

ROLE OF IMAGING IN CHEMOTHERAPY-INDUCED HEPATIC PARENCHYMAL CHANGES

¹Sharifa Skiandar, ²Muhammad Saleem, ³Zeeshan Rashid Mirza, ⁴Gulzar Hussain

¹Postgraduate Resident, Department of Diagnostic Radiology, Provincial Headquarters Teaching Hospital (PHQTH), Gilgit, Pakistan.sharifaunahar@gmail.com

²Department of Diagnostic Radiology, Provincial Headquarters Teaching Hospital (PHQTH), Gilgit, Pakistan.

³Department of Diagnostic Radiology, Provincial Headquarters Teaching Hospital (PHQTH), Gilgit, Pakistan.

⁴Department of Radiology, Institute of Nuclear Medicine and Oncology Lahore (INMOL), Lahore, Pakistan.

*Corresponding Author: Sharifa Skiandar, sharifaunahar@gmail.com

ABSTRACT

Acute appendicitis represents the most frequent indication for emergency surgery worldwide. Appendectomy, the standard treatment, can be performed via open or laparoscopic techniques. Although laparoscopic appendectomy is increasingly preferred due to its minimally invasive nature, its advantages must be weighed against longer anaesthesia duration and increased resource demands, especially in resource-limited settings.

Study Design: Comparative Cross-Sectional Study.

Setting: Department of Surgery, Mardan Medical Complex, MTI Mardan, Khyber Pakhtunkhwa, Pakistan. The study was conducted from 11 February to 11 July 2026.

The study included sixty patients aged 18 to 60 years diagnosed with acute appendicitis who underwent appendectomy. Patients underwent either open appendectomy (n=20) or laparoscopic appendectomy (n=40), with the surgical approach determined by the operating surgeon's clinical judgment, resource availability, and patient preference. Outcome measures comprised anaesthesia duration, length of hospital stay, time to tolerance of oral intake postoperatively, and postoperative analgesic requirement. We analysed data using IBM SPSS version 26. Independent-samples t-tests were applied for continuous variables, and Chi-Square or Fisher's exact tests for categorical variables. We defined statistical significance as $p < 0.05$.

The mean age of patients was 30.10 ± 7.22 years; 36 (60.0%) were male, and 24 (40.0%) were female. The laparoscopic group had a significantly longer anaesthesia duration compared to the open group (77.95 ± 10.81 minutes vs. 65.30 ± 7.18 minutes; $p < 0.001$). Laparoscopic appendectomy was also associated with a significantly shorter hospital stay (1.77 ± 0.46 days vs. 3.67 ± 0.61 days; $p < 0.001$), earlier tolerance of oral intake (15.51 ± 3.98 hours vs. 27.87 ± 5.57 hours; $p < 0.001$), and a lower postoperative analgesic requirement (30.0% vs. 70.0%; $p = 0.003$).

Laparoscopic appendectomy is superior to open appendectomy in early postoperative recovery, as indicated by shorter hospital stay, earlier resumption of oral intake, and reduced analgesic requirements, despite longer anaesthesia duration. It may be considered the first-line surgical intervention for selected patients with uncomplicated acute appendicitis in institutions possessing sufficient laparoscopic expertise and resources.

KEYWORDS: Acute appendicitis; Appendectomy; Laparoscopy; Open appendectomy; Hospital stay; Postoperative pain; Oral intake.

INTRODUCTION

Acute appendicitis is among the most common emergency surgical diagnoses and places a significant burden on surgical services worldwide. The lifetime risk of developing acute appendicitis is estimated at 7–8%, with peak incidence in the second and third decades of life.¹ Definitive management typically involves appendectomy, performed either laparoscopically or via an open approach.² Open appendectomy, first described by McBurney in 1894, has historically been the standard procedure due to its simplicity, minimal equipment requirements, and accessibility in low-resource settings.³ However, open appendectomy is associated with greater incisional trauma, higher postoperative pain scores, prolonged immobilisation, and extended hospital stay. Laparoscopic appendectomy, introduced in 1983 by Semm, offers advantages such as enhanced intra-abdominal visualisation, smaller incisions, reduced tissue trauma, and shorter postoperative stay.⁵ It is particularly beneficial in cases of diagnostic uncertainty, atypical presentations, or suspected alternative intra-abdominal pathology.⁶ Nevertheless, laparoscopic appendectomy requires general anaesthesia, creation of pneumoperitoneum, specialised instruments, and advanced surgical skills. In less experienced or low-volume centres, these factors may increase operative and anaesthetic times. The selection of surgical approach should be guided by institutional capability, surgeon experience, patient characteristics, and measurable postoperative outcomes, rather than theoretical benefits alone.⁹ Key outcomes include anaesthesia duration, hospital stay, postoperative analgesic requirement, and time to oral intake following appendectomy.¹⁰ These variables influence patient recovery, resource utilisation, and healthcare costs.¹¹ Local outcome data are essential due to institutional differences in case selection, surgical training,

perioperative care, and discharge practices. This study compared open and laparoscopic appendectomy for acute appendicitis management at Mardan Medical Complex, MTI Mardan, Pakistan.^{1, 2}

We conducted a comparative cross-sectional study in the Department of Surgery, Mardan Medical Complex, MTI Mardan, Khyber Pakhtunkhwa, Pakistan, over a five-month period from February 11, 2026, to July 11, 2026. We obtained Institutional Ethics Committee approval before initiation and secured written informed consent from participants after providing a detailed explanation of the study objectives, procedures, and potential risks and benefits. We calculated the sample size using OpenEpi, referencing previously published proportions of postoperative analgesic requirement (65.5% for open appendectomy and 20.7% for laparoscopic appendectomy), with 95% confidence and 80% power, resulting in a total of 60 patients. Inclusion criteria comprised adult patients aged 18–60 years, clinically diagnosed with acute appendicitis, who underwent open or laparoscopic appendectomy. Exclusion criteria included prior abdominal surgery likely to affect the surgical approach, gangrenous or perforated appendicitis, pregnancy, and other abdominal or pelvic diseases necessitating a secondary operative procedure. Assignment to open or laparoscopic appendectomy was non-randomised and determined by the operating surgeon's clinical judgment, patient condition, surgical feasibility, and resource availability. Potential selection bias was acknowledged. The final distribution included 20 patients (33.3%) in the open group and 40 (66.7%) in the laparoscopic group. Data collected included age, gender, residence, socioeconomic status, comorbidities, and procedure type, using a standardised proforma. All patients underwent a protocol-mandated preoperative assessment, including comprehensive history and clinical examination. Outcome measures were anaesthesia duration (minutes), defined as the total time from induction to extubation (including preparation, port placement, pneumoperitoneum creation, surgery, and emergence); length of hospital stay (days), defined as the interval from surgery to discharge; time to tolerance of oral intake (hours), defined as the time after surgery until oral intake was tolerated without significant nausea, vomiting, or abdominal pain; and postoperative analgesic requirement, defined as the need for analgesia beyond routine perioperative medications. Data were entered and analysed using IBM SPSS Version 26. Continuous variables (age, anaesthesia duration, hospital stay, and time to oral intake) were presented as mean $\pm$ standard deviation. Categorical variables (gender, residence, occupation, comorbid conditions, procedure type, and need for analgesia) were reported as frequencies and percentages. Continuous outcomes were compared between groups using independent sample t-tests, while Chi-square or Fisher's exact tests were used for categorical variables. We set statistical significance at $p \leq 0.05$. This design facilitated comparison of perioperative and postoperative outcomes between conventional and laparoscopic appendectomy within a specific institutional context. Although non-randomised allocation may limit causal inference, the approach was intended to reflect routine surgical practice.

RESULTS

The study included 60 patients with acute appendicitis. The mean age was 30.10 ± 7.22 years; 36 (60.0%) were male, and 24 (40.0%) were female. Urban residents accounted for 24 patients (40.0%), while 36 (60.0%) were from rural areas. Socioeconomic status was intermediate in 34 patients (56.7%), low in 14 (23.3%), and high in 12 (20.0%). Diabetes mellitus was present in 3 patients (5.0%) and hypertension in 5 (8.3%); the remaining 52 (86.7%) had no comorbidities. The cohort primarily consisted of young adults, with a male majority and a slight predominance of rural residents. Most patients belonged to the intermediate socioeconomic group and were generally medically well or had only minor conditions. Of the total, 40 (66.7%) underwent laparoscopic appendectomy, and 20 (33.3%) underwent open appendectomy (Table I). Postoperative analgesia was required in 26 patients (43.3%), while 34 (56.7%) did not require analgesics during the wake-up stage. The mean anaesthetic time was 73.73 ± 11.40 minutes. The average hospital stay was 2.40 ± 1.04 days, and the mean time to tolerate oral intake was 19.63 ± 7.42 hours (Table II). These values represent baseline characteristics before stratification by surgical approach.

The laparoscopic appendectomy group demonstrated a significantly shorter anaesthesia duration (77.95 ± 10.81 minutes vs. 65.30 ± 7.18 minutes; $p < 0.001$) and achieved earlier tolerance of oral intake (15.51 ± 3.98 vs. 27.87 ± 5.57 hours; $p < 0.001$). The requirement for postoperative analgesia was also significantly lower in the laparoscopic group (30.0%) compared to the open group (70.0%; $p = 0.003$) (Table III; Figures 1–4). All differences were statistically significant ($p < 0.05$). These findings indicate that, although laparoscopic appendectomy is associated with a longer anaesthetic duration, it confers advantages of shorter hospital stay, earlier resumption of oral intake, and reduced postoperative analgesic requirement compared to open appendectomy in this cohort.

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	18–30	35	27.6
	31–45	52	40.9

	46–60	40	31.5
Gender	Male	48	37.8
	Female	79	62.2
BMI (kg/m ²)	Normal (18.5–24.9)	45	35.4
	Overweight (25.0–29.9)	51	40.2
	Obese (≥ 30.0)	31	24.4
Tumour type	Breast cancer	38	29.9
	Colorectal cancer	35	27.6
	Ovarian cancer	20	15.7
	Gastric cancer	18	14.2
	Other gastrointestinal cancers	16	12.6
Tumour stage	Stage II	25	19.7
	Stage III	52	40.9
	Stage IV	50	39.4
Chemotherapy regimen	FOLFOX/CAPOX	42	33.1
	FOLFIRI/CAPIRI	28	22.0
	Anthracycline-based	30	23.6
	Taxane-based	17	13.4
	Platinum-based	10	7.9

Table 2. Pre-treatment liver assessment.

Parameter	Mean $\pm$ SD or frequency
Liver stiffness	5.2 $\pm$ 1.8 kPa
Liver-to-spleen attenuation ratio	1.20 $\pm$ 0.15
METAVIR-equivalent F0-F1	127 (100%)
METAVIR-equivalent F2	0 (0%)

METAVIR-equivalent F3	0 (0%)
METAVIR-equivalent F4	0 (0%)
Hepatic steatosis	0 (0%)
Pseudocirrhosis-like morphology	0 (0%)

Table 3. Post-treatment hepatic parenchymal changes.

Hepatic change	Frequency (n)	Percentage (%)	95% CI (%)
Hepatic steatosis	31	24.4	16.9–31.9
Elastography-detected increased liver stiffness (≥F2)	47	37.0	28.6–45.4
Pseudocirrhosis-like morphology	12	9.4	4.3–14.6

Figure 1. Prevalence of post-chemotherapy hepatic parenchymal changes.

Table 4A—stratification of hepatic steatosis by demographic and clinical factors.

Variable	Category	Steatosis present (%)	Steatosis absent n (%)	p-value
Age	18–30	7 (20.0)	28 (80.0)	0.312
	31–45	15 (28.8)	37 (71.2)	
	46–60	9 (22.5)	31 (77.5)	
Gender	Male	9 (18.8)	39 (81.2)	0.198
	Female	22 (27.8)	57 (72.2)	
BMI	Normal	6 (13.3)	39 (86.7)	0.027
	Overweight	14 (27.5)	37 (72.5)	
	Obese	11 (35.5)	20 (64.5)	
Tumour type	Breast	12 (31.6)	26 (68.4)	0.221
	Colorectal	9 (25.7)	26 (74.3)	
	Ovarian	4 (20.0)	16 (80.0)	
	Gastric	3 (16.7)	15 (83.3)	
	Other GI	3 (18.8)	13 (81.2)	

Tumour stage	Stage II	4 (16.0)	21 (84.0)	0.356
	Stage III	13 (25.0)	39 (75.0)	
	Stage IV	14 (28.0)	36 (72.0)	
Regimen	FOLFOX/CAPOX	11 (26.2)	31 (73.8)	0.874
	FOLFIRI/CAPIRI	7 (25.0)	21 (75.0)	
	Anthracycline-based	8 (26.7)	22 (73.3)	
	Taxane-based	3 (17.6)	14 (82.4)	
	Platinum-based	2 (20.0)	8 (80.0)	

*p-values are descriptive; no adjustment for multiplicity was applied.

Table 4B—stratification of elastography-detected increased liver stiffness by demographic and clinical factors.

Variable	Category	Stiffness present n (%)	Stiffness absent n (%)	p-value
Age	18–30	10 (28.6)	25 (71.4)	0.287
	31–45	22 (42.3)	30 (57.7)	
	46–60	15 (37.5)	25 (62.5)	
Gender	Male	16 (33.3)	32 (66.7)	0.421
	Female	31 (39.2)	48 (60.8)	
BMI	Normal	14 (31.1)	31 (68.9)	0.112
	Overweight	20 (39.2)	31 (60.8)	
	Obese	13 (41.9)	18 (58.1)	
Tumour type	Breast	16 (42.1)	22 (57.9)	0.041
	Colorectal	14 (40.0)	21 (60.0)	
	Ovarian	7 (35.0)	13 (65.0)	
	Gastric	5 (27.8)	13 (72.2)	
	Other GI	5 (31.3)	11 (68.8)	
Tumour stage	Stage II	7 (28.0)	18 (72.0)	0.089

	Stage III	20 (38.5)	32 (61.5)	
	Stage IV	20 (40.0)	30 (60.0)	
Regimen	FOLFOX/CAPOX	20 (47.6)	22 (52.4)	0.019
	FOLFIRI/CAPIRI	11 (39.3)	17 (60.7)	
	Anthracycline-based	10 (33.3)	20 (66.7)	
	Taxane-based	4 (23.5)	13 (76.5)	
	Platinum-based	2 (20.0)	8 (80.0)	

*p-values are descriptive; no adjustment for multiplicity was applied.

Table 4C—stratification of pseudocirrhosis-like morphology by demographic and clinical factors.

Variable	Category	Present n (%)	Absent n (%)	p-value
Age	18–30	3 (8.6)	32 (91.4)	0.612
	31–45	6 (11.5)	46 (88.5)	
	46–60	3 (7.5)	37 (92.5)	
Gender	Male	4 (8.3)	44 (91.7)	0.487
	Female	8 (10.1)	71 (89.9)	
BMI	Normal	4 (8.9)	41 (91.1)	0.923
	Overweight	5 (9.8)	46 (90.2)	
	Obese	3 (9.7)	28 (90.3)	
Tumour type	Breast	6 (15.8)	32 (84.2)	0.156
	Colorectal	4 (11.4)	31 (88.6)	
	Ovarian	1 (5.0)	19 (95.0)	
	Gastric	1 (5.6)	17 (94.4)	
	Other GI	0 (0.0)	16 (100.0)	
Tumour stage	Stage II	1 (4.0)	24 (96.0)	0.038
	Stage III	5 (9.6)	47 (90.4)	

	Stage IV	6 (12.0)	44 (88.0)	
Regimen	FOLFOX/CAPOX	4 (9.5)	38 (90.5)	0.427
	FOLFIRI/CAPIRI	2 (7.1)	26 (92.9)	
	Anthracycline-based	4 (13.3)	26 (86.7)	
	Taxane-based	2 (11.8)	15 (88.2)	
	Platinum-based	0 (0.0)	10 (100.0)	

*p-values are descriptive; no adjustment for multiplicity was applied.

Table 5. Post-chemotherapy elastography-equivalent METAVIR distribution.

Category	Description	Frequency (n)	Percentage (%)
F0-F1	No or mild fibrosis	80	63.0
F2	Moderate fibrosis	35	27.6
F3	Severe fibrosis	9	7.1
F4	Cirrhosis-range stiffness	3	2.4

Table 6. Correlation between hepatic parenchymal changes.

Parameter	Hepatic steatosis	Hepatic fibrosis	Pseudocirrhosis-like morphology
Hepatic steatosis	1.000	0.312*	0.198*
Hepatic fibrosis	0.312*	1.000	0.287*
Pseudocirrhosis-like morphology	0.198*	0.287*	1.000

*Pearson correlation coefficient; $p < 0.05$ for all.

Table 7. Mean liver stiffness values by elastography-equivalent METAVIR category.

Category	Mean liver stiffness (kPa)	Standard deviation	Range (kPa)
F0-F1 (n=80)	4.8	±1.2	3.2–6.9
F2 (n=35)	8.6	±1.8	7.0–11.9
F3 (n=9)	14.2	±2.7	12.0–17.8
F4 (n=3)	20.5	±3.1	18.2–24.1

Table 8. Imaging features among patients with pseudocirrhosis-like morphology (n=12).

Feature	Frequency (n)	Percentage (%)
Surface nodularity	11	91.7
Lobulations	10	83.3
Capsular retraction	9	75.0
Caudate lobe enlargement	6	50.0
Parenchymal atrophy	5	41.7
Parenchymal hypertrophy	4	33.3

Table 9. Comparison of pre-treatment and post-treatment liver parameters.

Parameter	Pre-treatment mean $\pm$ SD	Post-treatment mean $\pm$ SD	Mean change	p-value
Liver stiffness	5.2 $\pm$ 1.8 kPa	8.1 $\pm$ 3.2 kPa	+2.9 kPa	<0.001
Liver-to-spleen attenuation ratio	1.20 $\pm$ 0.15	1.02 $\pm$ 0.18	-0.18	<0.001

Table 10A—Multivariable predictors of hepatic steatosis.

Variable	Odds ratio	95% CI	p-value
BMI overweight/obese vs. normal	2.84	1.21–6.67	0.016
Breast cancer vs. other	2.12	1.02–4.41	0.044

Table 10B—multivariable predictors of elastography-detected increased liver stiffness.

Variable	Odds ratio	95% CI	p-value
FOLFOX/CAPOX regimen	3.21	1.34–7.69	0.009
Stage IV disease	2.45	1.08–5.56	0.032

Table 10C—multivariable predictors of pseudocirrhosis-like morphology.

Variable	Odds ratio	95% CI	p-value
Stage IV disease	4.12	1.23–13.79	0.021
Breast cancer	3.45	1.12–10.63	0.031

DISCUSSION

Setting: This observational pre-post study aimed to assess the frequency and imaging spectrum of hepatic parenchymal changes in patients receiving systemic chemotherapy at a tertiary-care centre in Gilgit-Baltistan. The main post-treatment features of interest were hepatic steatosis (24.4%), elastography-based increased liver

stiffness (37.0%), and pseudocirrhosis-like morphology (9.4%). The paired design facilitates interpretation, as imaging was normal at baseline and post-treatment evaluations using the same categories.

Hepatic steatosis occurred in 24.4% of our cohort, consistent with previously published data. In a retrospective study of patients on S-1 chemotherapy for pancreatic cancer, hepatic steatosis occurred in 23% of the patients. During systemic chemotherapy for gastrointestinal cancers, we reported transient elastography-based controlled attenuation parameter values characteristic of mild steatosis [2]. In addition, the study of patients with hepatic steatosis who were treated with chemotherapy showed that the rate of having received chemotherapy was 41.9%, and prior chemotherapy was a negative predictor of advancing hepatic fibrosis. Notably, our finding that BMI was significantly associated with steatosis ($p = 0.027$) corroborates existing knowledge that metabolic factors play a role in chemotherapy-associated steatosis and supports a "second hit" hypothesis in which systemic therapy targets an already vulnerable metabolic liver phenotype.

Elastography detected increased liver stiffness ($\geq F2$) in 37.0% of patients. Change in mean liver stiffness from 5.2 ± 1.8 to 8.1 ± 3.2 kPa. This increase was consistent with earlier experience in oxaliplatin-treated colon cancer patients, where clear changes in liver stiffness were seen following FOLFOX treatment, often normalising by 2 weeks. In a study of 28 patients comparing FibroScan and splenic volume index for early detection of oxaliplatin-induced hepatotoxicity, mean elasticity measurements at 3 months (16.2 vs 7.8 kPa, $P = 0.35$) and at 6 months (9.3 vs 6.7 kPa; $P = 0.009$) were significantly higher in those developing splenomegaly. Our results also echo a study of PNPLA3 p.148M allele carriers with chemotherapy-associated liver injury (CALI) that established the utility of liver stiffness measurements for serial evaluation of chemotherapy-associated hepatic alterations. As mentioned, histopathological correlation remains a limitation because transient elastography is affected by inflammation, cholestasis, hepatic congestion, tumour infiltration, and ascites. Therefore, the high prevalence of increased liver stiffness (37.0%) should be interpreted as an elastography-detected hepatic change, not histologically confirmed fibrosis.

The 9.4% prevalence of pseudocirrhosis-like morphology in our cohort is consistent with previously reported ranges in the literature. Pseudocirrhosis: a systematic review and meta-analysis was carried out on 389 patients from 62 articles, most of the patients (70%) having had breast cancer (80% in case reports and case series). Pseudocirrhosis usually occurs in about 5–20% of the patients with treated hepatic metastases. However, published series refer to patients with known liver metastases; therefore, we excluded patients with known hepatic metastases from our hospital study population. In the systematic review, the median time from pseudocirrhosis to death was 2 months, while patients with breast cancer and pseudocirrhosis had a median overall survival of 7.6–10.0 months from diagnosis. The presence of pseudocirrhosis-like morphology in a subset of subjects with no current evidence of hepatic metastases raises the possibility that chemotherapy-related parenchymal remodelling can occur without associated metastatic disease. However, undetectable micrometastases cannot be excluded.

The significant associations between changes in hepatic steatosis and increased liver stiffness and pseudocirrhosis-like morphology (Table 6) suggest these changes may share underlying pathophysiological mechanisms, such as oxidative stress, inflammation, and vascular injury. In the multivariable analysis, BMI class and breast cancer were independently associated with steatosis; the FOLFOX/CAPOX regimen and Stage IV disease were independently associated with increased liver stiffness; and Stage IV disease and breast cancer were independently associated with pseudocirrhosis-like morphology. These results are consistent with the reported hepatotoxicity profiles of oxaliplatin-based regimens. Sinusoidal obstruction syndrome has been reported in 54% of patients receiving oxaliplatin; nodular regenerative hyperplasia in 24.5%; and perisinusoidal fibrosis in 47%. Co-administration of bevacizumab can partially prevent oxaliplatin-associated lesions, reducing moderate/severe sinusoidal obstruction syndrome from 62.2% to 31.4%.

CLINICAL IMPLICATIONS: Given our findings, we suggest all patients starting systemic chemotherapy with potentially hepatotoxic agents have baseline liver imaging (CT or ultrasound) and, when available, transient elastography. This establishes a baseline to compare to in the future and identifies patients with existing liver disease who may be more vulnerable to injury as a result of receiving treatment with chemotherapy. Liver imaging after completing chemotherapy would be useful for our study's identified risk factors (obesity, breast cancer, the FOLFOX/CAPOX regimen, Stage IV disease). The optimal frequency of surveillance imaging during chemotherapy is not known and may require further investigation. Hepatology consultation is warranted in patients with imaging-detected hepatic changes where assessment of liver function or alternative aetiologies may influence decisions regarding chemotherapy dose modification, sequencing or surgical candidacy. We recognise that frequent imaging surveillance is also costly and resource-intensive, particularly in resource-scarce settings such as Gilgit-Baltistan. **Conclusions:** However, the imaging-detected changes in our cohort follow international frequencies and suggest that targeted surveillance in high-risk patients may be cost-effective in preventing chemotherapy-related complications, informing surgical planning, and identifying patients who may benefit from hepatoprotective strategies. Formal cost-effectiveness analysis is needed. Lastly, the use of hepatoprotective agents (eg, bevacizumab for oxaliplatin-associated liver injury, ursodeoxycholic acid, vitamin E, metformin) to prevent chemotherapy-associated liver injury also needs confirmation, but data are currently scant.

Limitations: This study has several limitations. One major limitation is the lack of a control group and blinded outcome assessment. Although two consultant radiologists reviewed all imaging and were blinded to the chemotherapy regimen and clinical outcomes, they were not blinded to the fact that the imaging was performed as part of a pre-post study (the very nature of pre-post studies may have introduced confounding through

expectation bias). The main limitations also include the lack of histopathological correlation: transient elastography is affected by inflammation, cholestasis, hepatic congestion, abdominal coagulation, ascites and especially by tumour infiltration. Third, the study was not powered for multivariable analysis, and the logistic regression results should be treated as hypothesis-generating. Fourth, the study was exploratory; thus, no adjustment for multiple comparisons was performed. Fifth, the margin of error used to calculate the sample size is 8%, which is quite large. Sixth, this was a single tertiary-care centre experience in a resource-limited setting, and so generalisability may be limited. Lastly, the observational period included only the duration of chemotherapy, and no longer-term consequences were evaluated.

Future Directions: Future studies require histopathological corroboration, control groups, standardised imaging protocols, and longer follow-up to validate these results and determine the most appropriate surveillance regimen. There is a clear need for consensus definitions for pseudocirrhosis-like morphology to compare studies. Finally, future studies should evaluate whether imaging-detected hepatic alterations translate into chemotherapy intolerance, surgical complications, or long-term survival.

CONCLUSION

AIM: This prospective observational study of patients (N=20,138) receiving systemic chemotherapy at a tertiary-care centre in Gilgit-Baltistan aims to document the high prevalence of imaging-detected hepatic parenchymal changes, such as steatosis, increased liver stiffness, and pseudocirrhosis-like morphology. These are in line with previously reported numbers worldwide and reinforce the recommendations to perform baseline imaging routinely and follow-up liver imaging in oncological patients, especially those with risk factors like obesity, breast cancer, advanced-stage disease or those treated with an oxaliplatin-based regimen. However, the lack of histopathological correlation and a control group hampers causal inference, and pseudocirrhosis-like morphology should be referred to as "pseudocirrhosis" only if hepatic metastases are excluded. Further studies are needed to validate these results in a histopathological context, particularly using control groups and standardised imaging protocols, to help elucidate the most effective surveillance strategy.

REFERENCES

1. Vernuccio F, Dioguardi Burgio M, Barbiera F, Cusma S, Badalamenti G, Midiri M, et al. CT and MR imaging of chemotherapy-induced hepatopathy. *Abdom Radiol (NY)*. 2019;44(10):3312-3324. doi:10.1007/s00261-019-02193-y.
2. Sharma A, Houshyar R, Bhosale P, Choi JI, Gulati R, Lall C. Chemotherapy-induced liver abnormalities: an imaging perspective. *Clin Mol Hepatol*. 2014;20(3):317-326. doi:10.3350/cmh.2014.20.3.317.
3. Calistri L, Rastrelli V, Nardi C, Maragheili D, Vidali S, Pietragalla M, et al. Imaging of chemotherapy-induced hepatic damage: yellow liver, blue liver, and pseudocirrhosis. *World J Gastroenterol*. 2021;27(46):7866-7893. doi:10.3748/wjg.v27.i46.7866.
4. Oliai C, Douek ML, Rhoane C, Bhutada A, Ge PS, Runyon BA, et al. Clinical features of pseudocirrhosis in metastatic breast cancer. *Breast Cancer Res Treat*. 2019;177(2):409-417. doi:10.1007/s10549-019-05311-y.
5. Pope MC, Olson MC, Flicek KT, Patel NJ, Bolan CW, Menias CO, et al. Chemotherapy-associated liver morphological changes in hepatic metastases (CALMCHeM). *Diagn Interv Radiol*. 2023;29(4):571-578. doi:10.4274/dir.2023.232299.
6. Haghshomar M, McComb BL, Shyn PB, Venkatesh SK. Diagnostic accuracy of CT for the detection of hepatic steatosis: a systematic review and meta-analysis. *Radiology*. 2024;311(3):e241171. doi:10.1148/radiol.241171.
7. Leung SY, Chiu WT, Law MKK, Wong HCA, Lai A, Luk YS. Imaging findings of post-chemotherapy non-metastatic hepatic parenchymal changes. *J Clin Imaging Sci*. 2025;15:24. doi:10.25259/JCIS_165_2024.
8. Myers RP, Pomier-Layrargues G, Kirsch R, Pollett A, Beaton M, Levstik M, et al. Feasibility and diagnostic performance of the FibroScan XL probe for liver stiffness measurement in overweight and obese patients. *Hepatology*. 2012;55(1):199-208. doi:10.1002/hep.24624.
9. Friedrich-Rust M, Ong MF, Martens S, Sarrazin C, Bojunga J, Zeuzem S, et al. Performance of transient elastography for the staging of liver fibrosis: a meta-analysis. *Gastroenterology*. 2008;134(4):960-974. doi:10.1053/j.gastro.2008.01.034.
10. Castera L. Noninvasive evaluation of liver fibrosis using transient elastography. *J Hepatol*. 2008;48(5):835-847. doi:10.1016/j.jhep.2008.02.008.
11. Vauthey JN, Pawlik TM, Ribero D, Wu TT, Zorzi D, Hoff PM, et al. Chemotherapy regimen predicts steatohepatitis and an increase in 90-day mortality after surgery for hepatic colorectal metastases. *J Clin Oncol*. 2006;24(13):2065-2072. doi:10.1200/JCO.2005.05.3074.
12. Rubbia-Brandt L, Audard V, Sartoretti P, Roth AD, Brezault C, Le Charpentier M, et al. Severe hepatic sinusoidal obstruction associated with oxaliplatin-based chemotherapy in patients with metastatic colorectal cancer. *Ann Oncol*. 2004;15(3):460-466. doi:10.1093/annonc/mdh095.
13. Kim SH, Lee JM, Han JK, et al. Hepatic stiffness measurement by using MR elastography: comparison with transient elastography and histopathologic findings. *Radiology*. 2013;267(1):143-152.
14. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis. *J Hepatol*. 2021;75(3):659-689.

15. Dietrich CF, Bamber J, Berzigotti A, et al. EFSUMB guidelines and recommendations on the clinical use of liver ultrasound elastography. *Ultraschall Med.* 2017;38(4):e16-e47.
 16. Villani R, Di Cosimo F, Sangineto M, Romano AD, Serviddio G. Pseudocirrhosis and portal hypertension in patients with metastatic cancers: a systematic review and meta-analysis. *Sci Rep.* 2022;12(1):19865. doi:10.1038/s41598-022-24241-2.
 17. Rubbia-Brandt L, Lauwers GY, Wang H, Majno PE, Tanabe K, Zhu AX, et al. Sinusoidal obstruction syndrome and nodular regenerative hyperplasia are frequent oxaliplatin-associated liver lesions and are partially prevented by bevacizumab in patients with hepatic colorectal metastasis. *Histopathology.* 2010;56(4):430-439. doi:10.1111/j.1365-2559.2010.03511.x.
 18. Phillips E, Sethi M, Vasanthakumar S, Sherpa G, Johnston S, Parton M, et al. The clinical features and outcomes of pseudocirrhosis in breast cancer. *Cancers (Basel).* 2024;16(16):2822. doi:10.3390/cancers16162822.
 19. Engelman D, Moreau M, Lepage C, et al. Metastatic breast cancer and pseudocirrhosis: an unknown clinical entity. *ESMO Open.* 2020;5(3):e000695. doi:10.1136/esmoopen-2020-000695.
 20. Gopalakrishnan D, Kasi PM, Haddad TC, et al. Pseudocirrhosis in breast cancer - experience from an academic cancer centre. *Front Oncol.* 2021;11:679163. doi:10.3389/fonc.2021.679163.
 21. Bouferra Y, El Chediak A, Shamseddine A, et al. Comparison between liver stiffness measurement by FibroScan and splenic volume index as non-invasive tools for the early detection of oxaliplatin-induced hepatotoxicity. *J Clin Exp Hepatol.* 2022;12(2):448-453. doi:10.1016/j.jceh.2021.06.007.
 22. Tsuji K, Mizukami Y, Furuya M, et al. S-1 induced hepatic steatosis in patients with pancreatic cancer: retrospective analysis. *World J Gastrointest Oncol.* 2017;9(8):314-318. doi:10.4251/wjgo.v9.i8.314.
 23. Reddy SK, Rehman S, Shah N, et al. Long-term influence of chemotherapy on steatosis-associated advanced hepatic fibrosis. *Med Oncol.* 2014;31(6):971. doi:10.1007/s12032-014-0971-y.
 24. Oki E, Kakeji Y, Yoshida R, et al. Transient elastography for the prediction of oxaliplatin-associated liver injury in colon cancer patients: a preliminary analysis. *J Gastrointest Cancer.* 2008;39(1-4):59-63. doi:10.1007/s12029-009-9063-1.
 25. Casper M, Grimm J, Kloor M, et al. Risk of chemotherapy-associated liver injury (CALI) in PNPLA3 p.I148M allele carriers: preliminary results of a transient elastography-based study. *Dig Liver Dis.* 2020;52(1):102-106. doi:10.1016/j.dld.2019.09.015.
- Figure 1.** Prevalence of post-chemotherapy hepatic parenchymal changes (steatosis, increased liver stiffness, pseudocirrhosis-like morphology) among 127 patients.
- Figure 2.** Distribution of elastography-equivalent METAVIR categories after chemotherapy (F0–F1, F2, F3, F4).
- Figure 3.** Frequency of individual pseudocirrhosis-like imaging features among 12 affected patients.
- Figure 4.** Mean liver stiffness (kPa) before and after chemotherapy, showing a significant increase ($p < 0.001$).
- Figure 5.** Liver-to-spleen attenuation ratio before and after chemotherapy, showing a significant decrease ($p < 0.001$).
- Acknowledgements:** The authors thank the Department of Radiology and the Department of Gastroenterology at Provincial Headquarters Teaching Hospital Gilgit for their support. We also thank the patients who participated in this study.
- Author Contributions:** SS: conceptualisation, data collection, imaging analysis, manuscript drafting. MS: imaging analysis, manuscript revision. ZRM: data analysis, manuscript revision. GH: clinical correlation, hepatology consultation, manuscript revision. All authors approved the final version.
- Funding:** None.
- Conflict of Interest:** The authors declare no conflicts of interest.
- Data Availability:** The data supporting the findings of this study are available from the corresponding author upon reasonable request.