLHA worldwide. [4 - 7] Recent data indicates that the incidence of cryptococcal infection is high in developing countries such as India. [8 - 9]
- It is the most common central nervous system (CNS) fungal pathogen in PLHAs. [9 - 11] The clinical signs and symptoms of *Cryptococcus neoformans* are indistinguishable from those of many other causes of meningitis. [12]

2. Materials and Methods

- The study was conducted in the Department Of Microbiology, a Tertiary Care Hospital Of Western Odisha (Vimsar, Burla), India from January 2023 to June 2023. A total of 68 HIV seropositive and clinically suspected cases of meningitis were included and processed further.
- The CSF samples of 68 cases were processed for fungal culture and biochemical test after preliminary microscopic examination, comprising wet mount, negative staining with India Ink and Gram's staining. The samples were inoculated on two sets of Sabouraud's Dextrose Agar (SDA) without antibiotics, one incubated at 37°c, another at 24°c in a special Biological Oxygen Demand (BOD) incubation.
- The colony morphology was noted. Cryptococcus neoformans was identified base on yeast like mucoid colony on SDA and Urease test. For a definite diagnosis colony from SDA was sub - cultured on Niger Seed agar which was incubated at 37°c and observed for appearance of brownish to blackish colored colonies due to melanin pigment production of *Crypptococcus neoformans.*
- A prospective study was undertaken in our institution with purpose of identifying laboratory diagnosis of CNS Cryptococcus in HIV reactive patients and their clinical findings.

Statistical Analysis
The data was entered in Microsoft office excel and analysis was done by appropriate statistical tool.

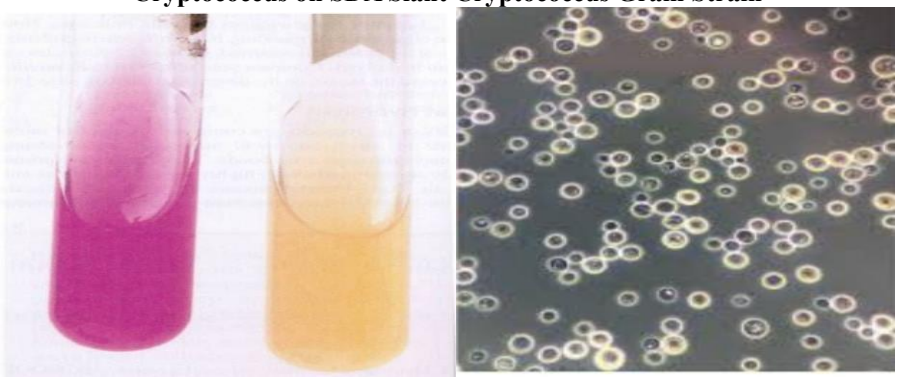
Ethical Approval
Taken from Institutional Ethics Committee (IEC) of VIMSAR, BURLA, ODISHA, INDIA.

3. Results

- Out of 68 processed CSF samples, 7 yielded growth of Cryptococcus neoformans, showing prevalence of 10%. Out of these 5 (72%) were male and 2 (28%) were female. All the positive patients were in the age group of 20 - 40 yrs (71%).
- The clinical presentation were almost same in most of the patients showing features of meningitis. Most common signs and symptoms being fever and headache (100%) followed by altered sensorium (71%), neck stiffness (57%), vomiting (28%). The CSF cell counts, glucose, and protein concentrations were non - specific.

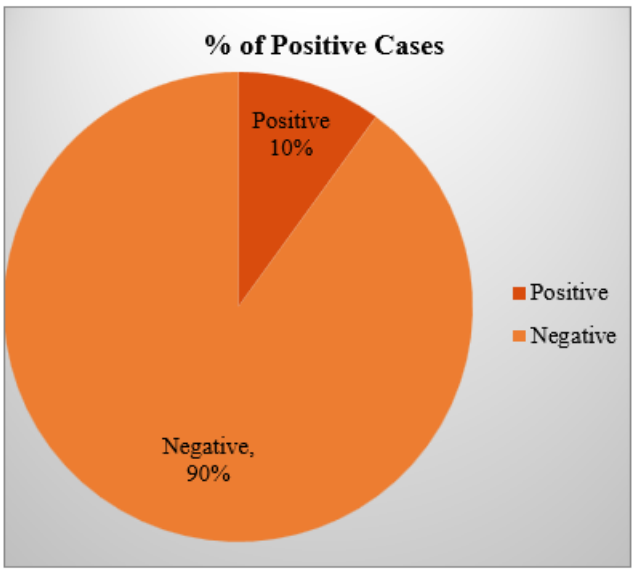


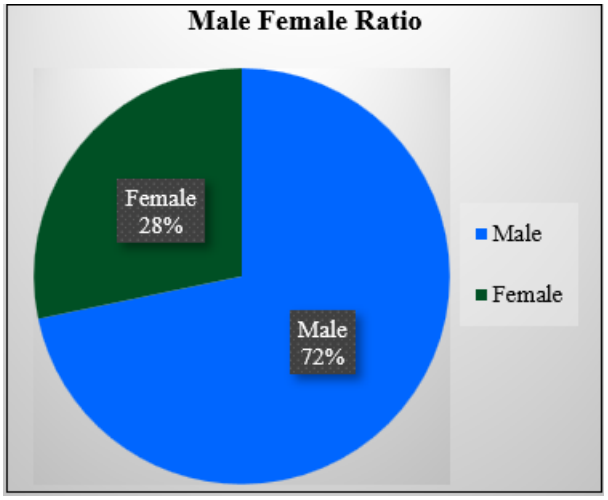
Cryptococcus on SDA Slant Cryptococcus Gram Strain

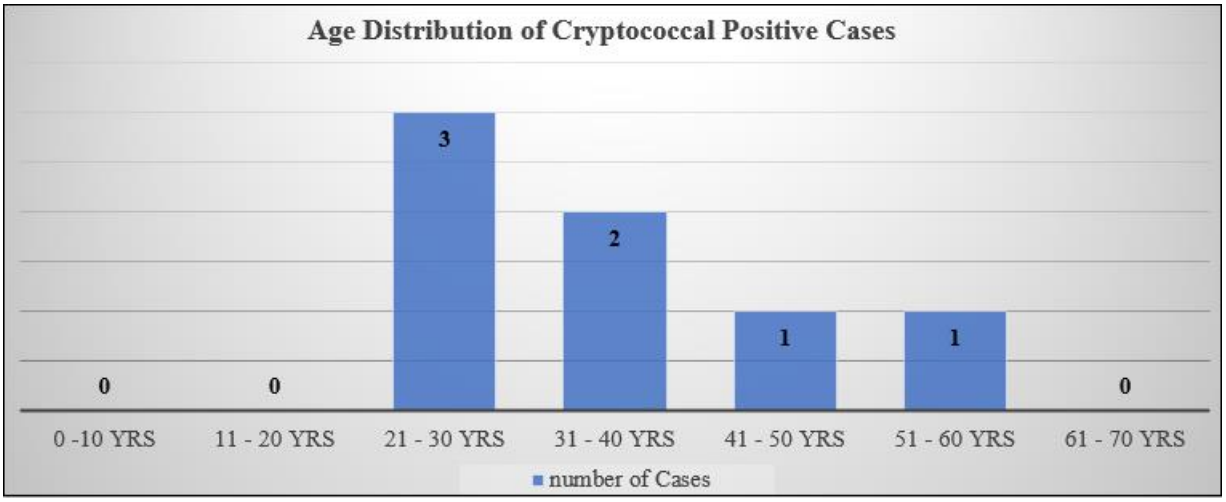


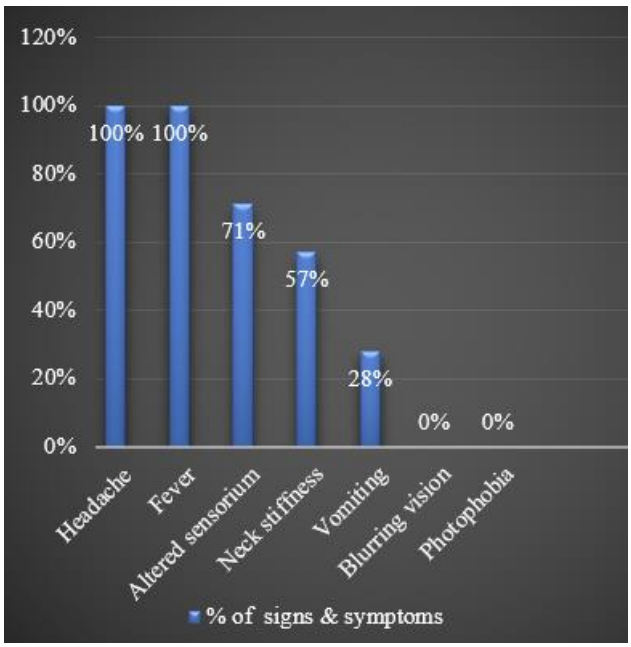
Positive Negative **Cryptococcus India Ink Strain**

Cryptococcus Urease Test









4. Discussions

- *Cryptococcus neoformans* is one of the most common opportunistic infection in AIDS. [1] The asexual form is characterized by oval to spherical budding yeast cells with a polysacchharide capsule, while the sexual or perfect stage is characterized by the presence of basidiospores. The sexual form has not been described in association with clinical specimens and is observed only during mating. The asxual form with capsule is frequently seen in clinical specimens. [13]
- Although cryptococcosis is an established disease, worldwide prevalence, was low before AIDS era. The HIV pandemic has a profound impact on the prevalence of cryptococcal disease. In India, HIV infection is wide spread and it was estimated that approximately 2.5 million were HIV - infected in 2006. [14]
- The asexual yeast *C. neoformans* has been classified as four serotypes based on the capsular polysaccharide, glucurononoxylomannan. Capsular types A through D correspond to the variants *C. neoformans var. grubii* (A), *C. neoformans var. gattii (*B and C), and *C. neoformans var. neoformans.* [15] It is a well - recognized opportunistic infection among cell - mediated immunodeficient patients, such as HIV infection, organ transplantation, and rheumatologic conditions requiring immunosuppressive agents. In HIV patients, it is classified as as acquired immunodeficiency syndrome (AIDS) - defining condition. [16]Characteristics of Cryptococcus that permit its survival within the host include a polysaccharide capsule, and phenol oxidase enzyme uses catecholamine as a substrate to produce melanin, which accumulates in the cell wall. It is the use of catecholamine that may produce a predilection for involvement of the CNS. [17]

- Over the years, three successive studies spanning over a period of 12 years (1992 - 2004), in AIIMS, it revealed that parallel to increase in number of HIV cases; HIV cryptococcosis co - infection increased from 20% in 1992 - 1993 to 30%, 1996 - 2000, 37% and 49% in 2000 - 2004. [18]In our study it was observed that males were involved slightly more than females, which may reflect a difference of exposure rather than a difference in host susceptibility, as it was noted earlier. Though children are less commonly affected, now there is increase in the prevalence of *Cryptococcal meninigitis* observed in HIV - infected children. [18 - 19]
- The clinical manifestation observed in the laboratory confirmed cases were fever and headache (100%), followed by altered sensorium (71%), neck stiffness (57%), vomiting (28%). Baradkar *et al*. noted headache, fever and altered sensorium (100%), neck stiffness (90%) and vomiting was present in (52.6%) cases, similar to our study. [20]Our findings are also comparable with a study conducted by Lakshmi *et al*. in India. [2] Prasad *et al.,* noted - headache in 89.5 % cases, fever in 78.9%, altered sensorium in 23.7%, neck rigidity in 13.2% and seizures in 10.5% cases. [21] Our findings are comparable with above studies in India. Other presentation such as lethargy, coma, papilledema, focal neurological deficits, and cranial neuropathies were observed by different workers, no such similar complications were noted in our study. [22]

5. Conclusion

As CM remain a significant cause of morbidity and mortality particularly among PLHA in source poor environments. As the clinical feature of Cryptococcal Meningitis is necessary for early definite diagnosis and subsequent initiation of appropriate therapy to decrease morbidity and mortality.

Source of Support: Nil

Conflict of Interest: None declared.

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