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POSTER ABSTRACTS

612.ACUTE LYMPHOBLASTIC LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Hepatitis B Reactivation without Hepatitis Is a Common Event in Adolescent/Adult Patients of Acute Lymphoblastic Leukemia with Occult Hepatitis B (OHBI) Treated on Pediatric Protocols and Warrants Prophylactic Antivirals: A Prospective Cohort Study

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Introduction:
Patients with occult Hepatitis B infection(OHBI) (HBsAg negative but HBcIgG &/or anti-HBs positive in the absence of immunization) are at an increased risk of Hepatitis B(HBV) reactivation while on and after chemotherapy. It can present over a spectrum ranging from asymptomatic or mild transaminitis to fatal hepatitis, affect the dose intensity of chemotherapy and compromise outcomes. The reported risk of reactivation is variable (1-24%, Yeo, 2009), and depends on the type of therapy and the method used to detect reactivation. Antiviral prophylaxis is recommended in patients with OHBI who are treated with antiCD20 monoclonal antibodies and those who undergo allogeneic stem-cell transplant, however this has not been evaluated in patients treated on pediatric-inspired ALL protocols comprising of several immunosuppressive drugs..

Methods:
This was a prospective longitudinal cohort study conducted at a single tertiary care center in India between October 2017 to July 2021 (CTRI/2017/01/007747). The primary objective was to study the incidence of HBV reactivation in patients with OHBI on ALL protocol, and secondary objectives were to study the incidence of OHBI, HBV related hepatitis and its impact on chemotherapy intensity. Newly diagnosed patients with ALL/LBL, aged ≥15 years were screened for the presence of OHBI. Patients with OHBI were considered for enrollment into the prospective part of the study if they were treated on intense protocol (modified BFM-90 ALL protocol), had normal liver function tests, and no co-infection with HCV, HIV or history of HBV vaccination. Liver functions were monitored twice weekly during the induction/reinduction phase, prior to the early and delayed intensification and once every 2-3 months during the maintenance phase. HBV DNA copies by quantitative PCR (threshold for detection 20 units/ml), were measured at baseline, week 4, week 8, week 20, 32, week 48, completion of maintenance and every 3-6 months for 1 year. If a patient developed hepatitis, serum was collected for HBV DNA levels, HBsAg, HB core IgM antibody, IgM HAV antibody, IgM HEV, HCV and CMV DNA levels.
HBV reactivation was defined as- either increase in serum HBV DNA level to more than 1 log higher than that of baseline or any copy numbers if it was negative at baseline. Seventy five patients with OHBI were to be studied to detect a true incidence of >10% HBV reactivation at a one-sided significance level of 5% and 90% power (Fleming's design)

Results:
A total of 566 patients were screened for the study, and 172(30.4% (95% C.I. (26.6-34.4)) patients were diagnosed with OHBI. 74 patients were enrolled in the prospective part of the study (Fig 1). The baseline characteristics of the study population are summarized in Table 1. HBV DNA was detectable at baseline in only 2(2.3%) patients. 51 patients (68.9%) completed all phases of treatment. The median follow-up was 21.6 months (range 0.03-53.5 months). A total of 402 HBV DNA tests were done in this cohort with an average of 5 tests per patient. HBV reactivation occurred in 5 patients ((6.7% 95% C.I.(1.03-12.47)), none of these patients developed hepatitis during HBV reactivation. In all the patients, reactivation occurred during the maintenance

phase. All of these patients were started on antivirals (Entecavir). Overall 15(20.3%) patients developed hepatitis during the study period and CMV viremia was the cause for hepatitis in 4(26.7%) patients and HCV infection was the cause in 1 (6.6%) patient. Median AST, ALT during the episodes of hepatitis were 363 and 459 respectively (range AST 150-3490, range ALT 218-1950). Two(2.7%) patients had a delay in administration of chemotherapy due to hepatitis and median duration of delay was 21 days (range 18-24).

Conclusion:

We conclude that the risk of HBV reactivation is significant in adolescent/adult ALL patients with OHBI treated on pediatric inspired ALL protocols. HBV related hepatitis is a late event, and monitoring with liver function tests alone is not sufficient. The use of prophylactic antivirals is justified in patients with ALL.

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Figure 1. Consort Diagram of Screening and Enrollement of Patients

Table 1. Baseline characteristics of study population

Characteristic	n = 74 (%)
Age in years, median (range)	29 (15-56)
Gender M/F	54/20 (73/27)
Diagnosis ALL LBL	 71 (95.9) 3 (4.1)
Risk factors 1. Past history of transfusions 2. Illicit drug use 3. History of Sexual exposure	 35 (47.3) 14 (18.9) 40 (54.1)
Past history of jaundice	1 (1.4)
Liver function tests- median(range) 1. Aspartate aminotransferase 2. Alanine aminotransferase 3. Total bilirubin	 32 (11-401) 40 (8-522) 0.77 (0.24-6.89)
HBV serology 1. Anti-HBs alone positive 2. Anti-HBs Borderline 3. Anti-HBcIgG alone positive 4. Both anti-HBcIgG and anti-HBs positive 5. Baseline HBV DNA positive	 40 (54) 3 (4) 9 (12.2) 21 (28.4) 2 (2.7) (<20 IU/ml in both cases)

Figure 1