

Spectrum and Severity of Anaemia in Chronic Liver Disease: A Prospective Cross-Sectional Study

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Received: 16th August, 2026; Revised: 8th September 2026; Accepted: 19th September, 2026; Available Online: 20th September, 2026

Abstract

Background: Chronic liver disease (CLD) accounts for a rising share of India's disease burden, and haematological abnormalities, anaemia foremost among them, frequently accompany its progression. Indian data linking anaemia severity and red-cell morphology to CLD stage, rather than to cirrhosis alone, remain limited.

Methods: After giving their informed consent, 100 of the 300 screened CLD patients who met the eligibility requirements were enrolled in this prospective, cross-sectional observational study at the Gastroenterology in-patient and out-patient departments of King George Hospital, Visakhapatnam. They were evaluated at a single baseline visit over the course of a 24-week recruitment period. During enrollment, the following values were determined: hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and peripheral blood smear morphology. For categorical data, the chi-squared test was performed, and for continuous variables, the unpaired Student's t-test or one-way/ two-way ANOVA, when appropriate (SPSS v29.0; GraphPad Prism v10.0); $p < 0.05$ was considered significant.

Results: Of 100 participants, 79 were male and 21 female ($\chi^2 = 18.36$, $p < 0.0001$), with the largest age band at 41–50 years ($n = 39$); age-group distribution did not differ significantly by gender (chi-square test, $p = 0.42$). Fifty patients were staged as CLD stage 2 (fibrosis), 34 as stage 3 (cirrhosis), 15 as stage 1, and 1 as stage 4; gender

distribution differed significantly across stages 1–3 (chi-square test, $p=0.024$; the single stage-4 patient was not included in this comparison). All 100 participants were anaemic. Mean Hb at screening was 8.5 ± 2.3 g/dL, lower in females (7.7 ± 2.0 g/dL) than males (8.7 ± 2.4 g/dL; unpaired t-test, $p=0.04$), and rose only marginally across CLD stages 1 to 4 (8.3 ± 2.4 , 8.3 ± 2.2 , 8.8 ± 2.3 , and 9.0 g/dL, respectively). Red-cell indices differed significantly by CLD stage (one-way ANOVA, $p=0.004$) but not by gender ($p=0.08$). Normocytic normochromic anaemia was the commonest morphology (41%), followed by microcytic hypochromic (34%) and normocytic hypochromic anaemia (12%).

Conclusion: Anaemia was universal in this CLD cohort, predominantly mild to moderate and normocytic normochromic in pattern — a picture more in keeping with gastrointestinal blood loss and anaemia of chronic disease than with isolated haematinic deficiency. Severity tracked only weakly with CLD stage, supporting routine haemogram and peripheral-smear screening at diagnosis, independent of disease stage, supplemented by ferritin, vitamin B12, and folate assays where morphology suggests a nutritional contribution. Ferritin, vitamin B12, and folate were not measured in this cohort, however, so the proposed mechanism remains inferential and should be confirmed biochemically rather than assumed.

Keywords: *chronic liver disease; anaemia; haemoglobin; cirrhosis; peripheral smear; red-cell indices*

How to cite this article: Soma Sekhar Pulamarasetti¹* Mr. Omkar Rai² Dr. N Swetapadma Rout³ Dr. Deepshikha Dey⁴ Dr. Perna Pandey⁵ Dr. Musunuri Sai Siri Phanisha⁶ Dr. Robin Singh⁷ Siddela Johnson⁸. Spectrum and Severity of Anaemia in Chronic Liver Disease: A Prospective Cross-Sectional Study. *Int J Drug Deliv Technol.* 2026;16(81s):1148-1155. DOI: 10.25258/ijddt.16.81s.145.

1. Introduction

Chronic liver disease (CLD) denotes a progressive loss of hepatic function persisting beyond six months, driven by sustained inflammation, parenchymal destruction, and regeneration that culminate in fibrosis and cirrhosis [1]. Cirrhosis, the histological endpoint of this process, is defined by diffuse nodular regeneration and disturbed hepatic architecture [2]. Early-stage fibrosis is now recognised as potentially reversible if the underlying insult resolves, but established cirrhosis is generally considered irreversible, and survival falls sharply once decompensation supervenes [3,4]. Cirrhosis caused an estimated 1.32 million deaths worldwide in 2017, and its global age-standardised mortality has continued to climb even as death rates from several other chronic diseases have fallen [5,6]. India contributed 18.3% of the two million liver-disease deaths recorded worldwide in 2015, and unlike China, where cirrhosis mortality has plateaued, the Indian trend has risen steadily since 1980 [7,8]. Alcohol-related liver disease and viral hepatitis, principally hepatitis B and, less commonly, hepatitis D, dominate the aetiological mix across South Asia, in contrast to the metabolic-disease-driven pattern that now prevails in high-income countries [9,10,11,12,13,14]. In India specifically, hepatitis C carries a documented national burden captured through dedicated task-force surveillance [15].

Clinical staging of CLD, moving from hepatitis or steatosis through fibrosis and cirrhosis to hepatocellular carcinoma, guides prognosis and treatment intensity, and relies chiefly on liver function tests, imaging, and, where indicated, histology [1]. Complications that accompany advancing CLD, including jaundice, coagulopathy, hepatic encephalopathy, portal hypertension, and variceal bleeding, are well described, yet the haematological consequences of the disease receive comparatively little routine attention in everyday

gastroenterology practice, where a haemogram is often ordered reactively rather than built into staging assessment [16,17].

Anaemia ranks among the most prevalent conditions worldwide and contributes substantially to years lived with disability across age groups [18,19]. In India, the National Family Health Survey (NFHS-5, 2019–21) recorded anaemia in 25.0% of men and 57.0% of women aged 15–49 years, a burden that extends well beyond the hepatology clinic [20]. Within CLD specifically, anaemia complicates an estimated 66–75% of patients with cirrhosis, arising through gastrointestinal blood loss, hypersplenism, nutritional deficiency, and direct marrow suppression, though its reported morphology varies with the cohort and aetiological mix under study [21,22]. Data linking anaemia severity and red-cell morphology to CLD stage as a continuum, rather than to cirrhosis in isolation, remain sparse in the Indian setting, and the relative contribution of gastrointestinal bleeding versus true haematinic deficiency in this population is not well defined [22,21].

This study set out to characterise the spectrum of anaemia, its severity and red-cell morphology, across the severity spectrum of CLD among patients attending a South Indian tertiary-care gastroenterology unit. The specific objectives were to determine the prevalence and severity of anaemia at each CLD stage, from hepatitis/steatosis through fibrosis and cirrhosis to hepatocellular carcinoma, and to characterise how red-cell indices and morphology vary with CLD stage and gender.

2. Materials and Methods

2.1 Study Design and Setting

This was a prospective, single-centre, cross-sectional observational study conducted at the in-patient and out-patient departments of Gastroenterology, King George Hospital, Visakhapatnam, Andhra Pradesh. Patients were

recruited over a 24-week period structured across three sequential phases: literature review and protocol development; patient screening, enrolment, and baseline assessment; and data compilation with statistical analysis. Each participant contributed a single baseline evaluation at the time of enrolment; the study did not follow participants longitudinally.

2.2 Ethics Approval and Consent

After receiving clearance from the Institutional Ethics Committee of King George Hospital, Visakhapatnam, the study was carried out in compliance with the Declaration of Helsinki. Written informed consent was obtained from every participant, with the study procedure explained in the presence of family members where applicable, before any study-related assessment. A signed copy of the consent form was retained by both the participant and the investigating team.

2.3 Sample Size

In order to determine With regard to the sample size, the following were the considerations:

Confidence level at 95%, which is $z = 1.96$

Margin of error at 5% = 0.05

Population proportion of CLD, $p = 0.072$, as reported in the National Program for Prevention and Control of Non-Communicable Diseases manual by the Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India (2023) [23,24]. This calculation yielded a minimum requirement of 102.7 participants ($0.072 \times 0.928 \times 1.96^2 / 0.05^2 = 102.7$), which was rounded to a practical enrolment target of 100, a shortfall of under 3% attributed to the fixed 24-week recruitment window.

2.4 Patient Selection

Inclusion criteria

- Adults of either gender aged 18 years or above.
- Diagnosis of CLD confirmed by laboratory and radiological findings.
- Willingness to provide informed consent and undergo the baseline clinical and laboratory assessment.

Exclusion criteria

- Age below 18 years, or unwillingness to provide informed consent.
- Recent surgery or trauma carrying a risk of substantial blood loss.
- Current use of medication known to independently cause anaemia.
- Concurrent enrolment in another interventional clinical study.
- Additional comorbidities or primary blood disorders independently contributing to anaemia.

2.5 Study Assessments

Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT), serum albumin and globulin, hemoglobin, MCV, MCH, MCHC, red blood cell count, packed cell volume, and peripheral

blood smear morphology were all measured during the baseline (enrollment) visit. Anaemia severity was classified against World Health Organization reference ranges as mild

(haemoglobin 9–10.9 g/dL), moderate (7–8.9 g/dL), or severe (<7 g/dL) [25,26]. CLD stage was assigned by the treating gastroenterologist on clinical, biochemical, and radiological grounds as stage 1 (hepatitis/steatosis), stage 2 (fibrosis), stage 3 (cirrhosis), or stage 4 (hepatocellular carcinoma). All analyses reported here are cross-sectional, describing the cohort's status at enrolment; the study did not include repeat assessment or longitudinal follow-up.

2.6 Statistical Analysis

IBM Corp., in Armonk, New York, USA, IBM SPSS Statistics 29.0; GraphPad Prism 10.0, by Dotmatics, Inc., in Boston, Massachusetts, USA; and Microsoft Excel 16.0, Microsoft Corporation, Redmond, Washington, USA, are software applications used for data analysis. Categorical variables such as gender, age group, and stage of CLD distribution are presented in numbers and percentages and compared using the chi-square test of independence, cross-checked with a Monte Carlo estimate of the Fisher–Freeman–Halton exact test (100,000 replicates) where expected cell counts were below five; where a comparison group contained fewer than two observations, it was reported descriptively rather than subjected to formal significance testing. The mean $\pm$ standard deviation of continuous variables, such as hemoglobin and red-cell indices, is used for comparisons between two groups, or between multiple grouping factors, using either one- or two-way analysis of variance (ANOVA), depending on the type of comparison being conducted. Statistical significance was maintained at all times when the p -value was less than 0.05.

3. Results

3.1 Baseline Demographic and Clinical Profile

Of 300 patients screened for CLD, 100 satisfied the eligibility criteria and were enrolled (Figure 1).

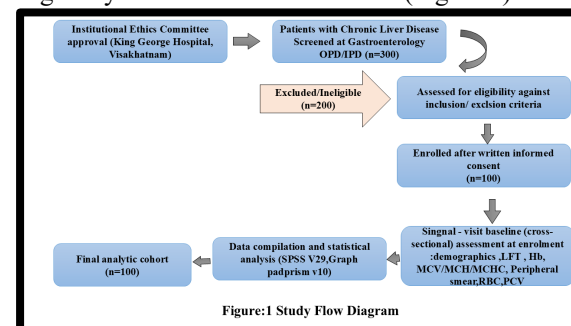
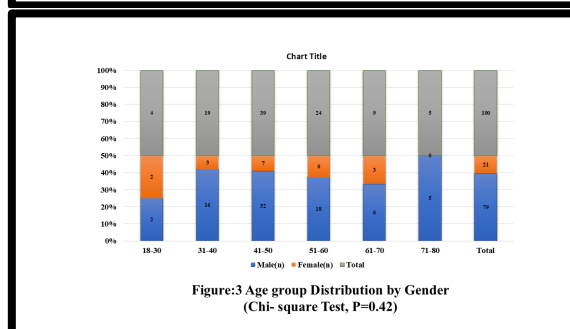
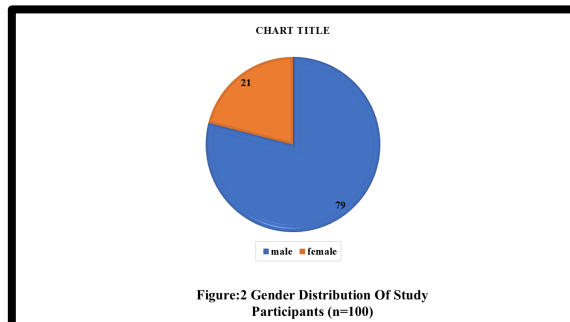


Figure:1 Study Flow Diagram

Men outnumbered women almost four to one, 79 (79%) against 21 (21%) ($\chi^2 = 18.36$, $p < 0.0001$; Figure 2). Participants clustered in mid-adulthood: 39 fell in the 41–50-year band, 24 in 51–60 years, 19 in 31–40 years, 9 in 61–70 years, 5 in 71–80 years, and 4 in 18–30 years. This age-group distribution

did not differ significantly between genders (chi-square test, $\chi^2=4.94$, $df=5$, $p=0.42$; Monte Carlo estimate of the Fisher–Freeman–Halton exact test, 100,000 replicates, $p=0.43$; Figure 3, Table 1), although roughly half the expected cell counts fell below five, so both results should be read as indicative rather than definitive.



By CLD stage, half the cohort ($n=50$) was classified as stage 2 (fibrosis), 34 as stage 3 (cirrhosis), 15 as stage 1, and a single patient as stage 4 (Figure 4, Table 1). Restricting formal comparison to stages 1–3, since the lone stage-4 patient could not support a meaningful cell-level test, gender distribution differed significantly across CLD stage (chi-square test, $\chi^2=7.48$, $df=2$, $p=0.024$; Monte Carlo estimate of the Fisher–Freeman–Halton exact test, 100,000 replicates, $p=0.021$), driven chiefly by the pronounced male skew at stage 3 (32 men versus 2 women). Across every stage, most participants reported a disease history of 12 months or less at enrolment, and only a small minority carried a documented history beyond two years.

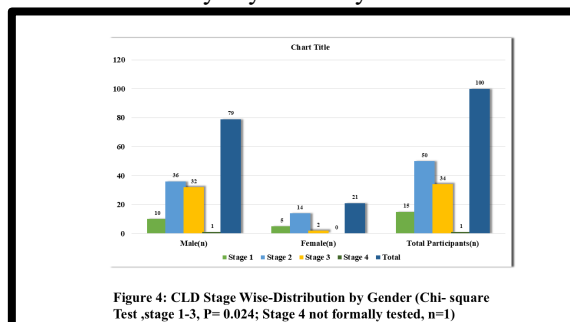


Table 1. Demographic and CLD Stage-Wise Distribution of Study Participants (N = 100)

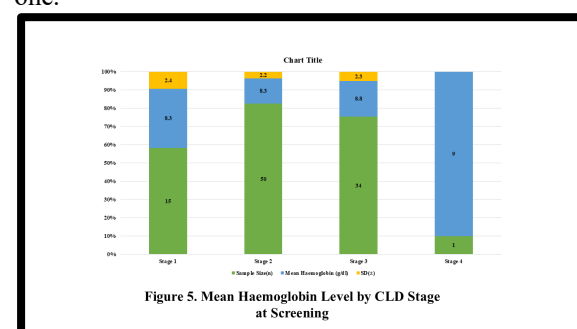
Characteristic	Male, n	Female, n	Total, n
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18–30 years	2	2	4
31–40 years	16	3	19
41–50 years	32	7	39
51–60 years	18	6	24
61–70 years	6	3	9
71–80 years	5	0	5
Age total	79	21	100
CLD stage			
Stage 1	10	5	15
Stage 2*	36	14	50
Stage 3	32	2	34
Stage 4	1	0	1
Stage total	79	21	100

*One patient was reassigned from male to female within CLD stage 2 to reconcile a discrepancy between the source case-report sub-totals (male $n=80$, female $n=20$ across CLD stages) and the overall gender total (male $n=79$, female $n=21$). This reassignment was made on statistical grounds alone — stage 2 is the largest stratum and therefore the most probable location of a single random misclassification — and was not traced to a specific patient in the original case-report forms, which were not re-audited during manuscript preparation. This correction should be verified against the source case-report forms before submission; if the true location of the discrepancy differs from stage 2, Table 1 and the associated stage-wise statistics (Section 3.1, Figure 4) should be revised accordingly.

3.2 Haemoglobin Levels and Anaemia Severity

All 100 participants met criteria for anaemia at screening. Mean haemoglobin was 8.5 ± 2.3 g/dL overall, consistent with moderate anaemia by WHO reference ranges (Table 2, Figure 5). Men measured higher than women, 8.7 ± 2.4 g/dL against 7.7 ± 2.0 g/dL (unpaired t-test, $p=0.04$; see Table 2 footnote on verifiability), placing men at a marginal-to-moderate deficit and women at a marginal-to-severe one.



Mean haemoglobin increased only marginally with advancing CLD stage: 8.3 ± 2.4 g/dL in stage 1, 8.3

± 2.2 g/dL in stage 2, 8.8 ± 2.3 g/dL in stage 3, and 9.0 g/dL in the single stage-4 patient. The stage-by-gender interaction did not reach significance (unpaired t-test, $p=0.178$). Across severity bands, mean haemoglobin in mild anaemia was near-identical between genders (10.78 ± 1.16 g/dL men, 10.8 ± 0.5 g/dL women), as it was in moderate (7.9 ± 0.6 versus 7.98 ± 0.6 g/dL) and severe anaemia (6.1 ± 0.82 versus 6.0 ± 0.83 g/dL; unpaired t-test, $p=0.90$; Figure 6, Table 2). Age-group comparisons showed a significant interaction between age and anaemia severity (two-way ANOVA, $p<0.001$), without a consistent linear trend across bands.

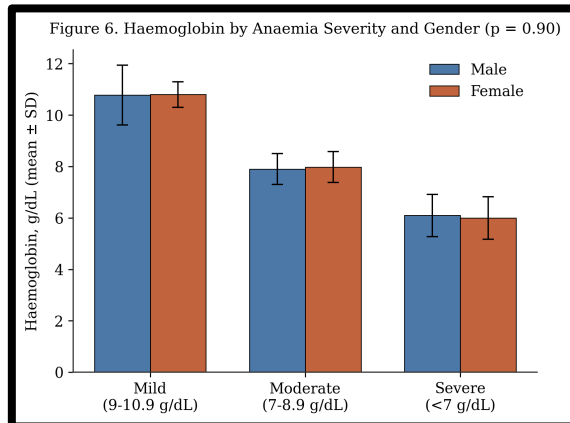


Table 2. Haemoglobin Levels by Gender, CLD Stage, and Anaemia Severity at Screening

Parameter	Male, Mean ± SD	Female, Mean ± SD
Overall (N = 100)	8.7 ± 2.4	7.7 ± 2.0
By CLD stage		
Stage 1 (n = 15)	8.3 ± 2.3	8.2 ± 2.9
Stage 2 (n = 50)	8.6 ± 2.5	7.3 ± 1.7
Stage 3 (n = 34)	8.9 ± 2.4	8.4 ± 2.1
Stage 4 (n = 1)	9.0	—
By anaemia severity (g/dL)		
Mild (9–10.9)	10.78 ± 1.16	10.8 ± 0.5
Moderate (7–8.9)	7.9 ± 0.6	7.98 ± 0.6
Severe (<7)	6.1 ± 0.82	6.0 ± 0.83

The male–female haemoglobin comparison (8.7 ± 2.4 g/dL, $n=79$ vs. 7.7 ± 2.0 g/dL, $n=21$) was originally reported as an unpaired t-test, $p=0.04$. Back-calculating a Welch's t-test from these rounded summary statistics gives $t=1.95$, $df=36.9$, two-tailed $p \approx 0.059$ — above the conventional 0.05 threshold and higher than the reported $p=0.04$; this held ($p=0.053$ – 0.065) across plausible ± 0.05 rounding perturbations of the reported SDs, so it is unlikely to be rounding noise alone. This most likely reflects

that the original test was computed on unrounded patient-level data, which are not available for re-verification here, rather than an error in the original analysis; nonetheless, the exact t-statistic and degrees of freedom from that original analysis should be confirmed and reported alongside the p-value before submission, consistent with the Monte Carlo cross-checks applied elsewhere in this report.

3.3 Red-Cell Indices

The mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) were 82.5 ± 14.0 fL, 27.0 ± 5.5 pg, and $31.6 \pm 2.8\%$, respectively, across the group (Table 3). Values did not differ significantly by gender alone (MCV 83.5 ± 14.3 fL in men versus 78.7 ± 12.4 fL in women; one-way ANOVA, $p=0.08$) but differed significantly across CLD stage (one-way ANOVA, $p=0.004$; Figure 7): the single stage-4 patient recorded the highest indices (MCV 88.9 fL, MCH 31.4 pg, MCHC 35.3%), while stage 2 recorded the lowest mean MCV (80.1 ± 16.5 fL). The stage-by-gender interaction was not significant (two-way ANOVA, $p=0.50$).

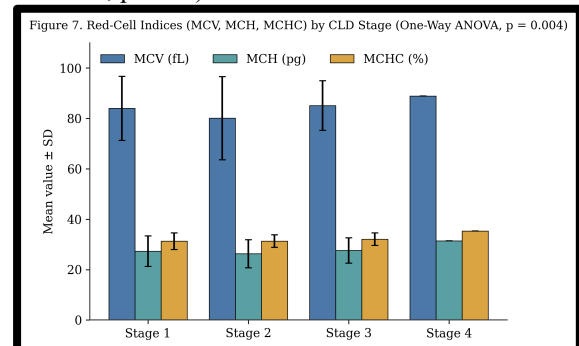


Table 3. Mean Corpuscular Volume, Mean Cell Haemoglobin, and Mean Cell Haemoglobin Concentration at Screening

Group	MCV, fL	MCH, pg	MCHC, %
Overall (N = 100)	82.5 ± 14.0	27.0 ± 5.5	31.6 ± 2.8
By gender			
Male	83.5 ± 14.3	27.7 ± 5.2	31.9 ± 2.8
Female	78.7 ± 12.4	24.7 ± 5.9	30.5 ± 2.3
By CLD stage			
Stage 1 (n = 15)	84.0 ± 12.7	27.3 ± 6.1	31.3 ± 3.3
Stage 2 (n = 50)	80.1 ± 16.5	26.3 ± 5.6	31.3 ± 2.5
Stage 3 (n = 34)	85.1 ± 9.9	27.6 ± 5.0	32.1 ± 2.5

Stage 4 (n = 1)	88.9	31.4	35.3
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3.4 Morphological Pattern of Anaemia

Peripheral smear examination classified 41 participants (41%) with normocytic normochromic anaemia, the single largest group, followed by 34 (34%) with microcytic hypochromic anaemia and 12 (12%) with normocytic hypochromic anaemia (Figure 8, Table 4). Macrocytic hyperchromic anaemia accounted for 5 participants (5%), dimorphic anaemia for 4 (4%), normocytic hyperchromic anaemia for 3 (3%), and macrocytic normochromic anaemia for a single participant (1%); no participant showed microcytic normochromic, microcytic hyperchromic, or macrocytic hypochromic morphology. The pattern held across genders: normocytic normochromic anaemia was the leading type in both men (33 of 79) and women (8 of 21), followed by microcytic hypochromic anaemia (23 men, 11 women).

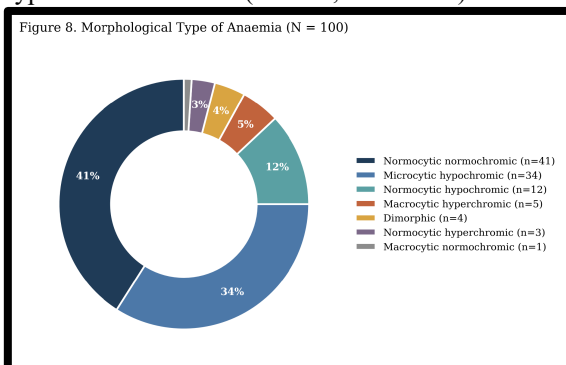


Table 4. Morphological Type of Anaemia by Gender (N = 100)

Type of anaemia	Male, n	Female, n	Total, n (%)
Normocytic normochromic	33	8	41 (41%)
Microcytic hypochromic	23	11	34 (34%)
Normocytic hypochromic	11	1	12 (12%)
Macrocytic hyperchromic	5	0	5 (5%)
Dimorphic anaemia	3	1	4 (4%)
Normocytic hyperchromic	3	0	3 (3%)
Macrocytic normochromic	1	0	1 (1%)
Microcytic normochromic	0	0	0 (0%)

Microcytic hyperchromic	0	0	0 (0%)
Macrocytic hypochromic	0	0	0 (0%)
Total	79	21	100 (100%)

Peripheral smear morphology was assessed by the hospital's routine haematology laboratory as part of standard clinical care; formal inter-rater reliability between readers was not assessed as part of this study protocol and is noted as a limitation (Section 4.5).

4. Discussion

4.1 Summary of Findings

Every participant in this cohort met laboratory criteria for anaemia, a pattern that sits within the high burden reported across cirrhotic populations worldwide. Anaemia skewed mild to moderate rather than severe, tracked only loosely with CLD stage, and carried a distinct male predominance shaped less by biological vulnerability than by exposure, principally alcohol use. Red-cell morphology pointed to normocytic normochromic anaemia as the leading pattern, ahead of microcytic hypochromic anaemia, a distribution that carries mechanistic implications discussed below.

4.2 Pathophysiological Contextualization

CLD disturbs erythropoiesis through several routes acting together: chronic low-grade gastrointestinal blood loss from portal hypertensive gastropathy or variceal bleeding, hypersplenism from portal hypertension that shortens red-cell survival, direct marrow-suppressive effects of hepatic dysfunction and alcohol, and impaired absorption or intake of iron, folate, and vitamin B12 [21,27,22]. The predominance of normocytic normochromic morphology in this cohort is more suggestive of gastrointestinal blood loss and anaemia of chronic disease than of an isolated nutritional deficiency, since iron or B12/folate deficiency would typically be expected to skew the distribution toward a microcytic or macrocytic pattern, respectively; this is a morphology-based inference, however, and was not confirmed against ferritin, vitamin B12, or folate assays, which were not part of the present protocol. Microcytic hypochromic anaemia, the second most frequent pattern here, is similarly compatible with either chronic iron loss, from gastrointestinal bleeding or, in women, menstrual blood loss, or the anaemia of chronic disease that commonly accompanies advanced liver dysfunction [22]; without biochemical confirmation, the two cannot be distinguished on morphology alone. Coexisting coagulopathy, itself a recognised complication of advancing CLD, may further compound gastrointestinal blood loss as a contributor to anaemia in this population [28].

4.3 Comparative Literature Analysis

Male predominance in this cohort (79%) mirrors the broader Indian pattern of alcohol-related CLD [29]. Adult alcohol-use-disorder prevalence in India runs higher in men than women; United States federal survey data likewise show men reporting higher rates of alcohol use than women [30], but the trajectory in India is distinct, with problematic drinking rising 43.6% among men and falling 8.5% among women between 2005–06 and 2015–16 [31]. Globally, alcohol use is linked to an estimated 3.3 million deaths annually and accounts for 5.1% of the world's disease burden, with average per-capita consumption among those above 15 years placed at roughly 13.5 g of pure alcohol per day [32]. The 41–50-year predominance recorded here coincides with the age band in which alcohol consumption peaks nationally, a pattern distinct from Western cohorts, where hepatitis-related CLD often presents earlier [33].

Stage 2 fibrosis accounted for half the cohort, a proportion at the high end of, though broadly consistent with, population-based fibrosis surveys, where significant fibrosis prevalence has been reported to rise from roughly 10% in adults under 40 years to close to 29% beyond age 75 [34]. The relative decline in stage-3 (cirrhosis) enrolment beyond 60 years in this cohort parallels reports that cirrhosis prevalence itself falls in the oldest age bands, plausibly reflecting differential survival, since median survival falls sharply with each transition from compensated to decompensated disease, and reduced continued alcohol exposure with age [34,4].

Drug-induced liver injury is generally an uncommon contributor to CLD cohorts of this kind: national surveillance places its incidence at 14–19 cases per 100,000 population, accounting for under 1% of acute liver injury presentations, and Indian DILI-network registry data indicate that anti-tubercular therapy and complementary or alternative medicines, rather than the analgesic overdoses common in Western series, dominate the local aetiological mix where drug-induced injury does occur [35,36]. This study did not record aetiology-specific case counts (viral, alcoholic, or drug-induced) for the enrolled cohort, so the actual contribution of drug-induced disease here cannot be quantified from the present data; this is addressed further under Limitations.

The overall anaemia burden recorded here sits within the 66–75% range reported across cirrhotic cohorts generally, and matches the observation that iron-deficiency anaemia specifically has been documented in 22% of compensated and 78% of decompensated cirrhosis [21]. Normocytic normochromic anaemia as the leading morphology, ahead of microcytic hypochromic and, more distantly, macrocytic patterns, is more in keeping with gastrointestinal bleeding and anaemia of chronic disease than with isolated haematinic

deficiency as the principal contributor in this population; the absence of ferritin, vitamin B12, and folate assays in the present protocol means this inference is indirect and should be confirmed, rather than assumed, in future work.

Women recorded lower mean haemoglobin than men despite comprising a smaller share of the cohort, a gap that plausibly reflects the added contribution of menstrual blood loss layered onto disease-related mechanisms. This is consistent with patterns described in the hepatitis-associated anaemia literature more broadly, where antiviral therapy itself is a recognised precipitant of anaemia in hepatitis-C-infected patients [27,22,37].

4.4 Clinical and Policy Implications

These findings support incorporating a baseline haemogram and peripheral smear into routine CLD work-up regardless of clinical stage, rather than reserving haematological assessment for patients with overt bleeding or advanced cirrhosis, since anaemia was already established by stage 1 in this cohort. Where peripheral smear indicates a microcytic or macrocytic pattern, reflex testing for ferritin, vitamin B12, and folate would help distinguish a treatable nutritional deficiency from anaemia of chronic disease, guiding whether haematinic replacement, endoscopic evaluation for a bleeding source, or continued observation is the appropriate next step. In pharmacist-led medication review within gastroenterology settings, this argues for flagging CLD patients for haemogram monitoring at each clinic visit rather than only when symptomatic.

Anaemia's contribution to CLD morbidity extends beyond the laboratory abnormality itself: health-related quality of life in CLD patients is shaped by age, gender, family support, socioeconomic status, and self-rated health, and correcting anaemia where clinically indicated may meaningfully improve this dimension of care [38].

4.5 Study Limitations

- The single-centre design and modest sample size limit generalisability. The achieved enrolment of 100 fell marginally short of the calculated minimum of approximately 103 (Section 2.3), which may modestly reduce statistical power for smaller subgroup comparisons, most notably CLD stage 4 (n=1).
- This is a cross-sectional analysis: it captures anaemia status at a single point in time (enrolment) and cannot describe how anaemia evolves as CLD progresses. Longitudinal follow-up of the same patients across disease stages would be needed to establish that trajectory directly, rather than inferring it from between-stage comparisons made at one time point.
- Peripheral smear was the sole diagnostic test used to characterise anaemia morphology; without ferritin, vitamin B12, and folate

assays, the precise aetiology of the anaemia identified could not be confirmed. Formal inter-rater reliability for peripheral smear reporting was not assessed as part of this protocol.

- This analysis stratifies anaemia by CLD stage and severity but not by underlying aetiology (viral, alcoholic, or drug-induced); aetiology-specific case counts were not systematically recorded in this protocol. Future studies should capture this dimension directly, with appropriate risk-ratio analysis, to test the aetiology-specific hypotheses this design could not address.
- Stage and gender group-size imbalance, evident in the sparse stage-4 representation ($n=1$), constrains the statistical power of subgroup comparisons at the severe end of the disease spectrum.

5. Conclusion

Anaemia was present in every participant of this prospective CLD cohort, predominantly mild to moderate in severity and normocytic normochromic in morphology, a pattern more consistent with gastrointestinal blood loss and anaemia of chronic disease than with isolated haematinic deficiency. Ferritin, vitamin B12, and folate were not measured in this protocol, however, so this mechanistic interpretation remains inferential rather than confirmed and should not be taken as established. Severity rose only marginally across CLD stages and did not differ meaningfully by gender within severity bands, even though overall haemoglobin was lower in women than men. These results support routine haemogram and peripheral-smear screening at CLD diagnosis, independent of disease stage, with reflex ferritin, vitamin B12, and folate testing where red-cell morphology suggests a nutritional contribution, so that the underlying mechanism can be confirmed biochemically and appropriate supplementation or further gastrointestinal work-up can begin before anaemia compounds the course of liver disease.

Declarations

Ethics approval: The King George Hospital Institutional Ethics Committee in Visakhapatnam gave its approval. All participants were asked to sign a written informed consent form.

Conflict of interest: No conflicts of interest are disclosed by the authors.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Acknowledgements: The authors express their gratitude to the Andhra Medical College's Department of Gastroenterology at King George Hospital in Visakhapatnam and the hospital's Laboratory Centre for support with patient recruitment and peripheral blood smear reporting.

References

1. Sharma A, Nagalli S. Chronic liver disease. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
2. Anthony PP, Ishak KG, Nayak NC, et al. The morphology of cirrhosis: recommendations on definition, nomenclature, and classification by a working group sponsored by the World Health Organization. *J Clin Pathol.* 1978;31:395–414.
3. Somnay K, Wadgaonkar P, Sridhar N, Roshni P, Rao N, Wadgaonkar R. Liver fibrosis leading to cirrhosis: basic mechanisms and clinical perspectives. *Biomedicine.* 2024;12:2229.
4. D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. *J Hepatol.* 2006;44:217–31.
5. Roth GA, Abate D, Abate KH, et al. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet.* 2018;392:1736–88.
6. Sepanlou SG, Safiri S, Bisignano C, et al. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Gastroenterol Hepatol.* 2020;5:245–66.
7. India State-Level Disease Burden Initiative Collaborators. Nations within a nation: variations in epidemiological transition across the states of India, 1990–2016 in the Global Burden of Disease Study. *Lancet.* 2017;390:2437–60.
8. Mukherjee PS, Vishnubhatla S, Amarapurkar DN, et al. Etiology and mode of presentation of chronic liver diseases in India: a multicentric study. *PLoS One.* 2017;12:e0187033.
9. Huang DQ, Terrault NA, Tacke F, et al. Global epidemiology of cirrhosis — aetiology, trends and predictions. *Nat Rev Gastroenterol Hepatol.* 2023;20:388–98.
10. Sarin SK, Kumar M, Eslam M, et al. Liver diseases in the Asia-Pacific region: a Lancet Gastroenterology & Hepatology Commission. *Lancet Gastroenterol Hepatol.* 2020;5:167–228.
11. Cheemerla S, Balakrishnan M. Global epidemiology of chronic liver disease. *Clin Liver Dis (Hoboken).* 2021. doi:10.1002/cld.1061
12. Moon AM, Singal AG, Tapper EB. Contemporary epidemiology of chronic liver disease and cirrhosis. *Clin Gastroenterol Hepatol.* 2020;18:2650–66.
13. World Health Organization. Hepatitis B (fact sheet) [Internet]. Geneva: WHO; 2023.

14. Stockdale AJ, Kreuels B, Henrion MYR, et al. The global prevalence of hepatitis D virus infection: systematic review and meta-analysis. *J Hepatol.* 2020;73:523–32.
15. Puri P, Anand AC, Saraswat VA, et al. Consensus statement of HCV Task Force of the Indian National Association for Study of the Liver (INASL). Part I: status report of HCV infection in India. *J Clin Exp Hepatol.* 2014;4:106–16.
16. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. *J Hepatol.* 2019;70:151–71.
17. Jepsen P, Younossi ZM. The global burden of cirrhosis: a review of disability-adjusted life-years lost and unmet needs. *J Hepatol.* 2021;75:S3–13.
18. Safiri S, Kolahi AA, Noori M, et al. Burden of anaemia and its underlying causes in 204 countries and territories, 1990–2019: results from the Global Burden of Disease Study 2019. *J Hematol Oncol.* 2021;14:185.
19. Kassebaum NJ, Jasrasaria R, Naghavi M, et al. A systematic analysis of global anaemia burden from 1990 to 2010. *Blood.* 2014;123:615–24.
20. International Institute for Population Sciences (IIPS), ICF. National Family Health Survey (NFHS-5), India, 2019–21. Mumbai: IIPS; 2021.
21. Manrai M, Dawra S, Kapoor R, Srivastava S, Singh A. Anaemia in cirrhosis: an underestimated entity. *World J Clin Cases.* 2022;10:777–89.
22. McHutchison JG, Manns MP, Longo DL. Definition and management of anaemia in patients infected with hepatitis C virus. *Liver Int.* 2006;26:389–98.
23. Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India. National Programme for Prevention and Control of Non-Communicable Diseases: Medical Officers' Manual for Prevention and Management of Chronic Liver Diseases. New Delhi: MoHFW; 2023.
24. Cochran WG. Sampling Techniques. 3rd ed. New York: John Wiley & Sons; 1977.
25. World Health Organization. Anaemia [Internet]. Geneva: WHO; 2019. Available from: <https://www.who.int/health-topics/anaemia>
26. Nutritional anaemias. Report of a WHO scientific group. World Health Organ Tech Rep Ser. 1968;405:5–37.
27. Turner J. Anemia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
28. Caldwell SH, Hoffman M, Lisman T, et al. Coagulation disorders and haemostasis in liver disease: pathophysiology and critical assessment of current management. *J Hepatol.* 2006;44:1039–46.
29. Singh SP, Panigrahi S, Mishra D, Khatua CR. Alcohol-associated liver disease, not hepatitis B, is the major cause of cirrhosis in Asia. *J Hepatol.* 2019;70:1031–2.
30. Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System [Internet]. Atlanta: CDC; 2017.
31. Shaikh R, Khan J. Gender and regional pattern of alcohol use and projection of problematic drinking in India, 1998–2016. *Alcohol.* 2021.
32. World Health Organization. Global status report on alcohol and health 2014. Geneva: WHO; 2014.
33. Singal AK, Mathurin P. Diagnosis and treatment of alcohol-associated liver disease: a review. *JAMA.* 2021;326:165–76.
34. Trifan A, Muzica CM, Nastasa R, et al. High prevalence of liver fibrosis among general population: a Romanian population-based study. *Hepatol Commun.* 2023;7:e0032.
35. Hosack T, Damry D, Biswas S. Drug-induced liver injury: a comprehensive review. *Ther Adv Gastroenterol.* 2023;16:17562848231163410.
36. Devarbhavi H, Joseph T, Sunil Kumar N, et al. The Indian network of drug-induced liver injury: etiology, clinical features, outcome and prognostic markers in 1288 patients. *J Clin Exp Hepatol.* 2021;11:288–98.
37. Reau N, Hadziyannis SJ, Messinger D, Fried MW, Jensen DM. Early predictors of anaemia in patients with hepatitis C genotype 1 treated with peginterferon alfa-2a (40KD) plus ribavirin. *Am J Gastroenterol.* 2008;103:1981–8.
38. Šumskienė J, Kupčinskas L, Šumskas L. Health-related quality of life measurement in chronic liver disease patients. *Medicina (Kaunas).* 2015;51:201–8.