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PREVALENCE AND MOLECULAR DETECTION OF HEPATITIS B AND HEPATITIS C VIRUS INFECTION IN CHRONIC MYELOID LEUKEMIA PATIENTS RECEIVING BCR-ABL TYROSINE KINASE INHIBITOR THERAPY

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ABSTRACT

Background: Tyrosine kinase inhibitors (TKIs) have improved the survival of patients with chronic myeloid leukaemia (CML), but prolonged treatment may affect immune function and increase the risk of hepatitis B virus (HBV) and hepatitis C virus (HCV) infection or reactivation. Data on these viral infections in CML patients receiving TKI therapy in India are limited.

Objectives: To assess the occurrence of HBV and HCV infection among BCR-ABL-positive patients receiving TKI therapy.

Methods: This observational study was conducted at a tertiary care hospital in Jaipur, Rajasthan, from October 2024 to July 2026. Real-time RT-PCR for BCR-ABL was performed in 66 patients suspected of having Philadelphia chromosome-positive acute lymphoblastic leukaemia or CML. BCR-ABL-positive patients were tested for HBV and HCV at baseline and during follow-up after starting TKI therapy using third-generation ELISA and real-time PCR. Descriptive statistics were used for analysis.

Results: BCR-ABL was detected in 51/66 patients (77.3%). All BCR-ABL-positive patients were negative for HBV and HCV at baseline. During follow-up, five patients (9.8%) developed HBV positivity and two (3.9%) developed HCV positivity, with no dual infections. Overall, 13.7% developed either HBV or HCV positivity during TKI therapy, and most infections occurred after treatment initiation. ELISA and PCR results showed complete agreement.

Conclusions: HBV and HCV positivity occurred during TKI therapy despite negative baseline screening. Pre-treatment screening and periodic monitoring may help detect infections early and support timely management in patients receiving TKI therapy.

KEYWORDS: Chronic myeloid leukemia, Tyrosine kinase inhibitor, Acute lymphoblastic leukemia, Hepatitis B virus, Hepatitis C virus

1.0 INTRODUCTION

Chronic myeloid leukemia (CML) is a slow-growing cancer of the blood-forming cells. It happens because of an abnormal genetic change called the Philadelphia chromosome, which forms when a piece of chromosome 9 breaks off and joins chromosome 22. This joining creates a new gene called BCR-ABL, which is found in almost every patient with CML.[1,2] The BCR-ABL gene makes an abnormal protein that keeps sending “grow and divide” signals to blood cells, without stopping, and this is the main reason CML develops.[3]

There are three common forms of the BCR-ABL protein, known as p190, p210 and p230, depending on where exactly the breakpoint occurs on the two chromosomes. The p210 form is most commonly seen in CML, while p190 is more often linked with Philadelphia-positive acute lymphoblastic leukemia (ALL). The p230 form is rare and is linked with a milder disease course.[2]

The discovery of tyrosine kinase inhibitors (TKIs), starting with imatinib, completely changed the outlook for CML patients. TKIs block the abnormal activity of the BCR-ABL protein and allow most patients to live a near-normal life with long-term therapy.[1,3] Newer TKIs such as dasatinib, nilotinib, bosutinib and ponatinib are now used, especially in patients who do not respond well to imatinib or who develop resistance; in Indian centers, such resistance has often been traced to mutations in the kinase domain of the BCR-ABL gene.[3,4] However, because CML patients usually need TKI therapy for many years, or even lifelong, doctors need to keep a close watch for side effects, and for how these drugs affect the immune system and other organs, particularly the liver.

Hepatitis B virus (HBV) is one of the most common causes of liver infection in the world, and it spreads mainly through blood, body fluids, and from mother to child.[5] If not treated, chronic HBV can lead to serious liver disease, including cirrhosis and liver cancer.[5] In India, HBV is present at an intermediate level, and the country carries a

large share of the global HBV burden due to its population size.[6] Hepatitis C virus (HCV) is another blood-borne virus that can cause chronic liver disease, and in India it is estimated that around 15 million people carry HCV antibodies, with an average prevalence of about 2%.[7]

Cancer patients who are on chemotherapy or other treatments that affect the immune system are known to be at higher risk of HBV reactivation, especially those with blood cancers.[8] Even though TKIs are targeted drugs and not traditional chemotherapy, they still interfere with immune pathways, and several case reports from around the world have described HBV reactivation in CML patients treated with imatinib and nilotinib.[9,10,11] Larger reviews of cancer patients treated with tyrosine kinase inhibitors and other newer targeted agents have reached the same conclusion, namely that this risk is real enough to justify screening before treatment and watchfulness during it.[12,13] The Bruton tyrosine kinase (BTK) inhibitors, a related class of drugs used in other blood cancers, have also shown a moderate risk of HBV reactivation, supporting the idea that kinase-inhibiting drugs in general can disturb the balance between the virus and the immune system.[5,14]

Interestingly, the ABL kinase, the same protein family that is targeted by TKIs in CML, also plays a role in how the Hepatitis C virus enters and assembles inside liver cells. Laboratory studies have shown that imatinib and dasatinib can block HCV entry into cells, meaning that TKIs may have a mixed effect on HCV, either helping to control it or, on the other hand, altering how the immune system detects it.[15,16] Reactivation of hepatitis C has also been reported in cancer patients receiving targeted therapy, although it is described far less often than hepatitis B reactivation.[17] This dual, and still not fully understood relationship, makes it important to study HBV and HCV status in real-world CML patients who are actually receiving TKI therapy.

Since India carries a large burden of both viral hepatitis and blood cancers, but data connecting BCR-ABL positive CML patients with HBV/HCV status during TKI treatment from Indian centers is limited, the present study was planned to identify the BCR-ABL fusion gene in patients attending a haemato-oncology clinic, to detect HBV and HCV infection in these BCR-ABL positive patients, and to observe how HBV/HCV status changed during the course of TKI treatment, using real-time PCR based molecular methods at a tertiary care hospital in Jaipur, Rajasthan.

2.0 MATERIALS AND METHODS

2.1 Study Design and Setting

This was a hospital-based observational study carried out in the Department of Advanced Molecular Laboratory at a tertiary care hospital and research Centre in Jaipur, Rajasthan, in collaboration with the Department of Haemato-Oncology. The period Oct 2024 to July 2026.

2.2 Study Population and Sample Size

The study included patients suspected of Chronic Myelogenous Leukemia (CML) and Philadelphia-positive Acute Lymphoblastic Leukemia (ALL) who attended the haemato-oncology clinic for evaluation and tyrosine kinase inhibitor treatment. A purposive sampling technique was used. Based on the reported prevalence of BCR-ABL positivity in India, a sample size of 68 suspected patients was calculated at 95% confidence interval, 80% power, and 5% margin of error, using the standard formula for estimating a single proportion. During the actual study period, complete data of 66 patients on the BCR-ABL-suspected/positive master chart were available for final analysis.

2.3 Sample Collection

For BCR-ABL testing, 3 mL of whole blood was collected in an EDTA vacutainer. For HBV and HCV testing, 3 mL of whole blood was collected in a clot-activator vacutainer. All samples were transported to the laboratory at 2–8°C and processed within 24 hours of collection to prevent degradation of nucleic acids. Samples were centrifuged at 3000 rpm for 10 minutes, after which serum and plasma were aliquoted and stored at −80°C until further analysis. Nucleic acid (RNA/DNA) was extracted using standard spin-column based extraction kits, and extracted material was stored at −80°C for further use when required.

2.4 Serological Analysis

Serological screening was performed for HBV and HCV infection. HBsAg was detected using commercially available third-generation ELISA (Merilisa HBsAg, Meril Diagnostics) kits according to the manufacturer's protocol. In brief, serum samples and controls were added to microtiter wells coated with anti-HBs antibodies, incubated at 37°C, washed to remove unbound material, and then treated with enzyme conjugate and substrate solution. The reaction was read at 450 nm and 630 nm using an Merilyzer (EIAQuant) and samples with absorbance above the cut-off value were considered positive. Anti-HCV antibodies were detected using third-generation ELISA kits (Merilisa HCV, Meril Diagnostics) in which patient serum and controls were added to antigen-coated microplates, incubated and washed as per kit instructions, followed by addition of enzyme-labeled conjugate and substrate. Optical density was measured at 450 nm and 630 nm, and reactive samples were reported as anti-HCV antibody positive.

2.5 Molecular Testing
RNA was isolated from whole blood for detection of the BCR-ABL fusion transcript by one-step real-time reverse transcriptase PCR (RT-PCR) by Bio-Rad RT-PCR, using a fluorescent probe-based assay targeting the p210, p190 and p230 transcripts (FAM channel) along with the ABL1 housekeeping control gene (VIC channel). A sample was labelled BCR-ABL positive when the cycle threshold (Ct) value for the fusion transcript was below 42, along with a valid internal ABL1 control.
Patients who tested positive for BCR-ABL were further tested for HBsAg (marker of Hepatitis B) and HCV RNA using kit-based real-time PCR assays with an internal control channel, following the manufacturer's standard cycling protocol. Testing for HBV and HCV was repeated at baseline (before starting TKI) and then again during follow-up visits at intervals over the course of TKI treatment, so that changes in HBV/HCV status during therapy could be observed.

2.6 Statistical Analysis
Data collected from the case records and laboratory reports were entered into Microsoft Excel and analysed using descriptive statistics. Results were expressed as numbers and percentages, and were also represented using tables.

2.7 Ethical Considerations
The study was carried out after obtaining written informed consent from all participants (or their legal guardians, for minors), and patient identity was kept confidential throughout the study.

3.0 RESULTS
A total of 66 patients suspected of CML/ALL, who were being evaluated at the haemato-oncology clinic, were included in the final analysis. Their blood samples were tested for the BCR-ABL fusion gene, and those found positive were further followed up for HBV and HCV status during TKI treatment.

3.1 BCR-ABL Positivity
Of the 66 patients tested, 51 (77.3%) were found positive for the BCR-ABL fusion gene by real-time PCR, while 15 (22.7%) were negative.

Table 1: BCR-ABL PCR status among suspected patients (N = 66)

BCR-ABL Status	Number of Patients	Percentage
Positive	51	77.3%
Negative	15	22.7%
Total	66	100.0%

3.2 Demographic Profile
Among all 66 patients, 40 (60.6%) were male and 26 (39.4%) were female. The mean age of the whole group was 44.2 years (median 44.5 years), with the youngest patient being 4 months old and the oldest being 88 years old. Among the 51 BCR-ABL positive patients, 31 (60.8%) were male and 20 (39.2%) were female, with a mean age of 45.5 years (range 4 months to 77 years).

Table 2: Gender distribution according to BCR-ABL status

Gender	BCR-ABL Positive (n=51)	BCR-ABL Negative (n=15)	Total (n=66)
Male	31 (60.8%)	9 (60.0%)	40 (60.6%)
Female	20 (39.2%)	6 (40.0%)	26 (39.4%)

Table 3: Age-wise distribution of BCR-ABL positive patients (n = 51)

Age Group (years)	Number of Patients	Percentage
0 – 9	2	3.9%
10 – 19	2	3.9%
20 – 29	7	13.7%
30 – 39	5	9.8%
40 – 49	13	25.5%
50 – 59	7	13.7%

Age Group (years)	Number of Patients	Percentage
60 – 69	9	17.6%
70 – 79	6	11.8%
Total	51	100.0%

The largest number of BCR-ABL positive patients belonged to the 40-49 year age group (25.5%), followed by the 60-69 year age group (17.6%), showing that CML in this study population was most common in middle-aged and older adults, though children and young adults were also affected.

3.3 Hepatitis B and Hepatitis C Status at Baseline (Before TKI Therapy)

Before starting TKI treatment, all 51 BCR-ABL positive patients were screened for HBsAg and HCV. At this baseline testing, none of the patients (0%) were positive for HBV and HCV, neither by serology and by PCR.

Table 4: Baseline HBsAg and HCV status of BCR-ABL positive patients before starting TKI therapy (n = 51)

Marker	Positive, n (%)	Negative, n (%)
HbsAg Elisa	0 (0.0%)	51 (100.0%)
HCV Elisa	0 (0.0%)	51 (100.0%)
HBV PCR	0 (0.0%)	51 (100.0%)
HCV PCR	0 (0.0%)	51 (100.0%)

3.4 Hepatitis B and Hepatitis C Status During Follow-up on TKI Therapy

All 51 BCR-ABL positive patients were started on TKI therapy and were re-tested for HbsAg and HCV at successive follow-up visits during treatment.

Table 5: HBsAg and HCV positivity among BCR-ABL positive patients at successive follow-up visits during TKI therapy

Visit	Patients Tested	HCV Positive, by ELISA n (%)	HBsAg Positive, by ELISA n (%)	HCV Positive, by PCR n (%)	HBV Positive, by PCR n (%)
1st (Baseline)	51	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2nd Follow-up	50	2 (4.0%)	1 (2.0%)	2 (4.0%)	1 (2.0%)
3rd Follow-up	46	2 (4.3%)	5 (10.9%)	2 (4.3%)	5 (10.9%)
4th Follow-up	43	1 (2.3%)	5 (11.6%)	1 (2.3%)	5 (11.6%)

It is important to note that these are point-prevalence figures at each visit, not new cases each time; the same patients who turned positive largely remained positive on subsequent testing. The fall in HCV positive numbers at the 4th visit (from 2 to 1) reflects fewer patients having reached that visit within the study period, not a true fall in infection.

3.5 Cumulative HBV/HCV Positivity Among BCR-ABL Positive Patients

When the entire follow-up period was considered together, 2 out of 51 BCR-ABL positive patients (3.92%) were positive for HCV at some point, and 5 out of 51 (9.80%) were positive for HBsAg at some point. No patient showed both HBV and HCV positivity together (0% dual infection). Taking either HBV or HCV positivity together, a total of 7 out of 51 BCR-ABL positive patients (13.73%) showed evidence of infection with one of the two viruses during the course of the study.

Of the 2 HCV positive patients, one was positive at the 2nd follow-up and 3rd follow-up visit before becoming negative on the 4th visit, while the second patient was HCV-negative at baseline and turned positive for the first time during TKI therapy (from the 2nd follow-up visit onward). All 5 patients who were positive for HBsAg were negative at baseline and turned positive for the first time only after starting TKI treatment, and all of them remained persistently HBsAg positive on every subsequent visit until the end of their follow-up.

Table 6: Cumulative (ever-positive) HBV and HCV status among BCR-ABL positive patients on TKI therapy (n = 51)

Status	Number of Patients	Percentage
HCV positive (ever)	2	3.92%
HBsAg positive (ever)	5	9.80%
Both HCV and HBsAg positive	0	0.0%
Either HCV or HBsAg positive	7	13.73%
Newly positive only after starting TKI (seroconversion)	6	11.76%

3.6 Comparison with BCR-ABL Negative Patients

Among the 15 patients who tested negative for the BCR-ABL fusion gene and were therefore not started on TKI therapy, HBsAg and HCV tests were negative in all patients.

3.7 Gender Distribution of HBV/HCV Positive Cases

Among the 7 BCR-ABL positive patients who showed HBV or HCV positivity, 5 were female and 2 were male. Of the 5 HBsAg positive patients, 4 were female and 1 was male. Of the 2 HCV positive patients, one was male and one was female.

4.0 DISCUSSION

In this observational study from a tertiary care hospital in Jaipur, Rajasthan, 77.3% of patients suspected of CML/ALL were confirmed positive for the BCR-ABL fusion gene by real-time PCR. This high positivity rate is expected because the sample was purposively drawn from patients already referred to a haemato-oncology clinic with clinical or haematological suspicion of CML, rather than from the general population; population-based Indian studies have reported the overall annual incidence of CML to be much lower, in the range of 0.71 to 2.2 per 100,000 in males and 0.53 to 1.6 per 100,000 in females.[18] Indian series have also shown that the fusion gene, most often in its p210 form, is present in the large majority of confirmed CML cases.[19] The male preponderance observed in this study (60.8% male among BCR-ABL positive patients, ratio close to 1.5:1) is consistent with previous Indian data, where CML has repeatedly been reported to show a male predominance of about 1.3 to 1.4 to 1.[20] The mean age of BCR-ABL positive patients in this study (45.5 years) was also close to the mean age of 44.7 years reported in a North-West Punjab study on the demographic profile of CML patients.[21] Children and young adults were also present in our group, the youngest being an infant of four months; CML in adolescents and young adults is uncommon but has been well described from Indian tertiary care centres.[22]

The main focus of this study, however, was the status of Hepatitis B and Hepatitis C infection in these BCR-ABL positive patients during TKI therapy. At baseline, before starting TKI, HBsAg and HCV positivity was nil (0.00%), broadly comparable with community and hospital-based Indian seroprevalence figures for HCV, which have generally ranged between about 1% and 5% across different regions of the country.[7,23,24,25,26,27] This baseline picture is reassuring and reflects the effectiveness of routine pre-treatment screening in excluding patients with already active infection, as recommended in the study protocol.

What stands out in this study is the pattern seen during follow-up. Five of the seven BCR-ABL positive patients who eventually tested positive for HBV or HCV were negative at baseline and turned positive only after TKI treatment had begun, giving a cumulative HBsAg positivity of 9.80% and an overall HBV-or-HCV positivity of 13.73% among treated patients. This figure is markedly higher than HBsAg prevalence figures reported from general hospital populations in India, such as 0.87% from a Rajasthan hospital-based study,[28] 2.8% from a Dehradun tertiary-care study,[7] 3.71% from a five-year hospital-based study in Central India,[26] and 1.91% from a North Indian surgical population.[27] It is, however, close to the 8% HBsAg positivity rate reported specifically among cancer patients in a Kashmir-based study, cited in the Indian National Association for the Study of the Liver (INASL) guidelines, which also note that HBV prevalence tends to be highest among patients with haematological malignancies compared with other cancers or the general population.[6] This comparison supports the idea that CML patients on long-term TKI therapy may carry a meaningfully higher risk of new HBV positivity than the general Indian population, in keeping with international literature describing TKI-associated HBV reactivation in CML patients treated with imatinib and nilotinib.[9,10,11,12,29]

The pooled global reactivation rate for HBV during chemotherapy in patients with haematological malignancies has been reported at around 9–10% in large meta-analyses, and the INASL guidelines specifically classify tyrosine kinase inhibitors among the drug classes carrying a relevant risk of HBV reactivation, warranting screening and monitoring before and during therapy.[6] The 9.80% HBsAg positivity observed among TKI-treated patients in the present study sits well within this expected range, and reinforces the recommendation that BCR-ABL positive patients should be screened for HBsAg not only before starting TKI therapy, but also monitored periodically during the course of treatment, as reactivation may take many months to appear, as also seen in this study where positivity first emerged at the 2nd and 3rd follow-up visits rather than at baseline.

The overall HCV positivity of 3.92% observed among BCR-ABL positive patients in this study is comparable to, or slightly higher than, several Indian regional seroprevalence studies, including 2.3% from a tertiary hospital in western Uttar Pradesh,[23] 2.02% from a tribal population study in Andhra Pradesh,[24] and 1.05–1.91% from hospital-based screening studies in central and northern India.[26,27] One striking finding was a new (incident) case of HCV positivity that appeared only after TKI therapy had begun. This observation is biologically interesting in light of laboratory research showing that the ABL kinase family, the same molecular target of TKIs used in CML, plays a role in HCV cell entry and viral particle assembly.[15,16] While imatinib and dasatinib have been shown in vitro to reduce HCV entry into liver cells,[15] the overall effect of long-term TKI-related immune modulation on HCV acquisition or reactivation in real patients remains complex and is not yet fully understood, and hepatitis C reactivation during targeted anticancer therapy has been reported in other cancer settings as well.[17]

In the present study each BCR-ABL positive patient was tested by both ELISA and real-time PCR at every visit, and the two methods gave the same answer on every instance. This complete agreement deserves comment, because serology and PCR do not always point in the same direction. A large population-based survey from north-west Russia, covering St Petersburg and the surrounding Leningrad region, tested 6,773 apparently healthy volunteers by both approaches and reported HBV DNA in 1.7% of them. Only about two out of every three of these DNA-positive people also carried HBsAg. The remainder, forming 0.7% of the whole group, had virus circulating in the blood while their HBsAg test stayed negative — a situation described as occult hepatitis B infection. Cases of this kind made up close to 38% of all the ongoing HBV infections found in that survey, which is a reminder that screening based on HBsAg alone can miss a sizeable part of the true infection load.[30]

This point carries direct practical value for CML patients. HBsAg is usually the only hepatitis B test performed before a tyrosine kinase inhibitor is started, so a patient carrying an occult infection can easily be recorded as uninfected at the start of treatment. If HBsAg later becomes detectable during therapy, the change may be read as a new infection when it was in fact a hidden infection that woke up under drug-related immune suppression. Occult carriers are known to be at risk of reactivation when they are given chemotherapy or targeted anticancer drugs.[6,13,30] In our patients this concern is reduced, because the baseline samples were negative not only by ELISA but also by a nucleic-acid test; this lowers, though it cannot completely rule out, the possibility that hidden virus was already present before treatment started.

The same survey also reported that people with a history of surgery or blood transfusion were roughly eight times more likely to carry occult HBV, and that many infected volunteers had no idea of their status, since HBsAg was picked up in a small but definite share of those who firmly denied ever having had hepatitis.[30] Patients with chronic myeloid leukaemia undergo repeated venepuncture, bone marrow sampling and, at times, transfusion, so a comparable route of exposure is plausible in our setting. This supports the practice of testing every patient in the laboratory rather than depending on what the patient recalls or reports.

For hepatitis C, that survey revealed the opposite kind of gap, only about 15% of the volunteers who carried anti-HCV antibodies actually had HCV RNA in their blood.[30] Antibody positivity therefore often reflects an old infection that has either cleared by itself or been cured, and on its own it does not prove that the virus is still active. In the present study both anti-HCV reactive patients were also positive for HCV RNA, which points towards genuine ongoing infection rather than past exposure. This strengthens the case for confirming every antibody-reactive result by PCR in a cancer patient before any decision is taken about antiviral treatment or a change in the anticancer regimen.[17,30]

No patient in this study showed dual infection with both HBV and HCV, which is in agreement with several Indian studies reporting very low rates of HBV-HCV co-infection in hospital and community populations, generally below 0.2%.[7,26,27] A study among a tribal population in Andhra Pradesh similarly found no cases of dual infection despite testing for both viruses.[24] This suggests that HBV and HCV largely behave as separate, independent risks in this population rather than occurring together.

Notably, none of the 15 BCR-ABL negative patients, who were not started on TKI therapy, showed any HBV or HCV positivity during their period of follow-up. Although the number of negative patients and their duration of follow-up were both smaller than in the BCR-ABL positive group, this comparison lends some support to the idea that the positivity observed in the BCR-ABL positive, TKI-treated group is linked to the disease and its treatment rather than being a general feature of the referral population.

One patient in the BCR-ABL positive group died during follow-up. HBV reactivation in patients with haematological malignancies who are not receiving antiviral prophylaxis has been associated with significant morbidity, including liver failure in around a quarter of such patients internationally, and has been linked with elevated mortality in some large registry-based studies.[29]

Taken together, the findings of this study support existing recommendations, both international and from Indian bodies such as INASL, that HBsAg and anti-HCV screening should be performed before starting kinase-inhibitor therapy in CML, and that periodic monitoring should continue during treatment, since reactivation or new infection may not be apparent at the time of diagnosis and may only emerge several months into therapy.[6]

5.0 CONCLUSION

In this study from a tertiary care center in Jaipur, Rajasthan, the BCR-ABL fusion gene was detected in 77.3% of patients suspected of CML/ALL by real-time PCR. Among BCR-ABL positive patients started on tyrosine kinase inhibitor therapy, HBsAg positivity was observed in 9.80% and HCV positivity in 3.92% of patients over the

course of follow-up, with most of these cases appearing only after TKI treatment had begun, rather than being present at baseline. These figures are higher than most general population and hospital-based Hepatitis B and C prevalence figures reported from India, suggesting that CML patients on long-term TKI therapy may be at greater risk of new hepatitis virus positivity than the general population. Because serological tests and nucleic-acid tests can disagree, and because HBsAg-negative but DNA-positive infection is now well documented in population studies, screening that combines both approaches gives a more truthful picture than serology alone. These findings support the value of screening all CML patients for HBV and HCV before starting TKI therapy, and continuing periodic monitoring throughout the course of treatment, so that reactivation or new infection can be picked up and managed early, protecting both liver health and the success of cancer treatment.

DECLARATIONS

Ethical Approval and Consent to Participate

The study was conducted in accordance with the principle of the declaration of Helsinki. Ethical approval was obtained from the Institutional Ethical Committee of NIMS University Rajasthan, Jaipur, India (Approval No-IEC/P-874/2024). Written informed consent was obtained from all participants prior to enrollment.

Consent for Publication

Not applicable

Availability of Data and Materials

The Datasets generated and/or analysis during the current study are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare that they have no known competing financial interest or person relationships that could have appeared to influence the work reported in this paper.

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Author Contributions:

Md Rabiul Parwana: Study conception and design, literature review, sample collection, laboratory investigations, data collection, data analysis, interpretation of results, and manuscript preparation. **Dr. Yogesh Kumar Singh:** Supervision, guidance, study design, interpretation of findings, and critical revision of the manuscript. **Dr. Prachi Saban:** Co-supervision, methodological guidance, data interpretation, interpretation of results, and critical revision of the manuscript. **Dr. Natasha Modi:** Co-supervision, clinical guidance, and critical revision of the manuscript. All authors reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of the manuscript, the authors used Chat GPT (Open AI) solely to improve language, grammar, readability and manuscript organization. The authors carefully reviewed and edited the generated content and take full responsibility for the content of this publication.

REFERENCES

1. Press RD, Kamel-Reid S, Ang D. BCR-ABL1 RT-qPCR for monitoring the molecular response to tyrosine kinase inhibitors in chronic myeloid leukemia. J Mol Diagn. 2013;15(5):565-576.
2. Li S, Ilaria RL Jr, Million RP, Daley GQ, Van Etten RA. The P190, P210, and P230 forms of the BCR/ABL oncogene induce a similar chronic myeloid leukemia-like syndrome in mice but have different lymphoid leukemogenic activity. J Exp Med. 1999;189(9):1399-1412.
3. Amarante-Mendes GP, Rana A, Datoguia TS, Hamerschlak N, Brumatti G. BCR-ABL1 tyrosine kinase complex signaling transduction: challenges to overcome resistance in chronic myeloid leukemia. Pharmaceutics. 2022;14(1):215.
4. S A, Shah A, Ashish A, Kumar Singh N, Kaur M, Kumar Yadav A, et al. BCR-ABL kinase domain mutations in CML patients, experience from a tertiary care center in North India. Leuk Res Rep. 2023;21:100403. doi:10.1016/j.lrr.2023.100403.

5. Knoll BM, Seiter K. Infections in patients on BCR-ABL tyrosine kinase inhibitor therapy: cases and review of the literature. Infection. 2018;46(3):409-418.
6. Arora A, Anand AC, Kumar A, Singh SP, Aggarwal R, Dhiman RK, et al. INASL guidelines on management of hepatitis B virus infection in patients receiving chemotherapy, biologicals, immunosuppressants, or corticosteroids. J Clin Exp Hepatol. 2018;8(4):403-431.
7. Mittal G, Gupta P, Gupta R, Ahuja V, Mittal M, Dhar M. Seroprevalence and risk factors of hepatitis B and hepatitis C virus infections in Uttarakhand, India. J Clin Exp Hepatol. 2013;3(4):296-300. doi:10.1016/j.jceh.2013.10.006.
8. Voican CS, Mir O, Loulergue P, Dhooge M, Brezault C, Dreanic J, et al. Hepatitis B virus reactivation in patients with solid tumors receiving systemic anticancer treatment. Ann Oncol. 2016;27(12):2172-2184.
9. Lai GM, Yan SL, Chang CS, Tsai CY. Hepatitis B reactivation in chronic myeloid leukemia patients receiving tyrosine kinase inhibitor. World J Gastroenterol. 2013;19(8):1318-1321.
10. Kang BW, Lee SJ, Moon JH, Kim SN, Chae YS, Kim JG, et al. Chronic myeloid leukemia patient manifesting fatal hepatitis B virus reactivation during treatment with imatinib rescued by liver transplantation: case report and literature review. Int J Hematol. 2009;90(3):383-387.
11. Wait S, Chen DS. Towards the eradication of hepatitis B in Taiwan. Kaohsiung J Med Sci. 2012;28(1):1-9.
12. Savaliya BP, Shekouhi R, Mubarak F, Manaise HK, Jimenez PB, Kowkabany G, et al. Risk of hepatitis B virus reactivation in cancer patients undergoing treatment with tyrosine kinase inhibitors. World J Gastroenterol. 2024;30(24):3052-3058.
13. Mustafayev K, Torres H. Hepatitis B virus and hepatitis C virus reactivation in cancer patients receiving novel anticancer therapies. Clin Microbiol Infect. 2022;28(10):1321-1327.
14. Chiu CY, Ahmed S, Thomas SK, Wang LS, Mustafayev K, Fayad LE, et al. Hepatitis B virus reactivation in patients receiving Bruton tyrosine kinase inhibitors. Clin Lymphoma Myeloma Leuk. 2023;23(8):610-615.
15. Min S, Lim YS, Shin D, Park C, Park JB, Kim S, et al. Abl tyrosine kinase regulates hepatitis C virus entry. Front Microbiol. 2017;8:1129.
16. Miyamoto D, Takeuchi K, Chihara K, Fujieda S, Sada K. Protein tyrosine kinase Abl promotes hepatitis C virus particle assembly via interaction with viral substrate activator NS5A. J Biol Chem. 2022;298(4):101804.
17. Yazici O, Sendur MA, Aksoy S. Hepatitis C virus reactivation in cancer patients in the era of targeted therapies. World J Gastroenterol. 2014;20(22):6716-6724.
18. Arnestina S, Kaur R, John JM. Clinicohematological spectrum of chronic myeloid leukemia: a cross-sectional study from a tertiary care hospital in North India. Cureus. 2025;17(6). doi:10.7759/cureus.86680.
19. Romero-Morelos P, González-Yebra AL, Muñoz-López D, Lara-Lona E, González-Yebra B. Frequencies of BCR::ABL1 transcripts in patients with chronic myeloid leukemia: a meta-analysis. Genes (Basel). 2024;15(2):232. doi:10.3390/genes15020232.
20. Dikshit RP, Nagrani R, Yeole B, Koyande S, Banawali S. Changing trends of chronic myeloid leukemia in greater Mumbai, India over a period of 30 years. Indian J Med Paediatr Oncol. 2011;32(2):96-100. doi:10.4103/0971-5851.89792.
21. Kaur R, Gupta R, Chandey M, Singh P, Mohan G, Singh N, et al. Study of demographic, hematological profile and risk stratification in chronic myeloid leukemia patients, in and around North-West Punjab, India. Int J Adv Med. 2020;7(12):1789-1794. doi:10.18203/2349-3933.ijam20204999.
22. Yanamandra U, Sahu KK, Karunakaran P, Katoch D, Jain N, Khadwal A, et al. Adolescent and young adult chronic myeloid leukemia in real-world settings: experience from a tertiary care institute in Northern India. J Adolesc Young Adult Oncol. 2019;8(1):94-97. doi:10.1089/jayao.2018.0007.
23. Chaudhary R. Seroprevalence of HCV infection at a tertiary care hospital, Western Uttar Pradesh, India. 2019. doi:10.5281/zenodo.3988025.
24. Chandra M, Khaja MN, Farees N, Poduri CD, Hussain MM, Habeeb MA, et al. Prevalence, risk factors and genotype distribution of HCV and HBV infection in the tribal population: a community based study in south India. Trop Gastroenterol. 2003;24(4):193-195.
25. Garg R, Kaur S, Aseri R, Aggarwal S, Singh JP, Mann S, et al. Hepatitis B & C among farmers: a seroprevalence study. J Clin Diagn Res. 2014;8(11). doi:10.7860/JCDR/2014/9514.5185.
26. Çağlar Y, Dalmanoğlu E. Investigation of anti-HCV, anti-HIV, and anti-HAV IgG seroprevalence in HBsAg-positive patients. Viral Hepat J. 2025;31(1):13-18. doi:10.4274/vhd.galenos.2024.2024-9-2.
27. Agarwal S, Agarwal A, Azam S, Singh DK, Soni ES, Afaq N, et al. Seroprevalence of hepatitis B, hepatitis C and HIV 1/2 in patients undergoing surgery in a tertiary care hospital. J Neonatal Surg. 2025;14(32S):3106-3111.
28. Sood S, Malvankar S. Seroprevalence of hepatitis B surface antigen, antibodies to the hepatitis C virus, and human immunodeficiency virus in a hospital-based population in Jaipur, Rajasthan. Indian J Community Med. 2010;35(1):165-169. doi:10.4103/0970-0218.62588.
29. Wang LY, Chu SC, Lo Y, Yang YY, Chan KA. Association of BCR-ABL tyrosine kinase inhibitors with hepatitis B virus reactivation requiring antiviral treatment in Taiwan. JAMA Netw Open. 2021;4(4).
30. Popova AY, Ostankova YV, Olkhovskaya AY, Petrova OA, Shchemelev AN, Serikova EN, et al. Serological and molecular epidemiology of hepatitis B, C, and D viruses in Northwest Russia: a population-based cross-sectional study. Viruses. 2026;18(6):632.