

Research Article

The Prevalence of Steatohepatitis Declines with Age in Non-urban Individuals with Obesity

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Abstract

Background: Worldwide, the prevalence of the major health disorder, obesity, has risen. Obesity is a risk factor for development of steatohepatitis, a precursor to chronic liver disease. Alanine transaminase (ALT) is a recognized marker for steatohepatitis. The prevalence of steatohepatitis in aging populations with obesity has not been well delineated. **Objective:** Our hypothesis is that the prevalence of steatohepatitis would be lower in older subjects with obesity due to the increased morbidity and mortality related to chronic liver disease in individuals with obesity. **Method:** Consecutive individuals with obesity (n=400) have been evaluated in gastrointestinal clinic. Exclusions (n=72) include cirrhosis, hepatitis C, Celiac disease, >28 g/day alcohol, and >2 g/day acetaminophen. Definition of elevation of ALT in men and women is based on the American College of Gastroenterology guidelines. **Result:** Among 328 eligible subjects, 175 are ≤ 64 years-old and 153 are ≥ 65 years old. Mean body mass index (BMI) of individuals ≤ 64 years is 36.0+/-5.2 kg/m² and mean BMI of individuals ≥ 65 years is 34.9+/-4.1 kg/m² (t-test: p=0.036). Subjects with type 2 diabetes mellitus include 53 of 175 subjects ≤ 64 years and 94 of 153 subjects ≥ 65 years (Chi-square 2X2 Statistic: p<.001). The overall prevalence of ALT elevation is 47%. A Chi-square 2X2 statistic (p<.001) supports the hypothesis that ALT elevation is inversely dependent upon age, and a Chi-square 2X2 statistic (p=0.039) supports a higher prevalence of steatotic liver disease in younger subjects. **Conclusion:** The high prevalence of ALT elevation, consistent with steatohepatitis, in this non-urban population is statistically more common in subjects ≤ 64 years-old, supporting our hypothesis. This difference is not explained by type 2 diabetes, which is statistically more common in subjects ≥ 65 years-old, but is consistent with the higher prevalence of steatotic liver disease in subjects ≤ 64 years-old. The association between a higher prevalence of elevated ALT levels and a higher prevalence of hepatic steatosis supports the importance of weight loss to resolve hepatic steatosis in order to protect younger individuals with steatohepatitis.

Keywords

Liver, Fatty Liver, Enzymes, Obesity, Aging, Population

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1. Introduction

Worldwide, obesity continues to be an increasing risk factor against healthy aging [1]. The prevalence of obesity rose in all nations between 1990 and 2021 [1]. The authors predicted that more than half of the global adult population will be overweight or obese by 2050 [1]. Obesity as a health risk factor is well described [2] to be associated with the development of type 2 diabetes mellitus, cardiovascular diseases, at least 13 types of cancer [3], and chronic liver disease.

Obesity can lead to hepatic steatosis, which can be defined as fatty infiltration of the liver [4]. It has been suggested that hepatic steatosis develops when the combined uptake of fatty acids from plasma by the liver and fatty acid synthesis in the liver is greater than the combined oxidation of fatty acids in the liver and export of triglycerides from the liver [4]. The estimated worldwide prevalence of steatotic liver disease is 25.6% of women and 39.7% of men [5]. A major concern about the presence of hepatic steatosis is the development of steatohepatitis [6]. Chronic steatohepatitis can lead to progressive fibrosis of the liver, cirrhosis, and then hepatocellular carcinoma [6]. The importance of the linkage of obesity to hepatic steatosis and fibrosis of the liver is supported by a meta-analysis demonstrating an increased risk of mortality in individuals with hepatic steatosis and liver biopsy-confirmed fibrosis [7]. A recent study supported a global rise after 2016 in the prevalence of advanced hepatic fibrosis and cirrhosis, with obesity cited as a risk factor [8]. A second study described a steep global increase from 2000 to 2021 of primary liver cancer associated with steatotic liver disease [9]. Taken together, these studies support the concern that obesity is a major cause of global chronic liver disease.

The enzyme alanine transaminase (ALT) is produced almost exclusively by the liver and ALT is a recognized marker of hepatic inflammation [10-13]. Depending upon the levels of ALT considered normal, diagnosis of steatohepatitis based upon elevated ALT levels is reported to provide a pooled specificity of 74.4% and a pooled sensitivity of 63.5% when compared to liver biopsies [10]. The prevalence of steatohepatitis in aging populations with obesity has not been well delineated. In our study of a large urban population of 593 individuals considering bariatric surgery for treatment of obesity, we identified a 17.2% prevalence of elevated ALT levels [14].

Based upon the risks of morbidity and mortality related to chronic liver disease in individuals with obesity, we hypothesized that the prevalence of steatohepatitis would be lower in older subjects with obesity. The aims of this study are to define the prevalence of elevated ALT levels in obese individuals age \geq 65 years-old compared to obese individuals \leq 64 years-old in a non-urban population, and to evaluate potential risk factors involved in development of steatotic liver disease.

2. Materials and Methods

2.1. Ethical Approval and Consent to Participate

All studies involving human subjects were consistent with the ethical standards of the institutional research committee. The Salem Veteran Affairs Medical Center Institutional Review Board provided approval for human studies on November 5, 2021. This study was declared to be an exempt protocol by the Institutional Review Board. For this research study, the Institutional Review Board provided a waiver of informed consent.

2.2. Study Population

United States veterans who live in rural areas, small towns, and small cities (population < 100,000 individuals) of Southwest Virginia, Southern Virginia, Northern North Carolina, and Eastern West Virginia receive care at the Salem Veteran Affairs Medical Center. In this single center, retrospective study from 2021 to 2023, consecutively accrued non-urban patients with obesity (n=400) were evaluated in the gastroenterology clinic. Patients are excluded from this study (n=72) who have a diagnosis of cirrhosis, hepatitis C, Celiac disease, intake of >28 grams/day of alcohol in men or >14 grams/day of alcohol in women (based upon United States Dietary Guidelines) [15], intake of >2 grams/day of acetaminophen (based on the recommendation of the National Institute of Health) [16], or a serum glutamic-oxaloacetic transaminase (SGOT) level that is higher than serum ALT.

2.3. Data Collection

A diagnosis of type 2 diabetes mellitus, age, sex, weight, body mass index, racial background, findings from imaging of the liver that did or did not demonstrate the presence of hepatic steatosis, serum ALT, and serum SGOT have been collected from the 328 study-eligible patients. In this study, 173 subjects completed imaging of the liver by computerized tomography, 54 individuals completed imaging of the liver by ultrasound examination, and 2 individuals completed imaging of the liver by magnetic resonance imaging.

2.4. Determination of Alanine Transaminase

Serum ALT determination was performed by an automated spectrophotometric analysis [17]. Elevated serum ALT levels in men and in women are defined by the national recommendations of the American College of Gastroenterology based upon histopathology of liver biopsies [18]. Their recommendations have been supported by a study from South Korea [19].

2.5. Statistical Analysis

The significance of and impact of the effect size could not be estimated by a power analysis because of the retrospective design of the present study. StatView for Windows (SAS Institute Inc., Cary, NC, USA) was used to perform statistical analysis. Descriptive statistics have been calculated for all variables. Unpaired Student's t-tests were used to evaluate

possible differences in body mass index and body weights in individuals ≤ 64 years-old compared to individual ≥ 65 years-old. Nonparametric analysis utilized Chi-Square statistics. Chi-Square 2X2 table statistics have been performed to examine the potential relationships between age and serum ALT, between age and type 2 diabetes mellitus, and between age and hepatic steatosis (as identified by imaging of the liver).

3. Results

3.1. Demographics of the Study Population

Table 1. Demographics of 328 Study Subjects.

	N	MEAN VALUE	STANDARD DEVIATION	RANGE
Men	290 (88%)			
Women	38 (12%)			
Black Americans	68 (21%)			
White Americans	259 (79%)			
Ages (Years)				
Age ≤ 64 Years	175	52	8.3	26-64
Age ≥ 65 Years	153	73	4.9	65-88
Weights (kg)				
Age ≤ 64 Years	175	111	19	80-200
Age ≥ 65 Years	153	110	15	74-152
Body Mass Index (kg/m ²)				
Age ≤ 64 Years	175	36.0*	5.2	30.1-61.8
Age ≥ 65 Years	153	34.9*	4.1	30.1-55.6

*t-test: $p = 0.036$

There are 328 eligible individuals: 175 (53%) are ≤ 64 years-old while 153 (47%) are ≥ 65 years old (see Table 1). There are 38 women (12%) and 290 men (88%) with 68 black Americans (21%) and 259 white Americans (79%). The mean \pm -standard deviation (SD) age of individuals ≤ 64 years is 52 ± 8.3 years with a range of 26 to 64 years, while the mean \pm -SD age of individuals ≥ 65 years is 73 ± 4.9 years with a range of 65 to 88 years (see Table 1). The mean \pm -SD weight of individuals ≤ 64 years is 111 ± 18 kg with a range of 80 to 200 kg, while the mean \pm -SD weight of individuals ≥ 65 years is 110 ± 15 kg with a range of 74 to 152 kg (see Table 1). There is no significant difference in mean weights (t-test: $p > 0.05$). The mean \pm -SD body mass index of individuals ≤ 64 years is 36.0 ± 5.2 kg/m² with a range of 30.1 to 61.8 kg/m²,

while the mean \pm -SD body mass index of individuals ≥ 65 years is 34.9 ± 4.1 kg/m² with a range of 30.1 to 55.6 kg/m² (see Table 1). There is a statistically significant difference in mean body mass index, which is higher in individuals ≤ 64 years (t-test: $p = 0.036$).

3.2. Relationship Between Patient Ages and Elevated Serum ALT

The overall prevalence of elevated serum ALT in this study is 47%. As shown in Table 2, a Chi-square 2X2 table analysis ($p < 0.001$) supports our hypothesis that elevated serum ALT is inversely dependent upon age.

Table 2. Relationship Between Age and Serum Alanine Transaminase (Alt) Levels Chi-square 2x2 Statistic: 21.3; P < 0.001.

		ELEVATED ALT	NORMAL ALT	TOTALS
AGE (YEARS)	≤ 64	103	72	175
AGE (YEARS)	≥ 65	51	102	153
	TOTALS	154	174	328

3.3. Relationship Between Patient Ages and Diabetes Mellitus 2

The overall prevalence of type 2 diabetes mellitus in this study is 45%. As shown in Table 3, a Chi-square 2X2 table analysis ($p < 0.001$) supports a positive correlation of type 2 diabetes mellitus with age.

3.4. Relationship Between Patient Ages and Hepatic Steatosis

Based upon imaging of the liver, the overall prevalence of steatosis of the liver in this study is 47%. As shown in Table 4, a Chi-square 2X2 table analysis ($p=0.039$) demonstrates that the presence of hepatic steatosis is inversely correlated with increasing age.

Table 3. Relationship Between Age and Type 2 Diabetes Mellitus (Dm2) Chi-Square 2x2 Statistic: 32.0; P < 0.001.

		DM2	NO DM2	TOTALS
AGE (YEARS)	≤ 64	53	122	175
AGE (YEARS)	≥ 65	94	59	153
	TOTALS	147	181	328

Table 4. Relationship Between Age and Hepatic Steatosis Chi-Square 2x2 Statistic: 4.22; P = 0.039.

		Steatosis	No steatosis	Totals
AGE (YEARS)	≤ 64	62	53	115
AGE (YEARS)	≥ 65	46	68	114
	TOTALS	108	121	229

4. Discussion

Depending upon the levels of ALT considered as normal, a diagnosis of steatohepatitis using elevated ALT levels is reported to provide a pooled specificity of 74.4% and a pooled sensitivity of 63.5% when compared to liver biopsies [10]. Elevated serum ALT levels in men and in women in this study are defined by the national recommendations of the American College of Gastroenterology based upon histopathology of liver biopsies [18]. Their recommendations have been supported by a study from South Korea [19]. The results from our

present study support our hypothesis that the prevalence of elevated ALT levels as a marker of steatohepatitis would be lower in older, subjects with obesity in a non-urban population. The presence of cirrhosis of the liver is an exclusion in this study so that we can examine the risk of chronic obesity in younger and older subjects.

The findings of our study support the importance of weight loss in younger individuals as a means of treating steatohepatitis. Prior studies have demonstrated that losing weight can result in the resolution of steatohepatitis. In a study from Havana, Cuba, 90% of individuals who lost ≥10% of their total body weight had resolution of steatohepatitis [20]. In a study from the United States, individuals who lost ≥7% of their total

body weight had a significant improvement in their parameters of steatohepatitis [21].

In examining potential methods of weight loss, we have previously summarized the weaknesses of dietary changes and exercise programs in promoting weight loss [22]. For more than 20 years, there have been reports of resolution of steatotic liver disease after weight loss resulting from bariatric surgery [22]. It has been known since the 1980s [23] that there is an enteric peptide, enteroglucagon, that is distinct from pancreatic glucagon. In the past decade, treatment of steatohepatitis with Glucagon-like Peptide-1 (GLP-1) receptor agonists was proposed [24]. In 2021, a 72 week phase 2 liver biopsy trial comparing the GLP-1 receptor agonist semaglutide to placebo reported a higher percentage resolution of steatohepatitis with no worsening of fibrosis in the individuals who received semaglutide [25]. Since then multiple studies using GLP-1 receptor agonists have examined their effects on steatohepatitis, and a recent systemic review and meta-analysis concluded that GLP-1 receptor agonists did improve steatosis of the liver [26]. The authors however warned that it was not yet clear whether these agents improved clinically significant outcomes. Since the development of cirrhosis of the liver may take years, demonstrating clinically significant outcomes remain a future goal of therapy when using these synthetic peptides.

The results of our present study, which included only obese subjects, are more specific than a prior population-based study of non-alcoholic fatty liver disease from 2010 to 2020 in the United States which provided evidence for a lower prevalence of non-alcoholic fatty liver disease in individuals ages 70-79 years and ages ≥ 80 years [27]. The results from that study are consistent with the results of our present study, but that prior study [27] did not suggest an explanation for a lower prevalence of non-alcoholic fatty liver disease in older individuals.

In our present study, obese subjects ≤ 64 years-old have a minimally higher body mass index when statistically compared to obese subjects ≥ 65 years-old. We speculate that body mass index does not entirely explain why younger individuals had a higher prevalence of elevated ALT levels.

Population studies have described an increasing number of prescriptions for medications with advancing age [28]. We speculate that it would be unlikely that the higher prevalence of elevated ALT levels in the younger population would be related to prescription medications.

In our present study, obese subjects ≥ 65 years-old have a higher prevalence of type 2 diabetes mellitus compared to obese subjects ≤ 64 years-old. Our present study parallels prior reports [29] describing a higher prevalence of type 2 diabetes mellitus in older populations. This raises the question of the relative importance of type 2 diabetes mellitus in the development of hepatic steatosis. The incidence of non-alcoholic fatty liver disease has been reported to be 48% higher in individuals with type 2 diabetes mellitus compared to individuals without diabetes mellitus [30]. By contrast, the incidence of non-alcoholic fatty liver disease has been reported to be 200%

higher in overweight/obese individuals compared to individuals with normal weight [30]. These findings support our greater concern with regards to the risk of steatotic liver disease in individuals with obesity.

Our present study did demonstrate that subjects ≤ 64 years-old have a statistically higher prevalence of hepatic steatosis as identified by imaging of the liver. An association between a higher prevalence of elevated ALT levels and a higher prevalence of hepatic steatosis in subjects ≤ 64 years-old is consistent with the concept that hepatic steatosis increases the risk of developing steatohepatitis. This association again supports the importance of promoting weight loss in younger individuals with steatohepatitis.

The limitations of this study include its being a retrospective study with enrollment of a high percentage of men and a single center enrollment. This study has a limited sample size with regards to imaging of the liver in enrolled subjects. This study was not designed to demonstrate a correlation between elevation of serum ALT level and liver biopsy findings of steatohepatitis. The results may not apply to urban patient populations or to countries outside of the United States because it is a single center study. Its organization may result in production of an inferior level of evidence because it is a retrospective study. A randomized controlled trial or a prospective cohort study could provide more information with regarding causality.

5. Conclusions

The high prevalence of ALT elevation, consistent with steatohepatitis, in this non-urban population is statistically more common in subjects ≤ 64 years-old compared to subjects ≥ 65 years-old. This difference is not explained by the presence of diabetes mellitus 2, which is statistically more common in individuals ≥ 65 years-old, but is consistent with the higher prevalence of steatotic liver disease in individuals ≤ 64 years-old. Prior studies have demonstrated that weight loss can result in the resolution of steatohepatitis. The association between a higher prevalence of elevated ALT levels and a higher prevalence of hepatic steatosis supports the importance of weight loss to resolve hepatic steatosis in order to protect younger individuals with steatohepatitis.

Abbreviations

ALT	Alanine Transaminase
BMI	Body Mass Index
SGOT	Serum Glutamic-Oxaloacetic Transaminase
SD	Standard Deviation
GLP-1	Glucagon-like Peptide-1
DM2	Type 2 Diabetes Mellitus

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Author Contributions

Timothy Koch: Conceptualization, Methodology, Formal Analysis, Writing – original draft

David Cronin: Conceptualization, Writing – review & editing

Ali Iranmanesh: Conceptualization, Writing – review & editing

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants, but are available from the corresponding author [TRK].

Conflicts of Interest

The authors declare no conflicts of interest.

References

- [1] Ng, M., Gakidou, E., Lo, J., Global Burden of Disease 2021 Adult BMI Collaborators. Global, regional, and national prevalence of adult overweight and obesity, 1990–2021, with forecasts to 2050: a forecasting study for the Global Burden of Disease Study 2021. *Lancet*. 2025, 405, 813-38. [https://doi.org/10.1016/S0140-6736\(25\)00355-1](https://doi.org/10.1016/S0140-6736(25)00355-1)
- [2] Jin, X., Qiu, T., Li, L., Yu, R., Chen, X., Li, C., Proud, C. G., Jiang, T. Pathophysiology of obesity and its associated diseases. *Acta Pharmaceutica Sinica B*. 2023, 13(6), 2403-24. <https://doi.org/10.1016/j.apsb.2023.01.012>
- [3] Steele, C. B., Thomas, C. C., Henley, S. J., Massetti, G. M., Galuska, D. A., Agurs-Collins, T., Puckett, M., Richardson, L. C. Vital Signs: Trends in Incidence of Cancers Associated with Overweight and Obesity — United States, 2005–2014. *MMWR Morbidity Mortality Weekly Report*. 2017, 66(39), 1052-58. <https://doi.org/10.15585/mmwr.mm6639e1>
- [4] Fabbrini, E., Sullivan, S., Klein, S. Obesity and nonalcoholic fatty liver disease: biochemical, metabolic, and clinical implications. *Hepatology*. 2010, 51(2), 679-89. <https://doi.org/10.1002/hep.23280>
- [5] Riazi, K., Azhari, H., Charette, J. H., Underwood, F. E., King, J. A., Afshar, E. E., Swain, M. G., Congly, S. E., Kaplan, G. G., Shaheen, A. A. The prevalence and incidence of NAFLD worldwide: A systematic review and meta-analysis. *Lancet Gastroenterology Hepatology*. 2022, 7(9), 851-61. [https://doi.org/10.1016/S2468-1253\(22\)00165-0](https://doi.org/10.1016/S2468-1253(22)00165-0)
- [6] Polyzos, S. A., Kountouras, J., Mantzoros, C. S. Obesity and nonalcoholic fatty liver disease: From pathophysiology to therapeutics. *Metabolism*. 2019, 92, 82-97. <https://doi.org/10.1016/j.metabol.2018.11.014>
- [7] Taylor, R. S., Taylor, R. J., Bayliss, S., Hagström, H., Nasr, P., Schattenberg, J. M., Ishigami, M., Toyoda, H., Wai-Sun Wong, V., Peleg, N., Shlomai, A., Sebastiani, G., Seko, Y., Bhala, N., Younossi, Z. M., Anstee, Q. M., McPherson, S., Newsome, P. N. Association between fibrosis stage and outcomes of patients with nonalcoholic fatty liver disease: A systematic review and meta-analysis. *Gastroenterology*. 2020, 158(6), 1611-25. <https://doi.org/10.1053/j.gastro.2020.01.043>
- [8] Zamani, M., Alizadeh-Tabari, S., Ajmera, V., Singh, S., Murad, M. H., Loomba, R. Global prevalence of advanced liver fibrosis and cirrhosis in the general population: A systematic review and meta-analysis. *Clinical Gastroenterology Hepatology*. 2025, 23(7), 1123-34. <https://doi.org/10.1016/j.cgh.2024.08.020>
- [9] Danpanichkul, P., Suparan, K., Kaesri, C., Jatupornpakdee, P., Attia, A. M., Suenghataiphorn, T., Thongpiya, J., Sukphutanan, B., Huang, D. Q., Noureddin, M., Singal, A. G., Wijarnprecha, K., Yang, J. D. Global trend of MASH-associated liver cancer: A systematic analysis from the global burden of disease 2021. *Clinical Gastroenterology Hepatology*. 2025, 23(8), 1346-1355. <https://doi.org/10.1016/j.cgh.2024.10.026>
- [10] Verhaegh, P., Bavalua, R., Winkens, B., Masclee, A., Jonkers, D., Koek, G. Noninvasive tests do not accurately differentiate nonalcoholic steatohepatitis from simple steatosis: A systematic review and meta-analysis. *Clinical Gastroenterology Hepatology*. 2018, 16, 837-61. <https://doi.org/10.1016/j.cgh.2017.08.024>
- [11] Sanyal, A. J., Mofrad, P. S., Contos, M. J., Sargeant, C., Luketic, V. A., Sterling, R. K., Stravitz, R. T., Shiffman, M. L., Clore, J., Mills, A. S. A pilot study of vitamin E versus vitamin E and pioglitazone for the treatment of nonalcoholic steatohepatitis. *Clinical Gastroenterology Hepatology*. 2004, 2(12), 1107-15. [https://doi.org/10.1016/s1542-3565\(04\)00457-4](https://doi.org/10.1016/s1542-3565(04)00457-4)
- [12] Lavine, J. E., Schwimmer, J. B., Molleston, J. P., Scheimann, A. O., Murray, K. F., Abrams, S. H., Rosenthal, P., Sanyal, A. J., Robuck, P. R., Brunt, E. M., Unalp, A., Tonascia, J., Nonalcoholic Steatohepatitis Clinical Research Network Research Group. Treatment of nonalcoholic fatty liver disease in children: TONIC trial design. *Contemporary Clinical Trials*. 2010, 31(1), 62-70. <https://doi.org/10.1016/j.cct.2009.09.001>
- [13] Praveenraj, P., Gomes, R. M., Kumar, S., Karthikeyan, P., Shankar, A., Parthasarathi, R., Senthilnathan, P., Rajapandian, S., Palanivelu, C. Prevalence and predictors of non-alcoholic fatty liver disease in morbidly obese South Indian patients undergoing bariatric surgery. *Obesity Surgery*. 2015, 25(11), 2078-87. <https://doi.org/10.1007/s11695-015-1655-1>
- [14] Nath, A., Shope, T. R., Pardo Lameda, I. L., Koch, T. R. Utility of the non-alcoholic fatty liver disease fibrosis score in the evaluation of individuals with medically-complicated obesity: A retrospective study. *International Journal Gastroenterology Hepatology Diseases*. 2024, 3(1), E26662906296409. <https://doi.org/10.2174/0126662906296409240826050717>

- [15] U.S. Department of Agriculture and U.S. Department of Health and Human Services. IN *Dietary Guidelines for Americans, 2020-2025*. 9th ed., 2020.
- [16] National Institute of Health. Bethesda, Maryland: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury: Acetaminophen [accessed 2025 May 3]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK548162/>
- [17] Knight, J. A., Hunter, D. T. Aspartic transaminase, alanine transaminase and lactate dehydrogenase determination by automated spectrophotometric analysis. *Journal Medical Laboratory Technology*. 1968, 25, 106–11.
- [18] Kwo, P. Y., Cohen, S. M., Lim, J. K. ACG clinical guideline: evaluation of abnormal liver chemistries. *American Journal of Gastroenterology*. 2017, 112(1), 18-35. <https://doi.org/10.1038/ajg.2016.517>
- [19] Choi, J., Jo, C., Kim, S., Ryu, M., Won-Mook, C., Lee, D., Shim, J. H., Kim, K. M., Lim, Y-S., Lee, H. C. Updated reference intervals for alanine aminotransferase in a metabolically and histologically normal population. *Clinical Gastroenterology Hepatology*. 2024, 22, 2240-49. <https://doi.org/10.1016/j.cgh.2024.04.031>
- [20] Vilar-Gomez, E., Martinez-Perez, Y., Calzadilla-Bertot, L., Torres-Gonzalez, A., Gra-Oramas, B., Gonzalez-Fabian, L., Friedman, S. L., Diago, M., Romero-Gomez, M. Weight loss through lifestyle modification significantly reduces features of nonalcoholic steatohepatitis. *Gastroenterology*. 2015, 149(2), 367-78. e5. <https://doi.org/10.1053/j.gastro.2015.04.005>
- [21] Promrat, K., Kleiner, D. E., Niemeier, H. M., Jackvony, E., Kearns, M., Wands, J. R., Fava, J. L., Wing, R. R. Randomized controlled trial testing the effects of weight loss on nonalcoholic steatohepatitis. *Hepatology*. 2010, 51(1), 121-9. <https://doi.org/10.1002/hep.23276>
- [22] Koch, T. R., Shope, T. R., Smith, C. I. Diet and activity programs are ineffective in nonalcoholic steatohepatitis. *Mayo Clinic Proceedings*. 2016, 91(5), 683-4. <https://doi.org/10.1016/j.mayocp.2016.02.021>
- [23] Go, V. L. W., Koch, T. R. Distribution of gut peptides. *Comprehensive Physiology* 1989. 1989(12S17), 111-122. <https://doi.org/10.1002/j.2040-4603.1989.tb01340.x>
- [24] Kalogirou, M., Sinakos, E. Treating nonalcoholic steatohepatitis with antidiabetic drugs: Will GLP-1 agonists end the struggle? *World Journal of Hepatology*. 2018 Nov 27, 10(11), 790-794. <https://doi.org/10.4254/wjh.v10.i11.790>
- [25] Newsome, P. N., Buchholtz, K., Cusi, K., et al. A placebo-controlled trial of subcutaneous semaglutide in nonalcoholic steatohepatitis. *New England Journal of Medicine*. 2021, 384, 1113-24. <https://doi.org/10.1056/NEJMoa2028395>
- [26] Potter, K. J., Phinney, J., Kulai, T., Munro, V. Effects of GLP-1 receptor agonist therapy on resolution of steatohepatitis in non-alcoholic fatty liver disease: a systematic review and meta-analysis. *Journal of the Canadian Association of Gastroenterology*. 2025 Jan 29, 8(2), 47-57. <https://doi.org/10.1093/jcag/gwae057>
- [27] Hamid, O., Eltelbany, A., Mohammed, A., Alsabbagh Alchirazi, K. The epidemiology of non-alcoholic steatohepatitis (NASH) in the United States between 2010-2020: A population-based study. *Annals of Hepatology*. 2022, 27(5), 100727. <https://doi.org/10.1016/j.aohep.2022.100727>
- [28] Zhong, W., Maradit-Kremers, H., St Sauver, J. L., Yawn, B. P., Ebbert, J. O., Roger, V. L., Jacobson, D. J., McGree, M. E., Brue, S. M., Rocca, W. A. Age and sex patterns of drug prescribing in a defined American population. *Mayo Clinic Proceedings*. 2013, 88(7), 697-707. <https://doi.org/10.1016/j.mayocp.2013.04.021>
- [29] Xia, M., Liu, K., Feng, J., Zheng, Z., Xie, X. Prevalence and risk factors of type 2 diabetes and prediabetes among 53,288 middle-aged and elderly adults in China: A cross-sectional study. *Diabetes Metabolic Syndrome Obesity*. 2021, 14, 1975-1985. <https://doi.org/10.2147/DMSO.S305919>
- [30] Younossi, Z. M., Henry, L. Understanding the burden of non-alcoholic fatty liver disease: Time for action. *Diabetes Spectrum*. 2024, 37(1). 9-19. <https://doi.org/10.2337/dsi23-0010>