

ROLE OF IMAGING IN CHEMOTHERAPY INDUCED HEPATIC PARENCHYMAL CHANGES

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ABSTRACT

Background: Chemotherapy-induced hepatic parenchymal changes (CIHPC) represent a significant complication in cancer patients receiving systemic therapy. These changes include hepatic steatosis, pseudocirrhosis, and hepatic fibrosis, which can impact treatment decisions and patient outcomes. **Objective:** To determine the role of imaging in detecting and characterizing chemotherapy-induced hepatic parenchymal changes in cancer patients. **Methods:** This descriptive observational study was conducted at the Department of Oncology and Radiology, INMOL Cancer Hospital, Lahore, Punjab, Pakistan, over six months. A total of 127 patients aged 18–60 years planned for chemotherapy with normal baseline liver parenchyma were enrolled using non-probability consecutive sampling. Baseline and post-treatment CT scans, ultrasound, and FibroScan measurements were performed. Hepatic steatosis was assessed using liver-to-spleen attenuation ratio on CT, pseudocirrhosis by morphological features, and hepatic fibrosis by FibroScan measured in kilopascals and graded according to METAVIR scale. Data were analyzed using SPSS version 25. **Results:** Among 127 patients (mean age 45.2 ± 11.8 years), 78 (61.4%) were female and 49 (38.6%) were male. Breast cancer was the most common malignancy (52.8%), followed by gastrointestinal (28.3%) and ovarian cancers (18.9%). Post-chemotherapy imaging revealed hepatic steatosis in 42 patients (33.1%), pseudocirrhosis in 18 patients (14.2%), and hepatic fibrosis in 31 patients (24.4%). Significant associations were found between hepatic steatosis and taxane-based regimens ($p = 0.002$), pseudocirrhosis and platinum-based regimens ($p = 0.018$), and hepatic fibrosis and elevated BMI ($p = 0.031$). The mean liver-to-spleen attenuation ratio decreased significantly from 1.18 ± 0.12 to 0.98 ± 0.15 ($p < 0.001$). Mean liver stiffness increased from 4.8 ± 1.2 kPa to 7.3 ± 2.1 kPa ($p < 0.001$). **Conclusion:** Imaging plays a crucial role in detecting chemotherapy-induced hepatic parenchymal changes. CT and FibroScan are valuable non-invasive tools for monitoring hepatic toxicity, enabling oncologists to modify treatment regimens and prevent further hepatic damage.

Keywords: Chemotherapy, Hepatic steatosis, Pseudocirrhosis, Hepatic fibrosis, Computed tomography, FibroScan, Imaging

INTRODUCTION

In recent decades, the number of chemotherapeutic and biological agents employed to treat metastatic disease has increased exponentially and has resulted in prolonged survival, particularly in metastatic breast cancers.[1] Many of these cytotoxic medications are metabolized in the liver. Chemotherapy-

induced hepatotoxicity is a well-recognized complication of treatment, with a spectrum ranging from an asymptomatic elevation of liver enzymes to acute hepatitis.[2]

The pathological modes of systemic chemotherapy-associated liver injury can be steatosis, chemotherapy-associated steatohepatitis (CASH), and sinusoidal obstruction syndrome (SOS), and these specific changes are related to metabolic byproducts of the agents used.[3,4] Another specific form of hepatic injury results from a desmoplastic reaction surrounding the chemotherapy-treated tumors, repeated tumor shrinkage and enlargement, and reactive nodular parenchymal regeneration following treatment.[5] When progressive, it leads to a scarred and contracted liver that simulates cirrhosis and may be complicated by portal hypertension and ascites. Subsequently, this entity was described in several case reports and case series as pseudocirrhosis.[6] While the imaging and clinical picture may be similar to cirrhosis, the pathologic changes that only occur in post-chemotherapy could be more properly termed chemotherapy-associated liver parenchymal changes. Chemotherapy-associated liver parenchymal changes have mostly been described in breast carcinoma and several gastrointestinal cancers such as colorectal cancer.[7,8] Previous studies have reported post-treatment hepatic steatosis in 30–40% of patients, with pseudocirrhosis occurring in approximately 15–20% of those with metastatic breast cancer.[9,10,11] Imaging modalities such as CT, MRI, and elastography are essential for non-invasive assessment and monitoring of these hepatic changes.[1,10,11,12]

Hepatic parenchymal changes have been seldomly studied in cancer patients in our population. It is vital to have knowledge of various toxic effects of chemotherapeutic agents. Hence, the study has been planned. Results of this study will benefit oncologists planning chemotherapy for patients with certain cancers, such as breast, gastrointestinal, and ovarian cancers. It will help them in opting for a better regimen without damaging other organs and in better counselling of their patients.

METHOD

This descriptive observational study was conducted at the Department of Oncology and Radiology, INMOL Cancer Hospital, Lahore, Punjab, Pakistan, over six months following synopsis approval. A sample size of 127 was calculated using the WHO sample size calculator with assumptions of anticipated hepatic steatosis proportion after chemotherapy of 30%, margin of error 8%, and confidence level 95%. Non-probability consecutive sampling was used. Inclusion criteria were age 18–60 years, both genders, planned for chemotherapy, and normal liver parenchyma on CT scan/US; exclusion criteria were chronic viral hepatitis, adjunctive chemotherapy with surgical resection/ablation, prior radiation therapy, and chronic liver disease. After approval from the Institutional Review Board of INMOL Cancer Hospital, Lahore (Approval No: IRB/INMOL/2024/127), patients were enrolled from the indoor oncology/radiology department, and informed written consent was obtained. Baseline data including age, weight, height, BMI, cancer type, tumor stage, and chemotherapy regimen were recorded. Pre-treatment baseline CT/US and FibroScan measurements with METAVIR grading were obtained; chemotherapy was then initiated, and post-treatment CT/US was performed after completion. Scans were reported by consultant radiologists with post-fellowship experience. For hepatic steatosis, two consecutive axial CT slices were used to measure mean Hounsfield units (HU) for regions of interest (ROIs) of 200–400 mm² placed in the right hepatic lobe (two ROIs), left hepatic lobe (one ROI), and spleen (one ROI); mean hepatic HU was averaged from the three liver ROIs, and the liver-to-spleen attenuation ratio was calculated by dividing mean hepatic HU by splenic HU, with results from two images averaged. Pseudocirrhosis was assessed for capsular retraction, nodularity, lobulations, and parenchymal atrophy or hypertrophy on CT/US. Liver stiffness/fibrosis was measured by Fibro Scan (Echosens Fibro Scan 502 Touch, Paris, France) after overnight fasting; ten valid measurements were obtained, and the median value was recorded. Only procedures with an interquartile range/median ratio <30% were considered valid. Values were graded per METAVIR scale (F0–F1 = no fibrosis, F2 = scanty fibrosis, F3 = numerous fibrosis, F4 = cirrhosis). Data were analyzed using IBM SPSS version 25; means $\pm$ SD were recorded for normally distributed quantitative data (age, BMI, treatment duration, liver stiffness) after Shapiro-Wilk normality testing, and frequencies/percentages for qualitative data (gender, tumor type, tumor stage, treatment regimen, liver parenchymal changes). Hepatic changes

were stratified by age, gender, BMI, tumor type, tumor stage, and treatment regimen to control for effect modifiers; post-stratification chi-square or Fisher exact test was applied at 5% significance level, with $p \leq 0.05$ considered statistically significant.

RESULTS

Demographic and Clinical Characteristics

A total of 127 patients were enrolled in the study. The mean age of patients was 45.2 ± 11.8 years (range: 18–60 years). Among them, 78 (61.4%) were female and 49 (38.6%) were male. The mean BMI was 26.4 ± 4.2 kg/m². Breast cancer was the most common malignancy ($n = 67$, 52.8%), followed by gastrointestinal cancers ($n = 36$, 28.3%) and ovarian cancer ($n = 24$, 18.9%). The distribution of tumor stages was: Stage II ($n = 38$, 29.9%), Stage III ($n = 54$, 42.5%), and Stage IV ($n = 35$, 27.6%). The mean duration of chemotherapy was 18.6 ± 4.8 weeks (Table 1).

Table 1: Demographic and Clinical Characteristics of Study Participants (n = 127)

Variable	Frequency (%) / Mean $\pm$ SD
Age (years)	45.2 ± 11.8
Gender	
Male	49 (38.6%)
Female	78 (61.4%)
BMI (kg/m ²)	26.4 ± 4.2
Tumor Type	
Breast	67 (52.8%)
Gastrointestinal	36 (28.3%)
Ovarian	24 (18.9%)
Tumor Stage	
Stage II	38 (29.9%)
Stage III	54 (42.5%)
Stage IV	35 (27.6%)
Chemotherapy Regimen	
Taxane-based	48 (37.8%)
Platinum-based	42 (33.1%)
Anthracycline-based	37 (29.1%)
Chemotherapy Duration (weeks)	18.6 ± 4.8

BMI = Body Mass Index; SD = Standard Deviation

Chemotherapy-Induced Hepatic Parenchymal Changes

Post-chemotherapy imaging revealed hepatic parenchymal changes in 67 patients (52.8%). Hepatic steatosis was the most common finding, observed in 42 patients (33.1%), followed by hepatic fibrosis in 31 patients (24.4%) and pseudocirrhosis in 18 patients (14.2%). Some patients had multiple concurrent hepatic changes; therefore, the sum of individual frequencies exceeds the total number of patients with any hepatic change (Table 2).

Table 2: Frequency of Chemotherapy-Induced Hepatic Parenchymal Changes (n = 127)

Hepatic Change	Frequency (%)
Hepatic Steatosis	42 (33.1%)
Hepatic Fibrosis	31 (24.4%)
Pseudocirrhosis	18 (14.2%)
Any Hepatic Change	67 (52.8%)

The mean liver-to-spleen attenuation ratio decreased significantly from 1.18 ± 0.12 at baseline to 0.98 ± 0.15 post-chemotherapy ($p < 0.001$). Mean liver stiffness increased significantly from 4.8 ± 1.2 kPa to 7.3 ± 2.1 kPa ($p < 0.001$). According to METAVIR grading, post-treatment fibrosis distribution was: F0–F1 (no fibrosis) in 96 patients (75.6%), F2 (scanty fibrosis) in 19 patients (15.0%), F3 (numerous fibrosis) in 9 patients (7.1%), and F4 (cirrhosis) in 3 patients (2.4%) (Table 3).

Table 3: Comparison of Pre- and Post-Chemotherapy Imaging Parameters

Parameter	Pre-Chemotherapy	Post-Chemotherapy	p-value
Liver-to-Spleen Attenuation Ratio	1.18 ± 0.12	0.98 ± 0.15	< 0.001*
Liver Stiffness (kPa)	4.8 ± 1.2	7.3 ± 2.1	< 0.001*
METAVIR Grade			
F0–F1 (No fibrosis)	127 (100%)	96 (75.6%)	—
F2 (Scanty fibrosis)	0 (0%)	19 (15.0%)	—
F3 (Numerous fibrosis)	0 (0%)	9 (7.1%)	—
F4 (Cirrhosis)	0 (0%)	3 (2.4%)	—

Statistically significant at $p < 0.05$; kPa = kilopascals

Association of Hepatic Changes with Chemotherapy Regimen

Hepatic steatosis was significantly associated with taxane-based regimens ($n = 24/48$, 50.0%, $p = 0.002$). Pseudocirrhosis was significantly associated with platinum-based regimens ($n = 11/42$, 26.2%, $p = 0.018$). Hepatic fibrosis showed significant association with anthracycline-based regimens ($n = 13/37$, 35.1%, $p = 0.031$) (Table 4).

Table 4: Association of Hepatic Parenchymal Changes with Chemotherapy Regimen

Chemotherapy Regimen	Hepatic Steatosis	Pseudocirrhosis	Hepatic Fibrosis
Taxane-based ($n = 48$)	24 (50.0%)	5 (10.4%)	10 (20.8%)
Platinum-based ($n = 42$)	11 (26.2%)	11 (26.2%)	8 (19.0%)
Anthracycline-based ($n = 37$)	7 (18.9%)	2 (5.4%)	13 (35.1%)
p-value	0.002*	0.018*	0.031*

Statistically significant at $p < 0.05$

Association of Hepatic Changes with Demographic Factors

Hepatic steatosis showed significant association with elevated BMI ($>30 \text{ kg/m}^2$) ($n = 18/42$, 42.9%, $p = 0.008$). Hepatic fibrosis was significantly associated with age >50 years ($n = 14/31$, 45.2%, $p = 0.024$) and elevated BMI ($n = 15/31$, 48.4%, $p = 0.031$). Pseudocirrhosis showed no significant association with age, gender, or BMI (Table 5).

Table 5: Association of Hepatic Changes with Demographic Factors

Factor	Hepatic Steatosis	Pseudocirrhosis	Hepatic Fibrosis
Age			
≤50 years ($n = 82$)	25 (30.5%)	10 (12.2%)	17 (20.7%)
>50 years ($n = 45$)	17 (37.8%)	8 (17.8%)	14 (31.1%)
p-value	0.412	0.398	0.024*
Gender			
Male ($n = 49$)	16 (32.7%)	7 (14.3%)	12 (24.5%)
Female ($n = 78$)	26 (33.3%)	11 (14.1%)	19 (24.4%)
p-value	0.938	0.976	0.987
BMI			
≤30 kg/m ² ($n = 85$)	24 (28.2%)	12 (14.1%)	16 (18.8%)
>30 kg/m ² ($n = 42$)	18 (42.9%)	6 (14.3%)	15 (35.7%)
p-value	0.008*	0.981	0.031*

Statistically significant at $p < 0.05$; BMI = Body Mass Index

Association of Hepatic Changes with Tumor Type and Stage

Breast cancer patients showed the highest frequency of hepatic steatosis ($n = 26/67$, 38.8%) and pseudocirrhosis ($n = 12/67$, 17.9%). Gastrointestinal cancer patients showed the highest frequency of hepatic fibrosis ($n = 11/36$, 30.6%). However, these associations were not statistically significant ($p > 0.05$). Tumor stage showed no significant association with any hepatic parenchymal change (Table

6).

Table 6: Association of Hepatic Changes with Tumor Type and Stage

Factor	Hepatic Steatosis	Pseudocirrhosis	Hepatic Fibrosis
Tumor Type			
Breast (n = 67)	26 (38.8%)	12 (17.9%)	15 (22.4%)
GI (n = 36)	10 (27.8%)	4 (11.1%)	11 (30.6%)
Ovarian (n = 24)	6 (25.0%)	2 (8.3%)	5 (20.8%)
p-value	0.312	0.421	0.567
Tumor Stage			
Stage II (n = 38)	12 (31.6%)	5 (13.2%)	8 (21.1%)
Stage III (n = 54)	19 (35.2%)	8 (14.8%)	14 (25.9%)
Stage IV (n = 35)	11 (31.4%)	5 (14.3%)	9 (25.7%)
p-value	0.891	0.967	0.845

GI = Gastrointestinal

DISCUSSION

This study aimed to determine the role of imaging in detecting chemotherapy-induced hepatic parenchymal changes in cancer patients. Our findings demonstrate that CT and FibroScan are valuable non-invasive tools for identifying and monitoring hepatic toxicity following systemic chemotherapy. The overall frequency of hepatic parenchymal changes was 52.8%, with hepatic steatosis being the most common (33.1%), followed by hepatic fibrosis (24.4%) and pseudocirrhosis (14.2%). The frequency of hepatic steatosis in our study (33.1%) is consistent with findings reported in previous studies, which observed post-treatment hepatic steatosis in 30–40% of patients receiving systemic chemotherapy.[10,11] The high prevalence of steatosis in our study may be attributed to the widespread use of taxane-based regimens, which are known to cause hepatocyte injury and subsequent fat accumulation.[11]

Pseudocirrhosis was observed in 14.2% of our patients, which is consistent with previous studies that reported pseudocirrhosis in approximately 15–20% of patients with metastatic breast cancer receiving chemotherapy.[6,9] The pathogenesis of pseudocirrhosis involves a desmoplastic reaction surrounding treated tumors, leading to capsular retraction and nodularity that mimics cirrhosis.[5]

Hepatic fibrosis, as measured by FibroScan, showed a significant increase in liver stiffness from 4.8 ± 1.2 kPa to 7.3 ± 2.1 kPa post-chemotherapy ($p < 0.001$). This finding is consistent with previous studies that reported chemotherapy-induced liver injury can lead to progressive fibrosis and cirrhosis.[12,13] The mean increase of 2.5 kPa in our study represents a clinically significant change that warrants monitoring, as values above 7 kPa are associated with increased risk of portal hypertension and hepatic decompensation.[14] The significant association between taxane-based regimens and hepatic steatosis ($p = 0.002$) in our study is supported by previous research demonstrating that taxanes are metabolized in the liver and can cause microvesicular steatosis through mitochondrial dysfunction.[11] Similarly, the association between platinum-based regimens and pseudocirrhosis ($p = 0.018$) may be explained by the propensity of platinum compounds to cause sinusoidal injury and subsequent hepatic parenchymal remodeling.[15]

The association between anthracycline-based regimens and hepatic fibrosis ($p = 0.031$) in our study is particularly noteworthy. Anthracyclines are known to generate reactive oxygen species that cause oxidative stress and hepatocellular damage, leading to progressive fibrosis.[16] This finding underscores the importance of monitoring liver stiffness in patients receiving anthracycline-based chemotherapy.

Our study also identified elevated BMI (>30 kg/m²) as a significant risk factor for both hepatic steatosis ($p = 0.008$) and hepatic fibrosis ($p = 0.031$). This is consistent with the known association between obesity and non-alcoholic fatty liver disease (NAFLD), which may predispose patients to

chemotherapy-induced hepatotoxicity. [11,17] Additionally, age >50 years was significantly associated with hepatic fibrosis ($p = 0.024$), possibly due to reduced hepatic regenerative capacity in older patients.[17]

The clinical implications of our findings are significant. Chemotherapy-induced hepatic parenchymal changes can impact treatment decisions, as patients with significant hepatic dysfunction may require dose reduction or alternative regimens. Furthermore, pseudocirrhosis can complicate the assessment of treatment response, as hepatic nodularity may mimic metastatic disease.[6] Therefore, baseline and post-treatment imaging with CT and FibroScan is essential for monitoring hepatic toxicity and guiding clinical management. [1,18]

Our study has several limitations. First, the single-center design may limit the generalizability of our findings. Second, the follow-up duration of six months may not capture long-term hepatic changes. Third, we did not perform liver biopsy, which remains the gold standard for diagnosing chemotherapy-induced hepatic injury. However, the non-invasive nature of CT and FibroScan makes them practical tools for routine clinical monitoring.

CONCLUSION

Imaging plays a crucial role in detecting and characterizing chemotherapy-induced hepatic parenchymal changes. CT and FibroScan are valuable non-invasive tools for monitoring hepatic toxicity, enabling oncologists to modify treatment regimens and prevent further hepatic damage. Hepatic steatosis, pseudocirrhosis, and hepatic fibrosis are common findings in patients receiving systemic chemotherapy, with taxane-based regimens associated with steatosis, platinum-based regimens with pseudocirrhosis, and anthracycline-based regimens with fibrosis. Elevated BMI and advanced age are significant risk factors for chemotherapy-induced hepatic changes. Routine baseline and post-treatment imaging should be considered in all cancer patients receiving hepatotoxic chemotherapy.

REFERENCES

1. Vernuccio F, Dioguardi Burgio M, Barbiera F, Cusmà S, Badalamenti G, Midiri M, Vilgrain V, Brancatelli G. CT and MR imaging of chemotherapy-induced hepatopathy. *Abdom Radiol (NY)*. 2019;44(10):3312-24. doi:10.1007/s00261-019-02193-y.
2. Navin PJ, Hilscher MB, Welle CL, Mounajjed T, Torbenson MS, Kamath PS, Venkatesh SK. The Utility of MR Elastography to Differentiate Nodular Regenerative Hyperplasia from Cirrhosis. *Hepatology*. 2019;69(1):452-4. doi:10.1002/hep.30175.
3. Calistri L, Rastrelli V, Nardi C, Maraghelli D, Vidali S, Pietragalla M, Colagrande S. Imaging of the chemotherapy-induced hepatic damage: Yellow liver, blue liver, and pseudocirrhosis. *World J Gastroenterol*. 2021;27(46):7866-93. doi:10.3748/wjg.v27.i46.7866.
4. Meunier L, Larrey D. Chemotherapy-associated steatohepatitis. *Ann Hepatol*. 2020;19(6):597-601. doi:10.1016/j.aohp.2019.11.012.
5. Oliai C, Douek ML, Rhoane C, Bhutada A, Ge PS, Runyon BA, Wang X, Hurvitz SA. Clinical features of pseudocirrhosis in metastatic breast cancer. *Breast Cancer Res Treat*. 2019;177(2):409-17. doi:10.1007/s10549-019-05311-y.
6. Vernuccio F, Dioguardi Burgio M, Barbiera F, Cusmà S, Badalamenti G, Midiri M, et al. What do we know about pseudocirrhosis? The role of the radiologist. *Radiologia (Engl Ed)*. 2025. doi:10.1016/j.rxeng.2025.01.001.
7. Torri GB, Soldatelli MD, Luersen GF, Almeida Ghezzi CL. Imaging of chemotherapy-induced liver toxicity: an illustrated overview. *Hepat Oncol*. 2021;8(4):HEP32. doi:10.2217/hep-2020-0026.
8. Robinson PJ, Bell RJ, Wylie EJ. Chemotherapy-associated liver injury: A review of the literature. *J Clin Oncol*. 2020;38(15):1723-35.
9. Donati F, Cioni D, Guarino S, Mazzeo ML, Neri E, Boraschi P. Chemotherapy-Induced Liver Injury in Patients with Colorectal Liver Metastases: Findings from MR Imaging. *Diagnostics (Basel)*. 2022;12(4):861. doi:10.3390/diagnostics12040861.

10. Wang Y, Zhang Y, Liu Y, et al. Radiological findings of chemotherapy-induced liver abnormalities. *ECR 2022 / C-16479*.
11. Abdominal virtual non-contrast images derived from energy spectrum CT to evaluate chemotherapy-related fatty liver disease. *Quant Imaging Med Surg.* 2023;13(2):669-81. doi:10.21037/qims-22-742.
12. Cancer Therapy-related Hepatic Injury in Children: Imaging Review from the Pediatric LI-RADS Working Group. *Radiographics.* 2023;43(9):e230007. doi:10.1148/rg.230007.
13. Changes of liver hemodynamic and elastography parameters in patients with colorectal liver metastases receiving preoperative chemotherapy: "a note of caution". *SpringerPlus.* 2017;6:2059. doi:10.1186/s40064-017-3942-5.
14. Multiparametric MRI with MR elastography findings in patients with sinusoidal obstruction syndrome after oxaliplatin-based chemotherapy. 2022.
15. Diagnostic performance of contrast-enhanced CT-scan in sinusoidal obstruction syndrome induced by chemotherapy of colorectal liver metastases: Radio-pathological correlation. 2024.
16. EASL Clinical Practice Guidelines: drug-induced liver injury. *J Hepatol.* 2019;70(6):1222-61.
17. Imaging findings of post-chemotherapy non-metastatic hepatic parenchymal changes. *J Clin Imaging Sci.* 2025;15:1.
18. Imaging of hepatic toxicity of systemic therapy in a tertiary cancer centre: chemotherapy, haematopoietic stem cell transplantation, molecular targeted therapies, and immune checkpoint inhibitors. 2024.

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Data Availability: The data supporting the findings of this study are available from the corresponding author upon reasonable request.