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SCREENING FOR PRIOR EXPOSURE TO HEPATITIS B VIRUS INFECTION IN PATIENTS UNDERGOING CHEMOTHERAPY

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Abstract:

Introduction: *Chemotherapy in patients with occult hepatitis can lead to the reactivation of Hepatitis B and even acute liver failure in immunosuppressed patients. We investigated the current trend of screening for previous exposure to hepatitis B in patients receiving chemotherapy in Pakistan.*

Materials and Methods: *In this retrospective multicenter study we collected data from the medical records of patients who underwent chemotherapy during a period of six months. Data were collected to assess the screening for Hepatitis before chemotherapy.*

Results: *A total of 182 patients who underwent chemotherapy were studied. The mean age of patients was 52.8 ± 14.9 years; 101(55.5%) were male. 140 (76.9%) were diagnosed with having solid organ malignancies while 42 (23.1%) were reported to have hematological malignancies. In our sample, 103 (56.6%) patients were screened for HBsAg, and amongst these patients, 3 patients tested positive. Hepatitis B core antibody (HBcAb) was checked in only 3 (1.6%) of the patients. The mean level of liver enzymes including ALT, AST, GGT, and ALP were 42.09, 38.98, 63.48 and 138.81, respectively. Ultrasound reports were available for 113 patients and the most common finding was a normal ultrasound 43(38.1%), followed by fatty liver 29 (25.7%).*

Conclusion: *Approximately half of the patients receiving chemotherapy are screened for active hepatitis B infection and screening for occult Hepatitis is almost negligible. Strategies are needed to ensure that all patients receiving chemotherapy should undergo complete screening of Hepatitis B before commencing chemotherapy.*

Key Words: *Occult hepatitis B, HBsAg, HBcAb, Immunosuppression, Chemotherapy.*

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INTRODUCTION :

Hepatitis B virus infection (HBV) and its complications are amongst some of the most serious health-related problems in many parts of the world. Reports indicate that more than one-third of the world's population has had positive serological evidence of infection with HBV in the past or present and that there are 350–400 million carriers of hepatitis B [1]In endemic areas, chronic Hepatitis B infection has a carrier rate of 8–20%. Its average rate of prevalence is 2–7% in the Mediterranean, Central Asian and Middle Eastern countries and it is about 2.5% in Pakistan (2, 3). There is a high risk of Hepatitis B reactivation in patients who are undergoing chemotherapy and immunosuppressive therapy. In patients with cancer, chemoradiotherapy is associated with several complications, such as changes in liver transaminases and jaundice, which makes it challenging to differentiate between iatrogenic conditions and Hepatitis B reactivation. For this reason, knowing the virological status and liver profile of patients before therapy initiation can prove beneficial. This screening and evaluation includes the routine performance of Hepatitis B surface antigen (HBsAg) and ruling out previous exposure to Hepatitis B or any occult hepatitis B virus (HBV) infection by Hepatitis B core antibody (HBcAb)

Several reports have described the risk of flares of chronic Hepatitis B in patients treated by chemotherapy for hematologic and solid malignancies, with the highest risk occurring when chemotherapy is discontinued (4-6). Various studies show that the risk of reactivation of Hepatitis B is between 20% and 50% in HBsAg positive patients and 3% to 9% in HBsAg negative but HBcAb positive patients (7).

Serum samples positive for HBcAb, but negative for both HBsAg are compatible with acute, resolved, and chronic Hepatitis B virus (HBV) infection as well as with occult HBV infection. The identification of HBcAb in the absence of HBsAg in organ transplant donors and in candidate patients for chemotherapy and immunosuppressive therapy requires further investigation because of the risk of HBV reactivation. Given the lack of sufficient antecedent studies on the prevalence of occult Hepatitis B in patients receiving chemotherapy and/or immunotherapy, the present study aims to examine the prevailing system of screening patients for HBcAb undergoing these therapies to guide physicians' decision making.

MATERIALS AND METHODS:

After approval from the ethical review committee, all patients who underwent chemotherapy in the Oncology unit of Aga Khan University Hospital Karachi and Hayat Abad Medical Complex Peshawar from 1st January 2018 to 30th June 2018 were identified and their medical records were reviewed. Demographic information including age, gender were collected on the proforma designed for this study. Laboratory investigations including HBsAg, HbcAb, HBeAg, LFTs, other concerning labs and ultrasound (US) liver were recorded using the electronic record systems available. The type of malignancy and chemotherapeutic agents received were also recorded. Patients who are already immunocompromised, known cases of HBV, cirrhotic, or had incomplete data were excluded. Data were analyzed by descriptive statistics like means, median, range, standard deviations and percentage using SPSS version 20.

RESULTS:

A total of 227 patients were reviewed, of which 45 patients were excluded (9 were diagnosed cirrhotic patients, 12 were known cases of chronic Hepatitis B and 24 had incomplete data). A total of 182 patients were studied, of which 130 were from Karachi and 52 were from Peshawar, Pakistan. Patients characteristics are given in Table 1.

Table 1: Baseline characteristics of patients (n=182)

Age (years), median; range	52.8 (20-86)
Sex, n%	
Male	101 (55.5)
Female	81 (44.%)
Cancer type (n %)	
Gastrointestinal	42 (23.1%)
Breast	29 (15.9%)
Lymphoma	28 (15.3%)
Genitourinary	26 (14.3%)
Head and Neck	17 (9.3%)
Musculoskeletal	12 (6.6%)
Lungs	09 (4.9%)
Others	19 (10.4%)
Mean ALT level (n=175), IU/L	42.09
Mean AST level (n=123) , IU/L	38.98
Mean GGT level (n=168) , IU/L	63.48
Mean ALP level (n=166) , IU/L	138.81
Mean Bilirubin level (n=171), mg/dL	1.093

Out of 182 studied patients, 140 (76.9%) were diagnosed with solid organ malignancy while 42 (23.1%) were diagnosed with hematological malignancy. The most common type of solid organ cancer was GI cancer with a frequency of 42 (23.1%), followed by breast cancer with a frequency of 29 (15.9%), and genitourinary cancer with a frequency of 26 (14.3%) and the most common type of hematological malignancy was Lymphoma with a frequency of 28 (15.3%).

Out of a total of 182 studied patients, 103 (56.6%) were screened for HBsAg, and amongst these patients 3 patients tested positive. In our sample, only 3 (1.6%) were screened for HBcAb, amongst which 1 (33.3%) tested positive. HBeAg screening was not done for 98.4% of the population. It was positive in 66.7% of cases when available. HBV DNA by PCR was not done for 98.4% of the population. The viral load was 1423,46789 and 26772413 IU/ml in the three cases where this data was available.
Ultrasound liver reports were available for 113 (62.09%) patients of the population. The most common result was a normal ultrasound (43 patients, 38.1%), which was followed by a fatty liver (29 patients, 25.7%).

DISCUSSION:

The risk of hepatitis B reactivation increases with the onset of chemotherapy (8-10). Studies in other parts of the world highlight the importance of occult hepatitis B infection, where HBsAg is negative (11, 12). According to the EASL 2017 guidelines for Hepatitis B virus infection, patients undergoing immunosuppressive therapy (immunotherapy or chemotherapy) should be screened with Hepatitis B serum markers including HBsAg, HBsAb, and HBcAb.

AASLD guidelines also recommend the same protocol (13). Similarly, Asian Pacific guidelines recommend screening with HBsAg and HBcAb in patients undergoing immunosuppressive therapy (14). The risk of HBV reactivation in this group varies widely according to the virological profile, the underlying disease and the type and duration of the immunosuppressive regimen. These subjects can be tested for serum HBV DNA before immunosuppression. If viremic, they should be treated similarly to HBsAg-positive patients (15). Patients who are HBcAb positive without HBV viremia, are classified into those with high, moderate and low risk (16). In the high-risk group (reactivation risk >10%), antiviral prophylaxis is recommended. Prophylaxis should continue for at least 12-18 months after stopping immunosuppression and monitoring should continue for at least 12 months after prophylaxis withdrawal (17-20). In HBsAg negative, HBcAb positive subjects with moderate (1-10%) or low (<1%) risk of HBV reactivation, pre-emptive therapy, not prophylaxis, is generally recommended (21). Pre-emptive therapy is based upon monitoring HBsAg and/or HBV DNA every 1–3 months during and after immunosuppression and starting treatment in case of detectable HBV DNA or HBsAg seroreversion (21, 22).

Hepatitis B carries a significant burden in Pakistan (23). This study found that the Hepatitis B core antibody was infrequently tested in our population. Our study shows that while patients undergoing chemotherapy or immunotherapy are regularly tested for Hepatitis B through HBsAg screening, other Hepatitis markers are not checked as consistently. Current practices should address this gap by conducting thorough screening panels which would be in line with up-to-date guidelines. Potential barriers to Hepatitis core antibody screening include the costs of additional testing, being unaware of best practice guidelines and lack of resources to conduct these investigations.

The strengths of this study include that it took place in the Oncology departments of two major tertiary care hospitals in urban areas of Pakistan. This allowed us a good insight into the pattern of practice concerning Hepatitis B screening taking place in chemotherapy and immunotherapy related contexts in Pakistan's health care system. The population type was vast and covered patients with a variety of illnesses while addressing a specific research question. Limitations include the sample size as the inclusions of more centers would allow us to better assess screening practices.

CONCLUSION:

Approximately half of the patients receiving chemotherapy are screened for active hepatitis B infection and screening for occult Hepatitis is almost negligible. Patients undergoing immunosuppressive treatment are already at risk for several morbidities and conducting a full hepatitis B screening panel is an efficient way to prevent avoidable harm. Policymakers and physicians should work together to make this possible.

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