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High percentage of young men with meningitis in HIV positive patients: A tertiary hospital study from South India

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Abstract
Objective: To describe the demographic characteristics of HIV patients with meningitis.
Study Design: Cross-sectional, observational.
Methods: We studied the age, sex, occupation and etiological profile of meningitis in 116 people living with HIV from a tertiary care hospital in India over a period of four years. Results: Fifty four percent of the patients were young adults [<35 years]. They were overwhelmingly of the male sex [70.4%] and were more commonly employed in performing manual labour [71.4%] occupations for daily living. Tuberculous [82.6%] meningitis was the most common aetiology.
Conclusion: A focused clinical approach and public health program targeting this particular population at risk is much-needed.

Keywords: Meningitis, HIV, AIDS, People living with HIV, HIV Seropositive

Introduction
There are 36.7 million People Living with HIV [PLWH] in the world according to the 2016 UNAIDS report [1]. Asia is home to about 4.8 million of PLWH [2]. The Indian subcontinent, a major land mass of Asia has its unique racial and cultural characteristics. One half of PLWH in Asia are from India [3].
People Living With HIV are constantly under the shadow of a threat of serious infections such as pneumonia, severe parasitic infections and meningitis [4]. Meningitis [inflammation of the coverings of the brain] is a life threatening illness affecting many HIV seropositive individuals. It claims thousands of lives every year in HIV seropositive individuals [5].
Much of our understanding of meningitis in PLWH is derived from Western [6] and African studies [7]. In these studies most of the patients were men [52-92%] and the mean age of the patients was below 40 years [32-37%]. Cryptococcal meningitis was most common etiology in these studies. Data regarding meningitis in PLWH from Asia [8] is very limited. HIV infection being both a physical and social disease manifests with distinctive features in India. Indian data shows that meningitis claims 56.3% of all the neurological disorders in PLWH [9]. In Indian PLWH, Cryptococcal meningitis alone or in combination with tuberculous meningitis contributes to about 46.3% of all infections of the CNS [9]. This in contrast to the meningitis in HIV seronegative patients which is commonly [45.8%] due to bacterial infections [10]. The dynamics of age distribution, the gender characteristics, occupational and etiological profile of meningitis in PLWH from India have been discussed only rarely [9]. Knowledge of the demographic factors and etiological profile of meningitis, a grave illness in PLWH is important in guiding health policy and patient management that will have the greatest impact with constrained resources. Our objective was to present the detailed analysis of the demographic features of meningitis in PLWH from a semi urban South Indian Hospital.

Methods
Study Design: Cross sectional observational. We collected data from 116 consecutive adult [>14 years] HIV positive inpatients with the diagnosis of meningitis from 2016 to 2019 at the Government General Hospital, Guntur, an apex 1000 bedded tertiary referral medical college hospital in a semi urban locality in South India. It was a cross-sectional study.

The hospital caters to over 20 million people in the surrounding area. Women aged 45 years or more were considered as peri- and postmenopausal [11]. Persons occupied with unskilled work were categorised as manual labour. The diagnosis HIV infection was made as per standard guidelines [12]. All patients were on Oral once per day Tenofovir 300mg, Lamivudine 300mg and Efavirenz 600mg regimen.

Clinical diagnosis of meningitis was based on neck stiffness and signs of meningeal irritation with any of fever, headache, altered sensorium and focal neurological deficit. Diagnosis of tuberculous [13], Cryptococcal [14], Bacterial [15] and aseptic meningitis [16] was confirmed by CSF analysis and Imaging. Clinical assessment was done by the staff neurologist. CSF analysis was done as per standard techniques. CT scan brain was done and MRI Scan was performed when deemed necessary by the staff neurologist. Data was collected from the case records of the patients. Patients were reviewed every month for one year period. But the study data is from the first admission only.

All the patients provided written informed consent for lumbar puncture, CSF analysis and data collection. Institutional ethical Committee, Guntur Medical College, Guntur approved the study. Data was tabulated in MS Excel 2010 and was analysed by IBM SPSS version 21. Data was described as mean and SD and percentages. All missing data was excluded from analysis.

Results

We studied 116 HIV seropositive meningitis patients. 70.4% of them were men. The mean age of the study group was 35±9 years. Over 50% of the patients were young adults less than 35 years age and over 85% of the patients were less than 50 years old[Fig 1A]. Among women premenopausal age group constituted a high percentage of 81.6% [Fig 1B].

Overwhelmingly, 71.4% were employed in manual labour. Both men and women in the study had similar occupational profiles (p=0.06) [Fig 2A].

82.6% patients were diagnosed to have meningitis of tuberculous aetiology. Aseptic meningitis was diagnosed in 10% of the patients. There were no gender differences in the aetiology of meningitis (p=0.3) [Fig 2B].

Discussion

Our study of meningitis in the PLWH cohort showed an alarmingly high number of young adults employed in physical labour, a significant number composed of the male sex and most of them of tuberculous origin.

Elderly people are considered more vulnerable to serious infections than young adults [17]. It is surprising that in our study more than 50% of patients were young. One of the reasons may be poor anti retro viral drug adherence [18] due to a false sense of physical vigour in this age group. Since HIV infection is more common in persons with promiscuity and drug use [19], habits associated with the young rather than the elderly, meningitis may have surfaced more commonly in these people. As the youth constitute a major portion of the populace in a developing country like India, this age distribution of the disease is of paramount importance. Much of the intellectual, socio cultural and economic development of the country is dependent on its young adults. Hence, the disease is a threat of national importance which needs urgent attention. Jarvis [20] etal, Rajasingham [21] *et al*., and Hakim [22] *et al*., from the heavily HIV burdened African continent also reported a similar age grouping with a mean of 30-34 years. A 1995 study from USA [6] and a study from Indonesia [23] in 2009 also report the similar young age distribution of the disease. Hence, this characteristic age grouping is prevalent worldwide.

Majority of patients were men in our study. This may be due to the numerical superiority of men in the PLWH cohort in our region [24]. It may also be due to the higher sexual promiscuity [HIV infection risk] and alcoholism [HIV infection and meningitis risk] in men [19]. Similar male predominance was observed in studies from various parts of the world such as Indonesia [23] [76.6%], Uganda [21] [49%] and Cambodia [25] [76.4%].

Women of premenopausal age group appear to be more than the peri and post-menopausal group in this cohort. A systematic study of 2000 men and women in Kenya and Zambia [26] elegantly explains why young women have a higher prevalence of HIV than young men. 'Women often have older sexual partners, and men rarely have partners much older than themselves. Greater susceptibility of women to HIV infection is also an important factor in the male-female discrepancy in HIV prevalence. Also, Herpes simplex virus type 2 infection, which is more prevalent in young women than in young men, is probably one of the factors that increases women's susceptibility to HIV infection' the authors suggest [26].

Most of our patients [71.4%] were employed in work involving manual labour. Studies show that being employed in jobs involving manual labour is a risk factor for HIV infection [19]. This may be due to the lower health awareness in these people [27]. There are 300 million persons employed in manual labour in India [28]. As such this is the number of potential victims at risk for this fatal illness. A study from Ethiopia [29] found that 23.4% of PLWH with neurological disease are occupied in manual work. The relatively heavier burden of the disease on the prime productive age group is detrimental to national growth and development.

In our study TB meningitis was the most common etiology. Given the high prevalence of TB in our region [30] and the immunosuppression in HIV infected individuals this finding may be expected. But many other Indian studies such as Kumar [31] *et al*., in 2012 and Sharma [10] *et al*., in 2004 and Wadia [32] *et al*., in 2001 and Satishchandra [9] *et al*., in 2000 have reported that cryptococcal meningitis was the most common CNS infection in PLWH. A study from Beijing [8] also reported a high incidence of cryptococcal meningitis in HIV patients. Chilean [33], Mexican [34], Zimbabwean [22], Brazilian [35] and Thailand [36] studies show the same. Georgia [37] in Europe and Indonesia [23] however report higher tuberculous meningitis than others in PLWH.

As the state of Andhra Pradesh has one of the highest numbers of tuberculosis cases [30], this infection may be more common than Cryptococcus in our region. The national programs for HIV and tuberculosis control need to focus on this deadly manifestation of these co infections. The Hospital data collection and the small sample size are limitations of the study.

Our study of 116 meningitis patients over a four-year period is one of the largest reported demographic analysis of meningitis in HIV seropositive individuals from India. Our study shows that meningitis in PLWH is common in young men. This picture is similar to the disease demographics reported by other studies. Hence, global policies should

target the youth and the male gender in addressing meningitis in PLWH. We also have seen that, in our people, the meningeal inflammation is due to tuberculosis, unlike in studies from other parts of the world where it is due to cryptococcal infection. This calls for a tuberculosis tailored policies of prevention and treatment of the disease. People employed in unskilled work formed a high proportion of the subjects. This association of meningitis and occupation in PLWH has to be studied further in large populations from different geographic locations.

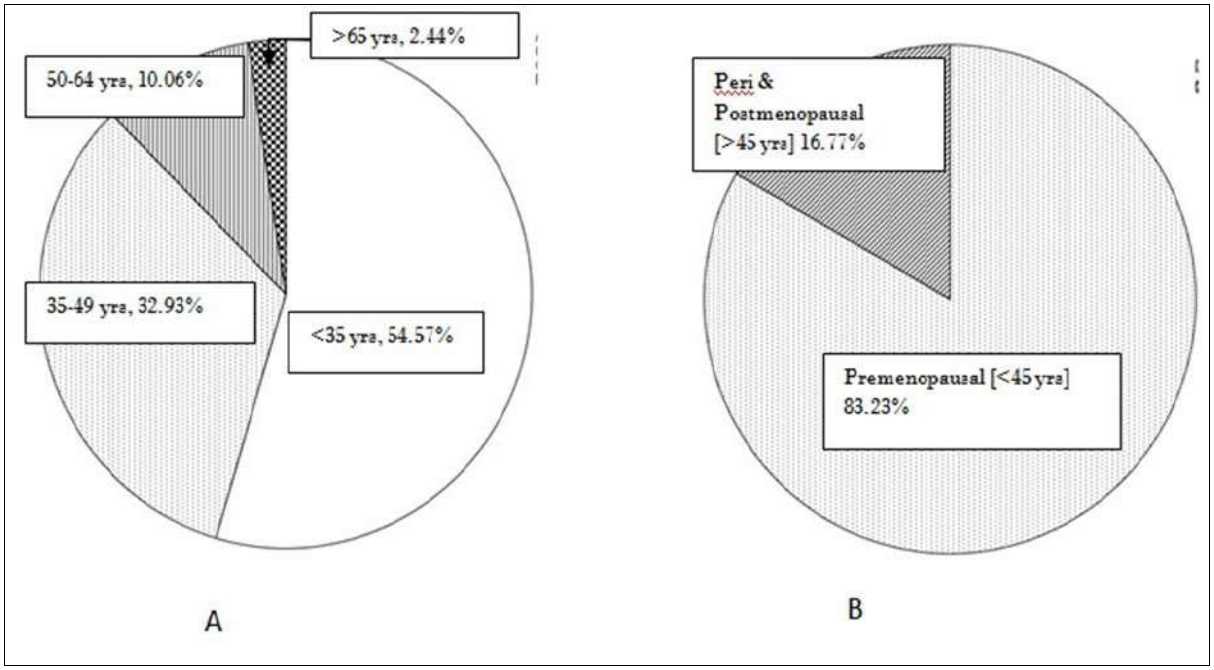

Fig 1A: Age distribution of PLWH diagnosed with meningitis, B) Age distribution in women with respect to menopause.

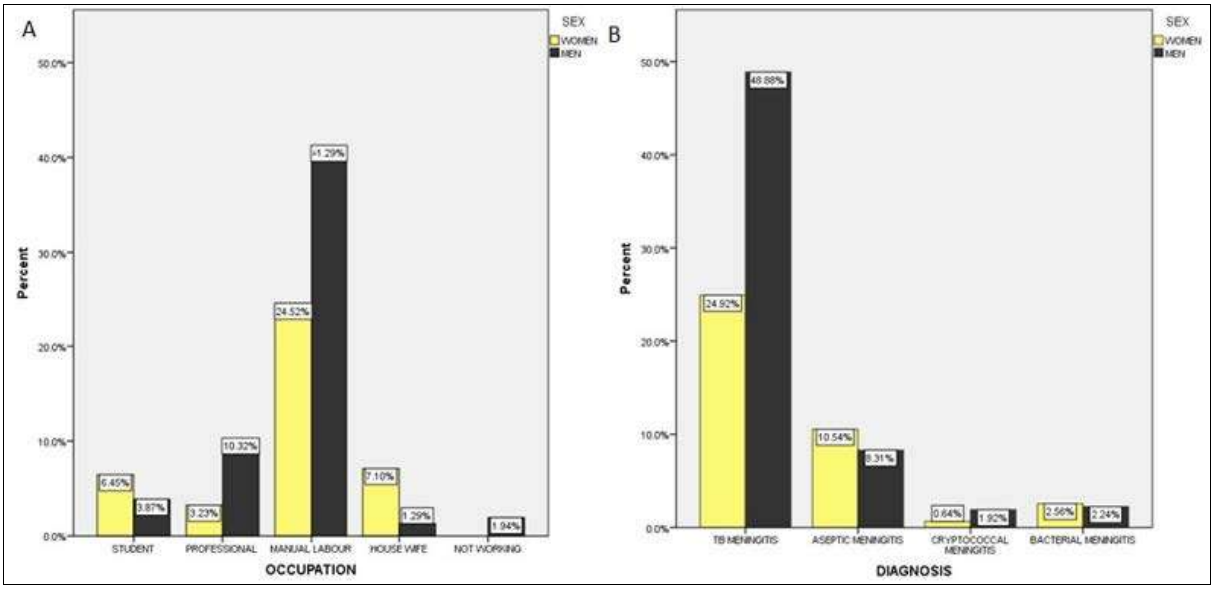

Fig 2A: Employment characteristics, B) Etiological profile of meningitis in PLWH

Authors' contributions

SA conceived the study and designed the study protocol; SA and KSG carried out the clinical assessment and interpretation of these data. SA drafted the manuscript; BJA SA and KSG critically revised the manuscript for intellectual content. All authors read and approved the final manuscript. SA and KSG are guarantors of the paper.

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Nil

Competing Interests

None declared

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None

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