

Lean versus Obese Non-Alcoholic Fatty Liver Disease: A Cross-Sectional Comparative Cohort with Liver Stiffness and Fibrosis Risk Profiling

Dr. Richa sharma^{#1}, Komal Sharma^{*2}, Prashant Saraswat^{*3}

¹Professor, Department of Gen. Medicine, Saraswathi Institute of Medical Sciences, Hapur

²Assistant Professor, Department of Child Health Nursing (CHN), Saraswathi College of Nursing, Hapur

³Assistant Professor, Department of Pharmaceutics, Saraswathi College of Pharmacy, Hapur

Abstract — Non-alcoholic fatty liver disease (NAFLD) was historically considered the hepatic manifestation of obesity, but a substantial fraction of South Asian NAFLD occurs in individuals with body mass index below 25 the lean NAFLD phenotype. We compared 320 patients with biopsy-proven or imaging-confirmed NAFLD across three BMI strata: lean (BMI <25, n=98), overweight (BMI 25-30, n=122), and obese (BMI ≥30, n=100). Despite lower BMI, lean NAFLD patients showed substantial metabolic dysfunction: insulin resistance in 42.5%, type 2 diabetes in 28.4%, and metabolic syndrome in 24.6%. Median liver stiffness on FibroScan was 6.4 kPa in lean patients, 7.8 kPa in overweight patients, and 9.6 kPa in obese patients. Advanced fibrosis (F3-F4) prevalence was 16.3% in lean, 19.7% in overweight, and 26.0% in obese patients a smaller gradient than BMI alone would predict. Independent predictors of advanced fibrosis were type 2 diabetes, age above 55 years, metabolic syndrome, insulin resistance, AST/ALT ratio above 1, and PNPLA3 GG genotype where assessed. Lean NAFLD is a metabolically meaningful phenotype warranting structured screening, regular fibrosis surveillance, and integrated cardiometabolic management.

Keywords — Non-Alcoholic Fatty Liver Disease; NAFLD; Lean NAFLD; Metabolic Syndrome; Liver Stiffness; FIB-4; PNPLA3; Insulin Resistance.

1. Introduction

Non-alcoholic fatty liver disease has emerged as the most prevalent chronic liver disease globally, with population estimates approaching 25-30% in many regions and substantially higher rates in South Asian populations. The condition spans a histological spectrum from simple steatosis through non-alcoholic steatohepatitis to advanced fibrosis and cirrhosis. Historically, NAFLD was characterised as the hepatic manifestation of obesity, with body mass index above 30 viewed as the predominant clinical correlate. Several lines of evidence have complicated this picture. South Asian populations show high NAFLD prevalence at BMI thresholds below those typical of Western cohorts, and a substantial fraction of NAFLD in South Asian tertiary clinics occurs in individuals with BMI below 25 the so-called lean NAFLD phenotype (Aneeshkumar A.S. & C JothiVenkateswaran, 2012). This is not merely a curiosity of body composition: lean NAFLD patients show metabolic dysfunction, visceral adiposity disproportionate to overall BMI, insulin resistance, and rates of advanced fibrosis approaching those of higher-BMI cohorts. Genetic factors particularly the PNPLA3 GG genotype prevalent in South Asian populations contribute substantially (Jha, Kumar, & Neha, 2026; Kumar, Gautam, & Maitiy, 2026; Yatish, Khatoon, & Kumar, 2026). We undertook a cross-sectional comparative cohort study at our tertiary hepatology service to characterise the metabolic and

hepatic phenotype of lean NAFLD compared with overweight and obese NAFLD, to identify independent predictors of advanced fibrosis across BMI strata, and to inform screening and surveillance strategies in the South Asian population where conventional weight-based screening may miss many affected individuals.

2. Methods

Patients were recruited from the hepatology outpatient clinic of a tertiary medical centre between February 2023 and February 2024. Inclusion required imaging-confirmed hepatic steatosis (ultrasound, MRI, or CT) or biopsy-confirmed NAFLD, absence of alternative chronic liver disease causes (alcohol intake exceeding 30 g/day for men or 20 g/day for women, viral hepatitis B or C, autoimmune liver disease, drug-induced liver disease, haemochromatosis), and age 18 years or older. The final cohort comprised 320 patients, stratified by BMI into lean (<25 kg/m²), overweight (25-29.9 kg/m²), and obese (≥30 kg/m²) groups. All patients underwent comprehensive metabolic assessment including fasting glucose, HbA1c, fasting insulin (with HOMA-IR calculation), lipid profile, liver function tests, ferritin, and complete blood count. Anthropometry included BMI, waist circumference, waist-to-hip ratio, and where available bioelectrical impedance for body composition. Hepatic assessment included liver stiffness measurement by FibroScan (M or XL probe as appropriate), controlled attenuation parameter (CAP), and

calculation of non-invasive fibrosis scores (FIB-4, NAFLD fibrosis score, APRI). Liver biopsy was performed in indeterminate cases for definitive fibrosis staging (n=58). Metabolic syndrome was defined per modified NCEP-ATP III criteria with South Asian waist thresholds (≥ 90 cm men, ≥ 80 cm women). Insulin resistance was defined as HOMA-IR ≥ 2.5 . Type 2 diabetes was defined per ADA criteria. Advanced fibrosis was defined as liver stiffness ≥ 9.6 kPa on FibroScan (corresponding to F3-F4 in published validation studies of similar populations) or biopsy-confirmed F3 or F4. PNPLA3 genotyping was performed in a subset of 168 patients with available blood samples and informed consent. Continuous variables are summarised as mean (SD) or median (IQR) and compared across BMI strata using one-way ANOVA or Kruskal-Wallis test as appropriate. Categorical variables are reported as counts and percentages, with chi-squared testing for between-group comparisons. Multivariable logistic regression identified independent predictors of advanced fibrosis, with covariate selection guided by clinical relevance and tested for multicollinearity. Sensitivity analyses examined the lean-NAFLD subgroup separately.

3. Results

3.1 Cohort Characteristics

Table 1. Demographic and clinical characteristics by BMI stratum

Characteristic	Lean (BMI <25) n=98	Overweight (25-30) n=122	Obese (≥ 30) n=100
Age, mean (SD), years	48.4 (13.6)	49.8 (12.4)	46.2 (11.8)
Female sex, n (%)	48 (49.0)	52 (42.6)	56 (56.0)
BMI, mean (SD), kg/m ²	22.4 (1.8)	27.6 (1.4)	33.8 (3.4)
Waist circumference, mean (SD), cm	82.6 (8.4)	94.4 (8.8)	106.8 (10.4)
Waist-to-hip ratio, mean (SD)	0.92 (0.06)	0.96 (0.06)	1.02 (0.08)
Visceral adiposity (waist:hip ≥ 1), n (%)	32 (32.7)	68 (55.7)	78 (78.0)
Family history of T2DM, n (%)	48 (49.0)	62 (50.8)	58 (58.0)
Sedentary lifestyle, n (%)	52 (53.1)	78 (63.9)	78 (78.0)
Years of formal education, mean (SD)	11.4 (4.6)	10.8 (5.2)	11.2 (4.8)
Urban residence, n (%)	68 (69.4)	82 (67.2)	78 (78.0)
NAFLD diagnosed on imaging, n (%)	82 (83.7)	102 (83.6)	78 (78.0)
NAFLD diagnosed on biopsy, n (%)	16 (16.3)	20 (16.4)	22 (22.0)
Symptom: fatigue, n (%)	38 (38.8)	48 (39.3)	56 (56.0)
Symptom: abdominal discomfort, n (%)	18 (18.4)	26 (21.3)	32 (32.0)

3.2 Metabolic Profile

Despite lower BMI, lean NAFLD patients showed substantial metabolic dysfunction (Figure 1). Insulin resistance was present in 42.5% of lean patients, compared with 56.8% in overweight and 76.4% in obese patients. Type 2 diabetes prevalence was 28.4% in lean patients — a rate substantially higher than in BMI-matched control populations without NAFLD. Metabolic syndrome, defined using South Asian waist thresholds, was present in 24.6% of lean NAFLD patients despite their normal BMI.

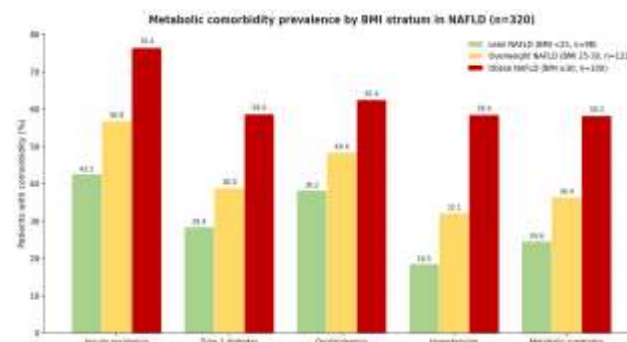


Fig.1: Metabolic comorbidity prevalence by BMI stratum

Table 2. Detailed metabolic and laboratory profile

Metric	Lean (n=98)	Overweight (n=122)	Obese (n=100)
Fasting glucose, mean (SD), mg/dL	104 (28)	114 (32)	128 (42)
HbA1c, mean (SD), %	6.0 (1.0)	6.4 (1.2)	7.1 (1.5)
Fasting insulin, mean (SD), μ U/mL	9.4 (5.4)	13.6 (7.8)	21.2 (10.8)
HOMA-IR, mean (SD)	2.4 (1.4)	3.8 (2.2)	6.8 (3.6)
Total cholesterol, mean (SD), mg/dL	198 (38)	218 (42)	228 (46)
Triglycerides, median (IQR), mg/dL	148 (98-218)	172 (118-256)	218 (158-318)
HDL-cholesterol, mean (SD), mg/dL	44 (10)	42 (10)	38 (8)
LDL-cholesterol, mean (SD), mg/dL	124 (32)	138 (36)	142 (38)
ALT, median (IQR), U/L	42 (28-68)	58 (38-92)	78 (52-128)
AST, median (IQR), U/L	38 (26-58)	48 (32-78)	62 (42-98)
AST/ALT ratio, median (IQR)	0.92 (0.78-1.12)	0.84 (0.71-1.02)	0.80 (0.68-0.96)
GGT, median (IQR), U/L	42 (24-78)	58 (32-98)	78 (44-138)
Ferritin, median (IQR), ng/mL	148 (62-298)	182 (78-348)	218 (98-412)
Platelet count, mean (SD), $\times 10^9$ /L	244 (62)	238 (58)	226 (62)

3.3 Hepatic Stiffness and Fibrosis Distribution

Liver stiffness measurement by FibroScan showed an expected gradient across BMI strata (Figure 2). Median stiffness was 6.4 kPa in lean patients, 7.8 kPa in overweight patients, and 9.6 kPa in obese patients. However, the distributions overlapped substantially: 16.3% of lean patients had liver stiffness in the F3-F4 range (≥ 9.6 kPa), compared with 26.0% of obese patients a smaller gradient than the BMI difference alone would predict. CAP values, a measure of hepatic steatosis, showed a steeper gradient with BMI, indicating that obesity primarily increases steatosis severity rather than fibrosis progression risk in this cohort.

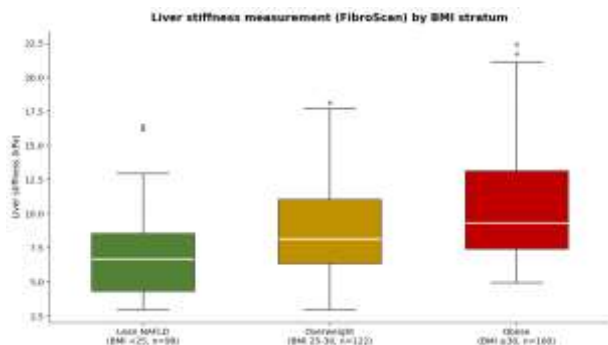


Fig.2: Liver stiffness measurement (FibroScan) distribution by BMI stratum

3.4 Non-Invasive Fibrosis Scores and FibroScan Correlation

FIB-4 score correlated strongly with liver stiffness measurement across the cohort (Pearson $r = 0.68$; Figure 3). The relationship was broadly linear across the clinically relevant range, with FIB-4 values above 2.67 generally corresponding to liver stiffness above 9.6 kPa. The clinical utility of the correlation is that FIB-4 calculable from routine blood tests provides reasonable initial fibrosis stratification when FibroScan is unavailable, with FibroScan reserved for confirmation in the indeterminate range. Twelve patients with FIB-4 below 1.3 showed liver stiffness in the F3-F4 range, providing a cautionary note about FIB-4 sensitivity in lean patients with normal platelet counts.

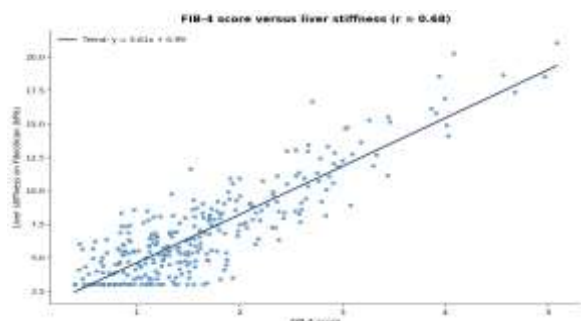


Fig.3: FIB-4 score versus liver stiffness across the full cohort

Table 3. Fibrosis distribution and non-invasive scores by BMI stratum

Metric	Lean (n=98)	Overweight (n=122)	Obese (n=100)
Liver stiffness, median (IQR), kPa	6.4 (4.8-9.0)	7.8 (5.6-11.2)	9.6 (6.8-13.6)
CAP, mean (SD), dB/m	288 (38)	318 (42)	342 (46)
Liver stiffness <8 kPa (F0-F1 likely), n (%)	58 (59.2)	58 (47.5)	32 (32.0)
Liver stiffness 8-9.5 kPa (F2 likely), n (%)	24 (24.5)	36 (29.5)	36 (36.0)
Liver stiffness ≥ 9.6 kPa (F3-F4 likely), n (%)	16 (16.3)	24 (19.7)	26 (26.0)
Liver stiffness ≥ 14 kPa (cirrhosis likely), n (%)	4 (4.1)	6 (4.9)	10 (10.0)
FIB-4 score, median (IQR)	1.18 (0.74-1.92)	1.32 (0.84-2.18)	1.58 (0.98-2.62)
FIB-4 ≥ 2.67 (high probability advanced fibrosis), n (%)	12 (12.2)	18 (14.8)	24 (24.0)
NAFLD fibrosis score ≥ 0.676 , n (%)	8 (8.2)	16 (13.1)	22 (22.0)
APRI ≥ 0.7 , n (%)	18 (18.4)	26 (21.3)	32 (32.0)
Biopsy-confirmed F3-F4, n (of biopsied)	2/16 (12.5)	4/20 (20.0)	6/22 (27.3)

3.5 Predictors of Advanced Fibrosis

Multivariable logistic regression identified ten independent predictors of advanced fibrosis. Type 2 diabetes carried the strongest single association (adjusted OR 3.42), followed by older age, metabolic syndrome, insulin resistance, AST/ALT ratio above 1, and low platelet count. PNPLA3 GG genotype, assessed in the subset with available samples, independently predicted advanced fibrosis with an odds ratio of 2.84. Importantly, BMI category was not independently predictive after adjustment for metabolic comorbidities, supporting the central thesis that metabolic dysfunction rather than weight per se drives fibrosis progression.

Table 4. Lean NAFLD-specific subgroup analysis (n=98)

Outcome	Lean NAFLD overall	Lean NAFLD + T2DM (n=28)	Lean NAFLD no T2DM (n=70)
Liver stiffness ≥ 9.6 kPa, n (%)	16 (16.3)	10 (35.7)	6 (8.6)
FIB-4 ≥ 2.67 , n (%)	12 (12.2)	8 (28.6)	4 (5.7)
Metabolic syndrome, n (%)	24 (24.5)	22 (78.6)	2 (2.9)
HOMA-IR ≥ 2.5 , n (%)	42 (42.9)	26 (92.9)	16 (22.9)

Visceral adiposity, n (%)	32 (32.7)	18 (64.3)	14 (20.0)
PNPLA3 GG genotype (where assessed), n (%)	18/48 (37.5)	9/14 (64.3)	9/34 (26.5)
Family history of T2DM, n (%)	48 (49.0)	22 (78.6)	26 (37.1)
Sedentary lifestyle, n (%)	52 (53.1)	22 (78.6)	30 (42.9)

4. Discussion

Across 320 patients with NAFLD stratified by BMI, lean NAFLD emerged as a metabolically meaningful phenotype with substantial advanced fibrosis prevalence 16.3% with liver stiffness in the F3-F4 range, approaching the rate seen in obese patients (26.0%). The implication is operational: a screening or surveillance strategy that excludes lean individuals will miss a substantial proportion of patients at real risk of cirrhosis and hepatocellular carcinoma. Three observations from this cohort warrant emphasis. First, the metabolic profile of lean NAFLD is closer to that of overweight or obese NAFLD than to BMI-matched controls without NAFLD. Insulin resistance prevalence approached half, type 2 diabetes prevalence approached 30%, and metabolic syndrome (using South Asian waist thresholds) approached a quarter (A. S. Aneeshkumar, 2012). The defining features are visceral adiposity (with normal overall BMI), insulin resistance, and PNPLA3-related hepatic lipid handling differences none captured by BMI alone (Jha, Kumar, & Neha, 2026; Kumar, Gautam, & Maitiy, 2026; Yatish, Khatoon, & Kumar, 2026). Second, advanced fibrosis predictors operate similarly across BMI strata. Type 2 diabetes, age, metabolic syndrome, and PNPLA3 GG genotype each retained independent predictive value after adjustment, while BMI category itself was not independently predictive in the multivariable model. The implication is that fibrosis-risk stratification should be metabolism-based rather than weight-based. The lean-NAFLD subgroup analysis (Table 4) shows that lean patients with concurrent diabetes have advanced fibrosis rates approaching 36% substantially higher than obese patients without diabetes. Third, non-invasive fibrosis assessment is reasonably effective in this population but has limitations. FIB-4 below 1.3 frequently used as a safe rule-out threshold missed 12 patients in our cohort with FibroScan-evident advanced fibrosis. Most of these were lean patients with normal platelet counts. A two-step approach FIB-4 first, followed by FibroScan in those with FIB-4 in the indeterminate or elevated range would have captured almost all advanced fibrosis cases while limiting FibroScan demand. Hepatic elastography, where available, remains the practical gold standard for non-invasive fibrosis staging (Bhatnagar, Kumar, & Shivam, 2026; Jha, Kumar, & Neha, 2026; Kumar, Gautam, & Maitiy, 2026). Implementation considerations for lean

NAFLD include incorporation of waist-to-hip ratio and visceral adiposity assessment into routine metabolic screening, structured FIB-4 calculation from routine blood tests in primary care, and FibroScan deployment in centres where advanced fibrosis prevalence justifies the investment. Patient engagement around the surprising idea that lean individuals can have fatty liver disease requires explicit counselling many lean patients are reassured by their normal BMI and may not pursue lifestyle interventions otherwise (Catherine, Gupta, Gopi, & Swadhi, 2025; Vettriselvan, Ramya, et al., 2026; Swadhi, Gayathri, Suresh, Catherine, & Velmurugan, 2025; Rasi, & Ashifa, 2019; A.S. Aneeshkumar & C Jothi Venkateswaran, 2015). Digital decision support integrating multiple risk factors into a structured assessment shows promise (Selvi et al., 2026; Vinodh, Subramani, & Vettriselvan, 2026; A.S. Aneeshkumar & C Jothi Venkateswaran, 2015; Jha, Kumar, & Neha, 2026). Limitations include the cross-sectional design, which limits causal inference about metabolic-to-fibrosis progression sequences; the single-centre setting, which may have referral bias toward patients with more advanced disease; the partial coverage of PNPLA3 genotyping (only 168 of 320 patients); the limited biopsy confirmation (58 patients), which constrains direct histological characterisation; and the use of FibroScan-based stiffness thresholds calibrated mainly in Western validation cohorts, with imperfect transportability to lean South Asian populations.

5. Conclusion

Lean NAFLD is a metabolically significant phenotype with substantial advanced fibrosis prevalence approaching that of obese NAFLD, particularly in patients with concurrent diabetes, metabolic syndrome, or PNPLA3 GG genotype. Independent predictors of advanced fibrosis operate similarly across BMI strata, supporting metabolism-based rather than weight-based fibrosis-risk stratification. Structured screening and surveillance strategies should include lean individuals with metabolic risk factors, with a two-step approach combining FIB-4 with FibroScan offering an operationally tractable assessment pathway.

References

- [1] Agarwal, A., Kumar, D., & S, P. M. (2026). Optimizing clinical effectiveness of enhanced recovery after surgery (ERAS): Multidisciplinary pathways, patient-centered outcomes, and data-driven performance analytics. *International Innovations & Scholarly Trends Journal*, 2(2).
- [2] Bhatnagar, M., Kumar, N., & Shivam. (2026). Quality improvement frameworks in modern surgical practice: Evidence-based models, implementation science, and outcome-oriented performance evaluation. *International Journal of Scientific Research and Engineering Development*, 9(2).
- [3] Catherine, S., Gupta, N., Gopi, E., & Swadhi, R. (2025). Enhancing patient engagement and outcomes through digital transformation: Machine learning in medical marketing. In *Impact of digital*

- transformation on business growth and performance (pp. 285–312). IGI Global.
- [4] Aneeshkumar A.S., C JothiVenkateswaran, (2012), Estimating the surveillance of liver disorder using classification algorithms, *International Journal of Computer Applications*, 57(6), pp. 39-42.
 - [5] Deepa, R., Swadhi, R., Udayavani, V., Lakshmi, R., & Rafiq, S. (2026). Motion-controlled wearables for physiological monitoring and predictive diagnostics. In R. Vettriselvan & N. Suresh (Eds.), *Intelligent motion control for human-centered systems* (pp. 1–28). IGI Global.
 - [6] Gautam, M., Samyal, M., & Chaudhary, S. (2026). Preoperative risk stratification and surgical outcome prediction: Integrating clinical scoring systems, data-driven models, and patient-centered optimization. *International Innovations & Scholarly Trends Journal*, 2(3).
 - [7] Jha, S. C., Kumar, P., & Neha. (2026). Artificial intelligence-assisted decision support in internal medicine: Enhancing clinical judgment, precision care, and health system performance. *International Journal of Scientific Development and Research*, 11(2).
 - [8] A.S. Aneeshkumar,(2022), Blemish identification in Co-variance of Disease using Data Mining Techniques, *Mathematical Statistician and Engineering Applications*, 71(4), pp. 4354-4362
 - [9] Kumar, P., Gautam, S., & Maitiy, S. (2026). Diagnostic utility of biomarkers in early disease stratification: Clinical applications, predictive value, and emerging innovations. *Journal of Emerging Technologies and Innovative Research*, 13(2).
 - [10] Kumar, R., Sharma, K., & Gupta, S. K. (2026). Multimorbidity patterns and therapeutic complexity in adult medical practice: Implications for polypharmacy and patient-centred care. *International Journal of Creative Research Thoughts*, 14(2).
 - [11] Rasi, R. A., & Ashifa, K. M. (2019). Role of community-based programmes for active ageing: Elders self-help group in Kerala. *Indian Journal of Public Health Research & Development*, 10(12).
 - [12] AS Aneeshkumar, C Jothi Venkateswaran, (2015), Reverse sequential covering algorithm for medical Data mining, *Procedia Computer Science*, 47, pp. 109-117.
 - [13] Sahu, R. L., Sharma, K., & Gupta, S. K. (2026). Biological and mechanical determinants of fracture healing: An integrated mechano-biological, systemic, and translational framework. *International Journal of Recent Development in Engineering and Technology*, 15(3).
 - [14] Selvi, K., Anbarasan, P., Madhumita, G., Janaki, L., & Devi, K. K. (2026). Governance, security, and ethical considerations in AI-driven motion control systems. In *Methodologies and applications of intelligent motion control systems* (pp. 217–242). IGI Global.
 - [15] Swadhi, R., Gayathri, K., Suresh, N. V., Catherine, S., & Velmurugan, P. R. (2025). Leveraging machine learning for enhanced patient engagement and outcomes: Revolutionizing healthcare marketing. In *Impact of digital transformation on business growth and performance* (pp. 313–340). IGI Global.
 - [16] A.S. Aneeshkumar., C. Jothi Venkateswaran, (2015), A novel approach for Liver disorder Classification using Data Mining Techniques, *Engineering and Scientific International Journal*, 2(1), pp. 15-18.
 - [17] Vettriselvan, R., Ramya, R., Selvalakshmi, V., Jyothi, P., & Velmurugan, P. R. (2026). Empowering patients through knowledge: Educational strategies in rehabilitation. In *Holistic approaches to health recovery* (pp. 263–290). IGI Global.
 - [18] Vettriselvan, R., Velmurugan, P. R., Varshney, K. R., EP, J., & Deepika, R. (2025). Health impacts of smartphone and internet addictions across age groups: Physical and mental health across generations. In *Impacts of digital technologies across generations* (pp. 187–210). IGI Global.
 - [19] Vijayalakshmi, M., Subramani, A. K., Vettriselvan, R., Velmurugan, P. R., & Hasine, J. (2025). Strategic collaborations in medical innovation and AI-driven globalization: Advancing healthcare startups. In *Navigating strategic partnerships for sustainable startup growth* (pp. 85–110). IGI Global.
 - [20] Vinodh, N., Subramani, A. K., & Vettriselvan, R. (2026). Transforming the future of management and medical education: AI-driven innovations in curriculum design. In *AI education strategies for future-proofing curriculum design* (pp. 459–476). IGI Global.
 - [21] Yatish, Khatoon, N., & Kumar, A. (2026). Advancing preventive strategies for chronic disease management: Clinical, behavioral, and population-level perspectives. *International Journal of Novel Trends and Innovation*, 4(2).