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Prevalence of Central Nervous System Cryptococcosis In A Tertiary Care Hospital.

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Abstract: *Cryptococcosis is a systemic opportunistic fungal infection caused by Cryptococcus neoformans. Cryptococcus neoformans is a capsulated opportunistic yeast fungi that predominantly affects HIV infected and other immonocompromised hosts involving the CNS either as meningitis or meningo encephalitis. Central nervous system Cryptococcus is an important cause of mortality among immuno compromised patients. A prospective study was conducted on a total no. of 150 patients who were suffering from CNS symptoms with cryptococcal meningitis and other co-morbid conditions like diabetes, corticosteroid use, chronic debilitating illness and in HIV/AIDS patients. The aim of the study was detection and isolation of cryptococcus neoformans in CSF samples of immunocompromised other co-morbid conditions like diabetes, corticosteroid use and chronic debilitating illness patients who suffered from suspected cryptococcal meningitis at Govt. General Hospital, Guntur. This study helps to assess the prevalence of CNS Cryptococcosis in immunocompromised individuals including HIV/AIDS patients. This helps the clinician and community to take proper measures & proper patient care. 150 CSF samples are screened by various cryptococcal investigations (India ink / gramstaining / culture / CALAS). Prospective study was conducted from July 2015 to December, 2015 for a period of 6 months. Of the total 150 cases, males were more commonly involved than females with the ratio 2:1. The total prevalences of Cryptococcus was 16% in high risk patients, where in HIV positive prevalence is 12.6% in diabetes mellitus 2.6% and others it is 0. 8%. Routine mycological evaluation is necessary for early definite diagnosis and proper treatment. This will decrease morbidity and mortality.*

Keywords: *Cryptococcus neoformans, cryptococcal meningitis, HIV/AIDS/CALAS immune compromised patients.*

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I. Introduction

Cryptococcosis is a systemic opportunistic fungal infection caused by Cryptococcus neoformans. Central nervous system Cryptococcosis is an important cause of mortality among immuno compromised patients. CM is acquired by inhalation of aerosalised form of Cryptococcus. It is found in soil contaminated with bird droppings particularly from pigeons and chickens[3]. Reactivation which occurs primarily among immune suppressed individual such as HIV/AIDS patients and other co-morbid conditions involving the CNS either as meningitis or menigoencephalitis[3]. The unique feature of Cryptococcus is the ability to cross blood-brain barrier of brain. Yeast cell migrate directly across the endothelium or carried inside the macrophages as 'Trojan horse'.[5] Cryptococcal meningitis presents as chronic meningitis with head ache, fever, sensory and memory loss, cranial nerve paresis and loss of vision (due to optic nerve involvement)[5]. Cryptococcus is worldwide distributed it accounts for nearly 1 million cases with more than 6,25,000 deaths annually.[3] The present study was conducted on total number of 150 cases who are suffering from suspected cryptococcal meningitis at Govt. General Hospital, Guntur.

Cryptococcus is the most common CNS fungal pathogen in HIV/AIDS patients. Clinical signs and symptoms of CM are indishguishable from other cause of meningitis.[9] This infection is fatal without treatment. Therefore rapid recognizing, diagnosing and treatment are required to decrease the morbidity and mortality.[3]

II. Material And Methods

Study population contains 150 cases suspected of Cryptococcal meningitis. 150 CSF samples are screened by various Cryptococcal investigations, by following SOP's 1ml of CSF sample is collected under aseptic conditions which is divided into three parts. First part for gram staining and india ink method, second part for fungal culture by inoculating on SDA and third part for antigen detection by latex agglutination test by using Meridian CALAS kit as per its guidelines. Direct microscopy examination - Take a clean glass slide add one drop of India ink sample cover with cover slip see under low power and high power. This will demonstrate

the capsule which appears as refractile delineated clear space surrounding the budding yeast cell against the black background. Capsule may be twice or thrice diameter of yeast cell. India ink stain is less sensitive ie. 60-70 %. In gram staining it shows gram positive budding yeast cell. In culture centrifuse sediment of CSF is inoculated on SDA without antibiotic, blood agar and chocolate agar and incubated at 37^0 c for 24 hours. Colonies appeared as mucoid creamy white. Conformation of crypotococcus species by inoculation into niger seed agar by urease test. Cryptococal antigen was detected from centrifuge sediment of 150 cases of CSF sample by using meridian cryptococal antigen latex agglutination test. The titre of 8 or more is conformed as positive for Cryptococcus. Definite diagnosis of CNS Cryptococcal infection is based on clinical features of chronic meningitis with laboratory findings such as positive India ink preparation, Gram's staining, positive culture of Cryptococcus and demonstration of Cryptococcal antigen in the CSF by latex agglutination test. CALAS is a rapid, sensitive (95% sensitivity) and specific test for diagnosis of Cryptococcal meningitis.

Tables:

Table -1Age and sex wise distribution of cryptococcal meningitis

Sno	Age group	Study group	
		Male	Female
1	15-45	10	6
2	26-35	23	10
3	36-45	55	20
4	46-55	12	14
	Total	100 (67%)	50 (33%)

Table -2 Analysis of clinical symptoms in chronic meningitis

Sno	Age group	Study group	Percentage
1	Head ache	140	93%
2	Fever	130	87%
3	Neck stiffness	11	7%
4	Altered sensorium	50	33%

Table -3 Prevalence of Cryptococcus in India ink/gram staining / culture /CALAS

Sno	Age group	India ink 12%	Gram staining 11.3%	Culture 12.6%	CALAS 16%
1	15 -25	2	2	2	2
2	26 – 35	3	3	3	3
3	36 -45	12	12	13	17
4	46 – 55	1	0	1	2
Total		18	17	19	24

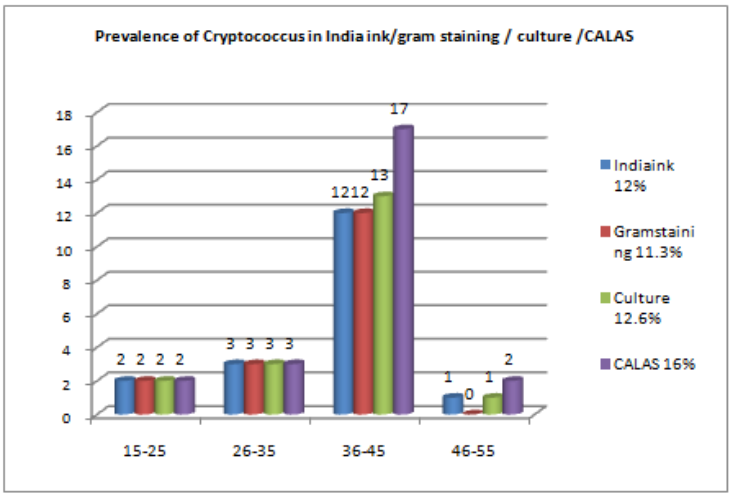

Table – 4 Prevalence of Cryptococcus in high risk patients

HIV	DM	Others
19 (12.6%)	4 (2.6%)	1 (0.8%)

III. Results

A total number of 150 clinically diagnosed meningitis were screened for Cryptococcus neoformans by various methods during the period of 6 months from July 2015 to December 2015. Table no. 1 shows analysis of age and sex distribution of chronic meningitis. The age of the patients ranging from 15-55 years. Males and females ratio is 2:1. Males were more exposed than females. Prevalence of chronic meningitis is more in 36-45 age group. Table no. 2 shows analysis of clinical symptoms in chronic meningitis patients. In this table headache was 93%, fever 87%, neck shiftness 7%, altered sensorium 33%Table no. 3 shows prevalence of Cryptococcus by Indiaink/gram staining/culture/CALAS. In this table positivity in India ink is 12%, gramstaining 11.3%, culture 12.6% and CALAS 16%. Table no. 4 shows prevalence of Cryptococcus in high risk group. In HIV/ AIDS it is 12.6%, diabetis milletus 2.6% and others 0.8%.

IV. Discussions

Cryptococcus neoformans is one of the most common opportunistic fungal infections in immunocompromised and debilitating individuals.[4]The group cryptococus contain atleast 39 species, but few are able to cause disease in human beings. Most of the human infections are due to cryptococus neoformans.[4]Cryptococus neoformans is an encapsulated yeast first identified as human pathogen in 1894, when it was isolated from tibia of a patient in Germany by Buese and Buschke in the same year it was also isolated from peach juice in sanfelice.[4]The first description of cryptococcal meningitis was published in 1905 by Van Han Semann4, although a case of chronic meningitis described in 1861 by Zenker prior to pathogen isolation, was probably first case history[9].Cryptococus neoformans exists in asexual or sexual forms. Asexual form is characterised by oval to spherical budding yeast cells with a polysaccharide capsule. The sexual form has not been described in association with clinical specimens and is observed in only during mating. The asexual form with capsule is frequently seen in clinical specimens[9].

Virulence is due to oxidase, protease enzymes and carbohydrate capsule when can be demonstrated by negative staining with 10% nigrosin in India ink Non capsulated mutant forms lack pathogenecity. [9]Infection occur through inhalation of yeast cells as respiratory pathogen, then remain dominant depending on host immune system. Dissemination is due to serious defect in host immune system.[13]The risk factors include advanced HIV stage, corticosteroid use, last stage of cancers organ transplantation, lymphomas, sarcoidosis, lymphoproliferation disorders, hypogamma globulinimia, systemic lupas erythmatosis. Although cryptococus is an established disease, worldwide prevalence was low before AIDS era. The HIV pandemic was an impact on the prevalence of cryptococal diseases.[13] Cryptococcal meningitis is an emerging opportunistic infection as documented in various Indian studies, especially among HIV infected patients and also important cause of mortality among the patients.[4]Published literature and the present findings clearly show the high prevalence of the infection in India. In our country leukemia and patients with diabetes mellitus have emerged as important risk groups besides HIV infected patients. In our study, it was observed that males are more commonly involved than female ratio was 2:1, which may reflect a difference of exposure rather than a difference in host susceptibility1. Male female ration (2:1). In present study the prevalence of cryptococus neoformans was 16% (24 out of 150). This value is comparable with the reports published by KV. Prasad et al, (16.6%) 2016, Mukti keth et al (14.3%) (2012).

Various studies have been conducted in different parts of the world including India, to find the prevalence of Cryptococcal meningitis in immunocompromised patients has been found to vary widely from 19.8% to 45.8%. In our study it was observed that prevalence of Cryptococcal meningitis in HIV infected patients is 19 out of 150 (12.6%). This value is comparable with reports of Lakshmi etal they found 10 986%) (2007). In our study it was observed that prevalence of cryptococcal meningitis in DM is (4 out of 150) 2.6% value compared with KN Prasad et al (3%). (2016 Clinical manifestations observed in present study were head ache 140/150 (93%), fever 130/150 (87%), were stiffness (20/150) 13%, altered sensorium 950/150) 35%. Muktikasu Das et al[3] noted head ache 100%, fever 100%, neck stiffness 90%, altered sensorium 100%. Prasad et al[1] noted headache 89.5%, fever in 78.9% altered sensorium 23.7%, neck stiffness 13.2%, Lakshmi et al noted head ache 92%, fever 49.79% altered sensorium 79%. Our findings are comparable with above studies in India.

Three successive studies conducted in AIMS, New Delhi over a period of 12 years (1992 – 2004) had revealed that parallel to increase in number of HIV cases : HIV crytococcosis coinfection increased from 20% in 1992-96 to 30% in 1996-2000 and 49% in 2000-04.[4]

In this present study (July – December, 2015) it was observed that the prevalence was decreased in over a period of 6 months due to advanced treatment with ART in HIV (AIDS) patients throughout India. Culture is considered to be the "gold stand" method of diagnosing for C. neoformans, but it takes at least 3 days to a maximum time of a month for growth. The other method is by demonstration of encapsulated yeast in India ink preparation from CSF which through specific stain poor sensitivity (-50-80%). Antigen detection represents

the most immediate and rapid way to enhance methods for diagnosis of Cryptococcus. It is a highly sensitive and rapid test and antigen can remain detectable for several months after infection.

V. Conclusions

Cryptococcal Meningitis remaining a significant cause of morbidity and mortality particularly among immune compromised patients mainly HIV/AIDS. Present study indicates a high prevalence of Cryptococcal Meningitis in immunocompromised patients in tertiary care hospital. Routine mycological evaluation is necessary for early definite diagnosis and subsequent indication of appropriate therapy as the majority of patients respond well to treatment. Antigen detection by latex agglutination proved to be both sensitive and specific method for the diagnosis of Cryptococcal Meningitis.

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