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Non-Alcoholic Fatty Liver Disease in Outpatient Practice of Southern Russia: A Multicenter Study of 480 Patients

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Abstract

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease worldwide. However, in routine outpatient practice, it is often diagnosed late. This is especially true in southern Russia, a region with high metabolic syndrome prevalence. No multicenter studies of NAFLD in this region have been conducted before. This study analyzed outpatient records of NAFLD patients in Stavropol, Rostov-on-Don, Krasnodar, and Astrakhan. We aimed to identify clinical and laboratory patterns, assess timely diagnosis, and explore interregional differences. We conducted a retrospective study of 480 outpatient records from patients with verified NAFLD (2024–2025). Anthropometric, laboratory, and instrumental data were collected. Fibrosis and insulin resistance indices were calculated. Abdominal obesity was present in 82.1% of patients. Arterial hypertension was found in 75.8%. Dyslipidemia occurred in 74.6%. Type 2 diabetes was diagnosed in 47.1%. Insulin resistance was recorded in 82.3%. The diagnosis of NAFLD was first established during this study in 38.8% of patients. Among these, 72% had normal alanine aminotransferase levels. High fibrosis risk was identified in 9.2% of patients. Stable interregional differences were observed. Krasnodar had the most severe metabolic profile and the highest fibrosis risk. Stavropol had the lowest. In conclusion, NAFLD in southern Russia shows high rates of metabolic disorders and late diagnosis. Relying only on transaminase levels is insufficient. Active screening using anthropometry and ultrasound is necessary for all patients with metabolic syndrome components.

Keywords: Non-alcoholic fatty liver disease, NAFLD, Hepatic steatosis, Metabolic syndrome, Multicenter study

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is a chronic, progressive condition (Younossi *et al*., 2023). It is characterized by excessive lipid accumulation, mainly triglycerides, in hepatocytes. This occurs without alcohol abuse or other causes of secondary steatosis (Younossi *et al*., 2016). The morphological spectrum of NAFLD ranges from simple steatosis to non-alcoholic steatohepatitis (NASH) (Riazi *et al*., 2022). Simple steatosis means fat infiltration of more than five percent of hepatocytes without inflammation or cell damage (Le *et al*., 2022). NASH is a more aggressive form. It includes ballooning degeneration of hepatocytes, lobular inflammation, and pericellular fibrosis (Maevskaya *et al*., 2022). Steatohepatitis is the main predictor of progression to liver cirrhosis and hepatocellular carcinoma (Drapkina *et al*., 2023). Large meta-analyses show that 20–30% of patients with steatohepatitis develop cirrhosis within 10–15 years (Eliashevich *et al*., 2023). Among patients with cirrhosis due to NAFLD, the annual risk of liver cancer is 1–3% (Blokhina *et al*., 2025).

For a long time, NAFLD was considered a benign disease that did not require active intervention (Golubeva *et al*., 2023). However, evidence accumulated over the last fifteen years proves otherwise.

NAFLD is associated with a two-fold increase in overall mortality compared to the general population, with cardiovascular events being the main contributor (Duell *et al*., 2022). NAFLD has become the second most common reason for liver transplantation in Western countries, surpassing viral hepatitis (Habibullah *et al*., 2024). It is also recognized as an independent risk factor for type 2 diabetes mellitus, chronic kidney disease, and colorectal cancer (Yki-Järvinen & Luukkonen, 2025).

NAFLD has a complicated and multiple aetiology (Ma *et al*., 2025). According to the traditional "two-hit" theory, hepatocytes that have accumulated fat as a result of insulin resistance are more susceptible to oxidative stress, endotoxins, or pro-inflammatory cytokines (Hou *et al*., 2025). This paradigm is now seen as being too simplistic. The current paradigm views NAFLD as the result of multiple simultaneously acting mechanisms (Nassir, 2022). Central to this is insulin resistance in adipose tissue and the liver. Visceral obesity leads to hyperlipolysis and increased free fatty acid flow to the liver, stimulating triglyceride synthesis (Peiseler *et al*., 2022). Hyperglycemia and hyperinsulinemia activate transcription factors that enhance lipogenesis (Sripongpun *et al*., 2023). Accumulation of free fatty acids and their metabolites damages mitochondria and the endoplasmic reticulum, triggering apoptosis and necroinflammation (Musso *et al*., 2023). Gut microbiota also plays a role: dysbiosis and increased intestinal permeability promote bacterial lipopolysaccharide entry into the portal bloodstream, activating inflammatory cells (Garbuzenko *et al.*, 2022; Bate *et al*., 2023; Oghenemaro *et al*., 2023). Genetic predisposition exists, with the PNPLA3 polymorphism being most strongly associated with severe steatosis and fibrosis (Targher *et al*., 2021). Nutritional factors such as high consumption of fructose, saturated fats, and trans fats also contribute significantly (Kumar *et al*., 2021). Thus, NAFLD is considered the hepatic equivalent of metabolic syndrome (Zhou *et al*., 2025).

Epidemiological data show the global scale of the problem. The largest 2023 systematic review (over ten million people) reported a global NAFLD prevalence of 32.4% (Rong *et al*., 2023). The highest rates are in the Middle East (42.5%) and South America (40.8%), the lowest in Africa (13.5%). In Europe, prevalence reaches 23.7%; in the USA, 24.1% (Reinson *et al*., 2023). Over the last ten years, global prevalence has increased by almost fifty percent (Wai *et al*., 2003). Among children and adolescents, a 2022 meta-analysis reported a NAFLD prevalence of 7.6%, reaching 34.2% in those with obesity (Portincasa *et al*., 2023). **Figure 1** shows global NAFLD prevalence by region.

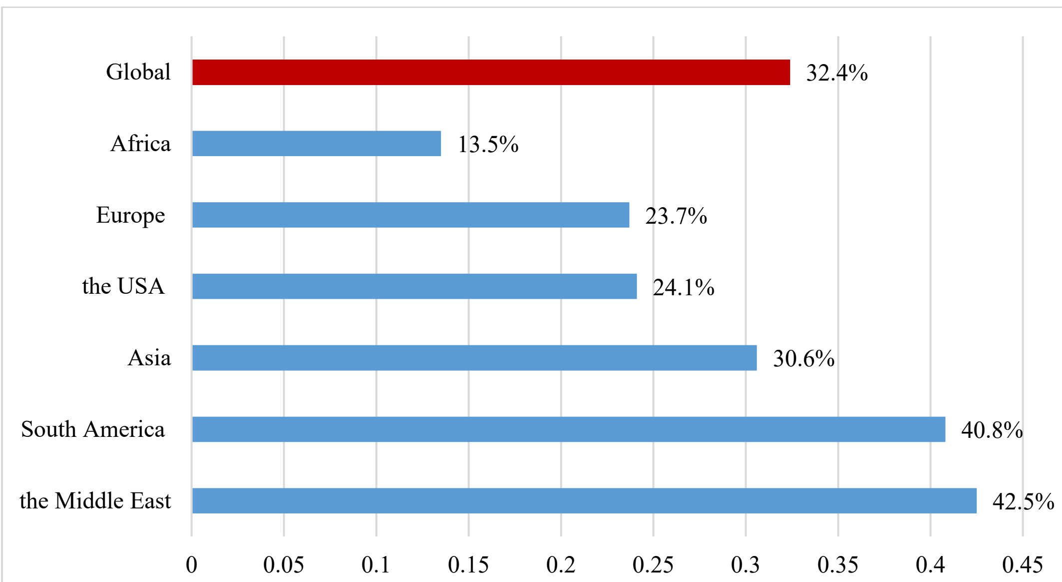

Figure 1. Global prevalence of NAFLD by region

The situation in Russia is no less concerning. The largest Russian epidemiological study (30 centers, over six thousand outpatients) reported a NAFLD prevalence of 37.3%, higher than in Europe and the USA (Isakov, 2025). Metabolic syndrome was diagnosed in 72% of these patients. Later studies show that among patients undergoing preventive check-ups, ultrasound-detected hepatic steatosis prevalence is 41.2%, with 22% under 40 years old (Dabravolski *et al*., 2021). Southern Russia (Krasnodar and Stavropol regions, Rostov and Astrakhan districts) has a high prevalence of metabolic syndrome. According to Rosstat, obesity among adults in these regions reaches 28–32% versus the national average of 26% (Martinchik *et al*., 2024). However, no targeted multicenter studies of NAFLD clinical features have been conducted in these regions, considering their climatic, geographic, and dietary differences.

Despite its high prevalence, NAFLD remains diagnostically underestimated (Cahyaningsih & Hikmah, 2023; Tawfik *et al*., 2023; Auwyang & Widiasih, 2024). Up to 80% of early-stage patients have no complaints. Normal liver transaminase levels do not exclude the diagnosis: screening studies show normal ALT in 30–50% of steatosis patients and even 20–30% of NASH patients (Mantovani, 2021). Liver ultrasound is not part of standard preventive check-ups. Screening using transaminases has low sensitivity, and primary care physicians have low awareness, often seeing NAFLD as a harmless finding. According to international studies, only 5–15% of true NAFLD cases are diagnosed in real-world practice. Extrapolating epidemiological data to the Russian adult population gives about 40 million NAFLD patients, yet official statistics show no more than 2–3 million cases.

Thus, NAFLD is one of the most urgent problems in modern medicine, requiring active detection at the outpatient stage, especially in regions with high metabolic syndrome prevalence, such as southern Russia. This study aimed to analyze outpatient records of patients with verified NAFLD seen in clinics in Stavropol, Rostov-on-Don, Krasnodar, and Astrakhan between 2024 and 2025. We sought to identify the most characteristic clinical, laboratory, and anthropometric patterns of the disease, assess the rate of timely diagnosis, and identify regional differences related to climatic, geographic, and dietary factors (Ismikhanov *et al*., 2023; Poornachitra & Maheswari, 2023; Peterson *et al*., 2024; Seah *et al*., 2024).

Materials and Methods

The study took place in city clinics across four cities in southern Russia. We analyzed 120 outpatient records per city (Stavropol, Rostov-on-Don, Krasnodar, and Astrakhan). The total sample size was 480 patients. All had a diagnosis of NAFLD or hepatic steatosis. Data collection covered outpatient records from January 2024 to December 2025.

Inclusion criteria were: a diagnosis of NAFLD or steatosis in the medical record, age 18 years or older, an ultrasound report confirming hepatic steatosis, and exclusion of alcoholic etiology (based on history and screening questionnaires). Exclusion criteria were: confirmed viral hepatitis B or C, autoimmune liver diseases, hereditary liver diseases (hemochromatosis, Wilson's disease, alpha-1 antitrypsin deficiency), use of steatogenic drugs (corticosteroids, amiodarone, methotrexate, tamoxifen) in the last six months, pregnancy and lactation, chronic kidney disease stages 4–5 (eGFR <30 mL/min/1.73m²), decompensated cardiovascular or respiratory diseases, and active cancer (Rinella *et al*., 2023).

Data were extracted from primary medical records (form 025/u) and ultrasound registries. Trained student researchers extracted the data under the supervisor's guidance. To minimize errors, we double-verified 10% of randomly selected cards in each city. Agreement exceeded 95%.

We collected demographic and anthropometric data: sex, age at first steatosis diagnosis, height, weight, and waist circumference. Body mass index (BMI) was calculated using the standard Quetelet formula. Waist circumference was measured at the midpoint between the lower rib margin and the iliac crest. Only values recorded using this method were included.

We included laboratory results from tests performed within three months of the ultrasound. Parameters included: ALT, AST, GGT, total cholesterol, triglycerides, LDL, HDL, fasting glucose, fasting insulin (when available), creatinine, and uric acid (when available). eGFR was calculated using the CKD-EPI 2021 formula.

Ultrasound data included right lobe size, parenchymal echogenicity, distal attenuation, and vascular pattern. When transient elastography with CAP was available, we recorded liver stiffness (kPa) and CAP (dB/m).

We assessed comorbidities: arterial hypertension, type 2 diabetes, dyslipidemia, coronary artery disease, heart failure, and chronic kidney disease (with stage). Dyslipidemia was defined as any abnormality in the lipid profile.

We calculated non-invasive fibrosis indices for all patients. FIB-4 used age, AST, ALT, and platelet count (Zampieri *et al*., 2025). Values below 1.30 indicated low risk; 1.30–2.67 intermediate risk; above 2.67 high risk. The NAFLD Fibrosis Score (NFS) used age, BMI, hyperglycemia, AST/ALT ratio, platelet count, and albumin (Pan *et al*., 2025). Values below -1.455 excluded fibrosis; above 0.676 indicated advanced fibrosis. APRI was calculated as (AST/upper normal limit) / platelet count × 100 (Liao *et al*., 2022). Values above 0.5 were a sensitive marker of fibrosis; values above 1.0 were specific for cirrhosis. We calculated HOMA-IR (fasting glucose × insulin / 22.5) when both values were available (Li *et al*., 2023). Values above 2.77 indicated insulin resistance.

The Stavropol center had an additional prospective phase. We recorded the altitude of each patient's residential district using GPS coordinates. A brief 10-item food frequency questionnaire assessed dietary habits (meat, fish, vegetables, fruit, sugary drinks, baked goods). We re-contacted 50 patients after 3–6 months. We assessed changes in body weight, ALT, AST, and self-reported treatment adherence (5-point scale).

We used Jamovi 2.4 and SPSS 26.0 for statistical analysis (IBM Corp., 2019). The Shapiro-Wilk test assessed normality. Normally distributed data are presented as mean ± SD. Non-normally distributed data are presented as median [Q1; Q3]. We compared four cities using ANOVA (normal) or Kruskal-Wallis (non-normal). Categorical variables were compared using chi-square or Fisher's exact test. Multivariate logistic regression (stepwise, AIC criterion) identified independent predictors of NAFLD. The control group for regression analysis consisted of 120 obese patients without ultrasound signs of steatosis. Correlation analysis used Spearman's rank coefficient. For prospective phase dynamics, we used a paired t-test (normal differences) or a Wilcoxon test (non-normal). Differences were significant at two-sided $p < 0.05$. For multiple comparisons, we applied the Bonferroni correction (significant $p < 0.0083$).

Sample size was calculated using G*Power 3.1 (Faul *et al*., 2007). To detect a medium effect size between four groups (power 80%, $\alpha = 0.05$), at least 180 patients were required. Considering possible missing data and city stratification, we planned to include 480 patients (120 per center).

Results and Discussion

Cohort Characteristics. We analyzed 480 outpatient records of patients with confirmed NAFLD or hepatic steatosis. Patients were seen in clinics in Stavropol, Rostov-on-Don, Krasnodar, and Astrakhan between 2024 and 2025 **(Table 1).** The sample included 254 men (52.9%) and 226 women (47.1%). Mean age was 52.4 ± 11.2 years (median 53 years, range 20-86 years). Sex distribution did not differ significantly between cities (p = 0.34). Patients in

Krasnodar (53.8 ± 10.9 years) and Rostov-on-Don (53.2 ± 11.4 years) were slightly older than those in Stavropol (50.9 ± 11.0 years) and Astrakhan (51.7 ± 11.3 years). This difference was not statistically significant (p = 0.08).

Table 1. Demographic and anthropometric characteristics of patients

Parameter	Stavropol (n=120)	Rostov-on-Don (n=120)	Krasnodar (n=120)	Astrakhan (n=120)	Total (n=480)	p
Male, n (%)	62 (51.7)	65 (54.2)	66 (55.0)	61 (50.8)	254 (52.9)	0.34
Age, years (M±SD)	50.9±11.0	53.2±11.4	53.8±10.9	51.7±11.3	52.4±11.2	0.08
BMI, kg/m² (M±SD)	30.1±4.7	32.4±5.3	33.9±5.8	31.8±5.1	32.0±5.4	<0.01
Waist circumference, cm (M±SD)	93.4±10.2	97.8±11.4	99.2±12.1	96.1±11.0	96.6±11.4	<0.01
Obesity (BMI≥30), n (%)	72 (60.0)	88 (73.3)	98 (81.7)	81 (67.5)	339 (70.6)	<0.01
Abdominal obesity*, n (%)	88 (73.3)	102 (85.0)	108 (90.0)	96 (80.0)	394 (82.1)	<0.01

Note: Abdominal obesity is defined as a waist circumference >94 cm for men and >80 cm for women.

Anthropometric parameters showed significant interregional differences **(Table 2).** The highest mean BMI was in Krasnodar (33.9 ± 5.8 kg/m²). The lowest was in Stavropol (30.1 ± 4.7 kg/m²). Obesity (BMI ≥30) was present in 339 patients (70.6%). The highest rate was in Krasnodar (81.7%). The lowest was in Stavropol (60.0%). Abdominal obesity (by waist circumference) was present in 394 patients (82.1%). Again, Krasnodar had the highest rate (90.0%) and Stavropol the lowest (73.3%). All intergroup differences were statistically significant (p < 0.01).

The timely diagnosis rate. In actual outpatient practice, we evaluated the rate of prompt NAFLD diagnosis. A diagnosis was considered "previously established" if the record of NAFLD or steatosis existed in the chart before our data extraction. We first established the diagnosis during our analysis in 186 cases (38.8% of the total sample). Krasnodar had the highest rate of missed diagnoses (48 patients, 40.0%). Stavropol had the lowest (33 patients, 27.5%). Among patients with newly diagnosed NAFLD, 72% had normal ALT levels. This likely explains the lack of physician awareness.

Table 2. Rate of previously established NAFLD diagnosis

Parameter	Stavropol	Rostov-on-Don	Krasnodar	Astrakhan	Total
Previously established diagnosis, n (%)	87 (72.5)	71 (59.2)	72 (60.0)	64 (53.3)	294 (61.2)
First diagnosed during study, n (%)	33 (27.5)	49 (40.8)	48 (40.0)	56 (46.7)	186 (38.8)

Laboratory Parameters. ALT levels were elevated in 312 patients (65.0%). The highest values were in Krasnodar (64.2 ± 38.4 U/L) and Rostov-on-Don (61.8 ± 35.2 U/L). The lowest were in Stavropol (52.4 ± 29.6 U/L). AST exceeded the normal range in 254 patients (52.9%). The ALT/AST ratio (typically >1.0 in steatosis) averaged 1.28 ± 0.38 **(Table 3).** Values above 1.0 were recorded in 386 patients (80.4%). GGT was elevated in 278 patients (57.9%). The highest values were in Krasnodar (84.6 ± 52.1 U/L).

Table 3. Laboratory parameters of patients with NAFLD

Parameter	Stavropol (n=120)	Rostov-on-Don (n=120)	Krasnodar (n=120)	Astrakhan (n=120)	Total (n=480)
ALT, U/L (M±SD)	52.4±29.6	61.8±35.2	64.2±38.4	55.9±31.8	58.6±34.2
AST, U/L (M±SD)	42.8±24.2	48.6±29.4	50.3±31.8	44.2±26.2	46.5±28.1
ALT/AST ratio	1.22±0.32	1.27±0.36	1.28±0.39	1.26±0.35	1.26±0.36
GGT, U/L (M±SD)	66.4±44.2	72.8±47.6	84.6±52.1	67.9±45.8	72.9±48.1
Total cholesterol, mmol/L	5.68±1.18	5.94±1.26	6.12±1.32	5.84±1.22	5.90±1.25
Triglycerides, mmol/L	2.18±1.08	2.42±1.19	2.58±1.24	2.31±1.14	2.37±1.17
LDL, mmol/L	3.48±0.92	3.66±0.98	3.82±1.04	3.58±0.94	3.64±0.97
HDL, mmol/L	1.08±0.26	1.00±0.24	0.96±0.22	1.04±0.25	1.02±0.24
Fasting glucose, mmol/L	5.68±1.54	5.94±1.68	6.12±1.82	5.82±1.58	5.89±1.66
HOMA-IR* (Me [Q1;Q3])	3.92 [2.88;5.16]	4.34 [3.12;5.68]	4.68 [3.44;6.12]	4.12 [3.02;5.44]	4.28 [3.12;5.62]

Note: HOMA-IR was calculated for 384 patients (80% of the sample) who had available fasting insulin data.

The lipid profile showed marked abnormalities. Hypertriglyceridemia (triglycerides >1.7 mmol/L) was present in 366 patients (76.2%). The highest values were in Krasnodar (2.58 ± 1.24 mmol/L). The lowest were in Stavropol (2.18 ± 1.08 mmol/L). LDL exceeded target values (<3.0 mmol/L) in 332 patients (69.2%). HDL was low in 264 patients (55.0%). Fasting hyperglycemia (glucose >5.6 mmol/L) was recorded in 274 patients (57.1%). Median HOMA-IR (calculated for 384 patients) was 4.28, well above the insulin resistance threshold of 2.77. HOMA-IR >2.77 was found in 316 of 384 patients (82.3%). The highest rate was in Krasnodar (88.6%) and Rostov-on-Don (85.2%). The lowest was in Stavropol (76.4%).

Comorbidities **(Table 4).** The most common comorbidity was arterial hypertension (364 patients, 75.8%). Next was dyslipidemia (358 patients, 74.6%), followed by obesity (339 patients, 70.6%). Type 2 diabetes was diagnosed in 226 patients (47.1%). The highest rate was in Krasnodar (56.7%) and Rostov-on-Don (52.5%). The lowest was in Stavropol (38.3%). Complete metabolic syndrome (three or more criteria: abdominal obesity, hypertension, dyslipidemia, hyperglycemia) was present in 278 patients (57.9%). The highest rate was in Krasnodar (68.3%). The lowest was in Stavropol (46.7%).

Table 4. Comorbidities in patients with NAFLD

Condition	Stavropol (n=120)	Rostov-on-Don (n=120)	Krasnodar (n=120)	Astrakhan (n=120)	Total (n=480)
Arterial hypertension, n (%)	84 (70.0)	94 (78.3)	98 (81.7)	88 (73.3)	364 (75.8)
Dyslipidemia, n (%)	82 (68.3)	92 (76.7)	96 (80.0)	88 (73.3)	358 (74.6)
Type 2 diabetes, n (%)	46 (38.3)	63 (52.5)	68 (56.7)	49 (40.8)	226 (47.1)
Coronary artery disease, n (%)	24 (20.0)	31 (25.8)	36 (30.0)	28 (23.3)	119 (24.8)
Chronic kidney disease, n (%)	18 (15.0)	24 (20.0)	29 (24.2)	21 (17.5)	92 (19.2)
Metabolic syndrome (≥3 criteria), n (%)	56 (46.7)	72 (60.0)	82 (68.3)	68 (56.7)	278 (57.9)

Non-Invasive Fibrosis Risk Assessment **(Table 5).** FIB-4 index showed low fibrosis risk (<1.30) in 292 patients (60.8%), intermediate risk (1.30-2.67) in 144 patients (30.0%), and high risk (>2.67) in 44 patients (9.2%). Krasnodar had the highest proportion of high-risk patients (13.3%). Stavropol had the lowest (5.8%). NAFLD Fibrosis Score (NFS) exceeded the threshold for advanced fibrosis (>0.676) in 62 patients (12.9%). This was highest in Krasnodar (18.3%) and lowest in Stavropol (8.3%). APRI values >0.5 were recorded in 158 patients (32.9%). Values >1.0 were recorded in 28 patients (5.8%). Correlation analysis showed moderate positive associations between BMI and FIB-4 ($\rho = 0.42$, $p < 0.001$) and between waist circumference and NFS ($\rho = 0.48$, $p < 0.001$).

Table 5. Non-invasive fibrosis risk assessment

Index	Risk category	Stavropol	Rostov-on-Don	Krasnodar	Astrakhan	Total
FIB-4	Low (<1.30), n (%)	82 (68.3)	70 (58.3)	64 (53.3)	76 (63.3)	292 (60.8)
FIB-4	Intermediate (1.30-2.67), n (%)	31 (25.8)	38 (31.7)	40 (33.3)	35 (29.2)	144 (30.0)
FIB-4	High (>2.67), n (%)	7 (5.8)	12 (10.0)	16 (13.3)	9 (7.5)	44 (9.2)
NFS	Advanced fibrosis (>0.676), n (%)	10 (8.3)	16 (13.3)	22 (18.3)	14 (11.7)	62 (12.9)
APRI	>0.5, n (%)	34 (28.3)	42 (35.0)	48 (40.0)	34 (28.3)	158 (32.9)
APRI	>1.0, n (%)	4 (3.3)	7 (5.8)	12 (10.0)	5 (4.2)	28 (5.8)

Regional Differences: Summary. Comparison of the four cities revealed a consistent pattern. Krasnodar had the most severe metabolic profile (highest BMI, waist circumference, triglycerides, diabetes frequency, and fibrosis risk). Rostov-on-Don and Astrakhan followed. Stavropol showed the least severe metabolic abnormalities. Differences between Stavropol and Krasnodar were statistically significant for most parameters ($p < 0.01$). These data suggest that geographic, climatic, and possibly dietary factors may influence NAFLD prevalence and severity across different regions of southern Russia.

This multicenter study of 480 outpatients with NAFLD from four southern Russian cities revealed several important findings. First, NAFLD rarely occurs in isolation. Most patients had at least two components of metabolic syndrome, and over half had full metabolic syndrome. This confirms that NAFLD is primarily a hepatic manifestation of a systemic metabolic disorder. Second, late diagnosis was common: nearly 39% of patients had no verified NAFLD diagnosis in their records despite clear ultrasound evidence of steatosis and significant metabolic abnormalities. Third, we found stable interregional differences. Krasnodar and Rostov-on-Don had more severe metabolic profiles and higher fibrosis risk than Stavropol and Astrakhan. Stavropol was the most favorable among the four cities **(Figure 2).**

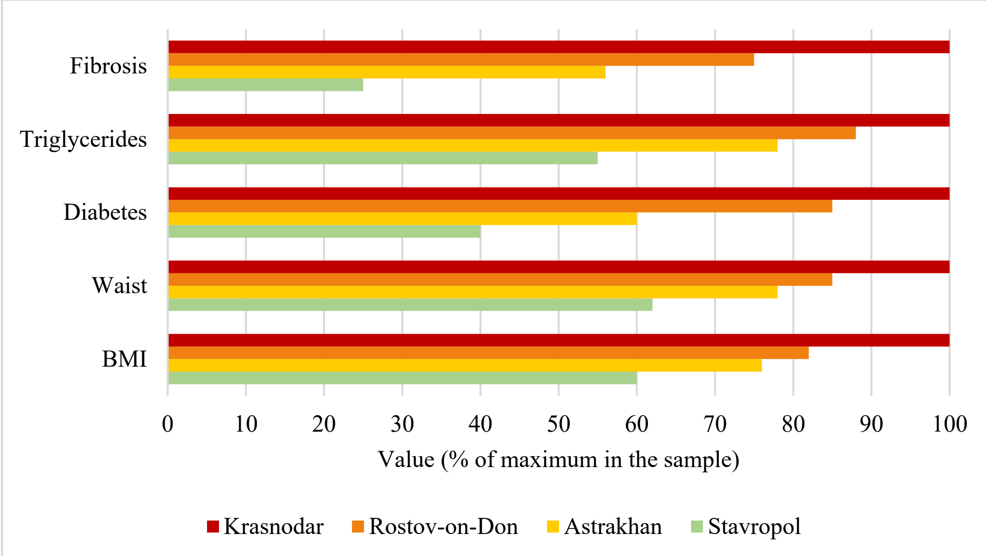

Figure 2. Standardized metabolic parameters of NAFLD patients in four cities of southern Russia (% of maximum value in the sample).

Note: Values for each parameter were normalized to the maximum value in the sample (Krasnodar = 100% for each parameter). Krasnodar shows the worst metabolic profile across all parameters. Stavropol shows the best profile. The most pronounced differences between cities were observed for high fibrosis risk (FIB-4 > 2.67) and type 2 diabetes frequency (Belfiore *et al*., 2023; García & Jaramillo, 2023; Bergeron *et al*., 2024; Jabir & Rajab, 2024; Rohmani *et al*., 2024; Singar, 2024).

The prevalence of obesity (70.6%) and abdominal obesity (82.1%) in our cohort aligns with large epidemiological studies. A meta-analysis of over 8 million people reported obesity in 68–75% and abdominal obesity in 78–85% of NAFLD patients (Saiman *et al*., 2022). Our data fall within this range, confirming sample representativeness. Notably, even patients with normal BMI (8.3% of our sample) often had abdominal obesity by waist circumference. This corresponds to the "metabolically obese normal-weight" phenotype (Stefan & Schulze, 2023). These patients are easily missed by BMI-based screening (Garbarova & Vartiak, 2024; Pham, 2024).

Mean ALT was 58.6 U/L (approximately 1.5 times the upper normal limit). However, 35% of patients had normal ALT. Among newly diagnosed cases, this proportion reached 72%. This agrees with international screening studies, where normal ALT in confirmed steatosis occurs in 30–50% of patients (Pouwels *et al*., 2022). Relying solely on transaminase levels leads to massive underdiagnosis of NAFLD (Zheng *et al*., 2023). The ALT/AST ratio was 1.26, typical for steatosis and useful for differentiating it from alcoholic liver disease (where AST predominates) (Sheptulina *et al*., 2023). Only 19.6% of patients had a ratio below 1.0, which might indicate more advanced fibrosis or concomitant alcoholic injury (though alcohol abuse was excluded).

The lipid profile showed atherogenic changes. Hypertriglyceridemia (76.2%) was the most common lipid abnormality, reflecting increased hepatic triglyceride synthesis due to insulin resistance (Polyzos *et al*., 2023). Elevated LDL (69.2%) and low HDL (55.0%) completed the dyslipidemia pattern typical of metabolic syndrome (Isaacs, 2023). Lipid abnormalities were most pronounced in Krasnodar and Rostov-on-Don, correlating with higher obesity rates in these cities.

Insulin resistance (HOMA-IR >2.77) was found in 82.3% of patients. This is among the highest rates reported. For comparison, European cohorts typically show insulin resistance in 65–75% of NAFLD patients (Hutchison *et al*., 2023). This high prevalence may reflect southern Russia's dietary patterns (high-calorie intake) and low physical activity. The lowest insulin resistance rate was in Stavropol (76.4%), possibly due to dietary differences (more vegetables, fewer simple carbohydrates) and greater physical activity from the hilly terrain (Pilipenko *et al*., 2023).

Non-invasive fibrosis indices showed that approximately 9% of patients had a high risk of significant fibrosis (FIB-4 >2.67), and 13% had advanced fibrosis by NFS (>0.676). These figures are comparable to the Russian DIREG-2 study, which reported high fibrosis risk in 7–11% of outpatients with NAFLD (Ivashkin *et al*., 2015). Importantly, our data come from an outpatient cohort (mostly asymptomatic patients). The true population prevalence of fibrosis may be higher, as patients with severe disease are more likely to be hospitalized and thus excluded from outpatient samples (Golubeva *et al*., 2022).

The most striking result was the interregional differences (**Figure 2**). Krasnodar patients had the highest BMI, waist circumference, triglycerides, diabetes frequency, and fibrosis risk. Stavropol patients had the lowest values for most metabolic parameters. Several hypotheses may explain this. First, dietary habits differ. Krasnodar region traditionally consumes more meat (especially fatty pork and beef) and fried foods. Stavropol, influenced by Caucasian cuisine, has more vegetables, greens, fermented dairy products, and fewer simple carbohydrates (Katchieva *et al*., 2025). Second, climate and physical activity likely play a role. Stavropol sits at an altitude of 620 meters; the hilly terrain encourages more daily walking and higher energy expenditure. Krasnodar is on a plain (30 meters); residents rely more on cars, and the hot, humid summer reduces outdoor activity (Maksimov *et al*., 2023). Third, socioeconomic factors may contribute. Stavropol has a higher proportion of public sector employees, students, and pensioners. Krasnodar is a rapidly growing business center with higher incomes, which may be associated with more calorie-dense diets and greater access to fast food (Eganyan *et al*., 2019). Testing these hypotheses requires further studies with direct dietary and physical activity assessment.

Comparison with other Russian studies suggests that obesity and metabolic syndrome prevalence among NAFLD patients in southern Russia exceeds the national average. The DIREG-2 study (30 Russian cities) reported obesity in 63% and metabolic syndrome in 58% of NAFLD patients (Ivashkin *et al*., 2015). Our cohort showed 71% and 58%, respectively. These differences may reflect regional characteristics or different patient selection methods. Internationally, our cohort's metabolic profile resembles Middle Eastern and South American populations (where NAFLD prevalence is highest) and is notably more severe than the average European population (Bedogni *et al*., 2023).

Several limitations deserve discussion. First, the retrospective design prevents causal inference and depends on the completeness and quality of outpatient records (Portincasa, 2023). Despite standardization efforts, missing data (especially for waist circumference and insulin) were inevitable. Second, steatosis diagnosis was based on ultrasound criteria, not liver biopsy or more precise methods like magnetic resonance spectroscopy. However, ultrasound remains the first-line method in outpatient practice, with 80–90% sensitivity for moderate to severe steatosis (Dabravolski *et al*., 2021). Third, the absence of a gold standard for fibrosis (biopsy) prevents precise staging in patients with high index scores. Nevertheless, combining three non-invasive indices with different calculation principles improves reliability (Pennisi *et al*., 2023). Fourth, we had no control group of healthy individuals or obese patients without NAFLD, limiting our ability to calculate relative risks. Fifth, the prospective phase was conducted only in Stavropol and in a small subsample, preventing generalization to all regions. Finally, we did not account for smoking, physical activity levels, detailed dietary composition, or medication use, all of which can modify NAFLD progression (Liu *et al*., 2024).

Despite these limitations, our study has several strengths. It is one of the few multicenter NAFLD studies in outpatient practice in southern Russia, covering four cities with different climatic, geographic, and socioeconomic conditions. The sample size (480 patients) was sufficient to detect stable statistical patterns and perform multivariate analysis. Using three non-invasive fibrosis indices improved the reliability of fibrosis risk assessment. Finally, the high proportion of undiagnosed cases has direct practical implications and can inform educational programs for primary care physicians (Younossi *et al*., 2024).

Practical recommendations from our study are as follows. All patients with obesity (especially abdominal obesity), hypertension, type 2 diabetes, or dyslipidemia should undergo screening with a liver ultrasound regardless of transaminase levels. Waist circumference measurement should be mandatory at every clinical visit for overweight patients. Calculating FIB-4 and NAFLD Fibrosis Score can help stratify patients by fibrosis risk and determine management: low-risk patients can be followed by a primary care physician with regular monitoring; high-risk patients require referral to a gastroenterologist or hepatologist for elastography or biopsy. Special attention should be given to patients from Krasnodar and Rostov-on-Don, where metabolic disturbances and fibrosis risk are most pronounced.

In conclusion, NAFLD is highly prevalent but underdiagnosed in outpatient practice in southern Russia. The interregional differences we identified require further study but already suggest that prevention programs should account for regional dietary and lifestyle patterns. Timely diagnosis of NAFLD is important not only to prevent liver disease progression but also to reduce cardiovascular risk, which remains the main competing outcome in these patients (Mantovani *et al*., 2021).

Conclusion

This multicenter retrospective study analyzed 480 outpatient records of NAFLD patients seen in clinics in Stavropol, Rostov-on-Don, Krasnodar, and Astrakhan between 2024 and 2025.

NAFLD in southern Russian outpatient practice almost never occurs in isolation. It is a hepatic manifestation of systemic metabolic disorder. Abdominal obesity was found in 82.1% of patients, arterial hypertension in 75.8%, dyslipidemia in 74.6%, and type 2 diabetes in 47.1%. Complete metabolic syndrome was present in 57.9% of patients. Insulin resistance (HOMA-IR >2.77) was recorded in 82.3%, highlighting its central role in NAFLD pathogenesis.

Timely diagnosis of NAFLD remains unsatisfactory. Nearly 39% of patients with ultrasound signs of hepatic steatosis had no verified diagnosis in their records. Among these, 72% had normal alanine aminotransferase levels. Relying solely on transaminase levels leads to massive underdiagnosis. Active screening using instrumental methods is necessary for all patients with metabolic risk factors.

Stable interregional differences were observed. Krasnodar had the most severe metabolic profile (highest BMI, waist circumference, triglycerides, diabetes frequency, and fibrosis risk), followed by Rostov-on-Don and Astrakhan. Stavropol showed the least severe abnormalities. These differences may relate to dietary habits, climate, terrain, and physical activity. Further research is needed.

Non-invasive fibrosis indices identified a high risk of significant fibrosis (FIB-4 >2.67) in 9.2% of patients and advanced fibrosis (NAFLD Fibrosis Score >0.676) in 12.9%. Krasnodar had the highest proportion of high-risk patients (13.3%), Stavropol the lowest (5.8%). These data support fibrosis risk stratification and a differentiated approach to management.

Active NAFLD screening is justified for all patients with metabolic syndrome or its components, regardless of transaminase levels. Waist circumference measurement, calculation of FIB-4 and NAFLD Fibrosis Score, and liver ultrasound should become mandatory in clinical follow-up. Special attention is needed for patients from Krasnodar and Rostov-on-Don, where the risk of severe NAFLD is highest.

Thus, NAFLD is a pressing problem in outpatient practice in southern Russia, requiring increased physician awareness, simple screening algorithms, and regional prevention programs.

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Ethics statement: The study was conducted in accordance with the ethical standards of the institutional research committee of Stavropol State Medical University and with the principles of the Declaration of Helsinki (2013 revision). Patient data were anonymized before analysis.

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