Reduced Lysosomal Acid Lipase Activity in Non-alcoholic Fatty Liver Disease: A Systematic Review of Current Evidence and Future Directions

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ABSTRACT

Background and Objectives

Non-alcoholic fatty liver disease (NAFLD) presents with accumulation of excessive intra-hepatic fat and acts as a major health burden globally. A multifactorial pathogenesis is reported to be involved. Reduced Lysosomal Acid Lipase (LAL) activity is suggested as one of the involved pathogenic mechanisms. This review summarizes the available evidence on role of reduced LAL activity in the pathogenesis of NAFLD.

Methodology

Four databases namely, PubMed/Medline, Science direct, Cochrane Library and Google scholar were searched to identify relevant observational records evaluating the role of LAL activity in pathogenesis of NAFLD. All studies were assessed for their quality by using Newcastle–Ottawa Scale (NOS) or The Joanna Briggs Institute (JBI) Critical Appraisal tools for cohort and cross-sectional studies, respectively. The estimates of LAL activity and other clinical outcomes were expressed as mean (SD) and number (%) as presented in the primary studies.

Results

A total of nine good quality studies with 1711 NAFLD patients and 877 controls from different groups (healthy volunteers, alcoholics, cryptogenic cirrhosis and HCV-positive) were included. From the NAFLD group, 59.55% were males and the overall mean age ranged between the studies from 12.6±8.5 months in paediatrics to 58.90±13.82 years in adults. In the NAFLD group, the LAL activity varied from 0.53±0.08 to 1.3±0.70 (nmol/spot/hr) between the studies which was less than all control groups except cryptogenic cirrhosis patients (0.5±0.15 nmol/spot/hr). Of the other outcomes of interest, ALT, AST, total cholesterol, triglyceride and LDL cholesterol were found elevated in NAFLD patients than in controls.

Conclusion

The current evidence suggests a potential correlation of reduced LAL activity with NAFLD pathogenesis according to its severity. Large-scale studies are recommended, more importantly in NAFLD patients having no metabolic or genetic involvement. Further LAL can act as a new non-invasive diagnostic biomarker to identify that specific NAFLD subgroup.

Clinical and biochemical characteristics of patients diagnosed with NAFLD in comparison with other controls

#	Authors (Year)	Country	Type of study	Type of patients	Total (N)	Age (years)	Sex (M/F)	LAL activity (nmol/spot/h)	AST (UI/L)	ALT (UI/L)	TC (mg/dl)	HDL-Cho (mg/dl)	TG (mg/dl)	FBS (mg/dl)	Pharmacotherapy N (%)
1	Thoen et.al, (2021)	Brazil	Prospective cross -sectional study	MAFLD (-steatohepatitis)	12	55.07 ± 13.41	4/8	**67.96 ± 55.85 pmol/ punch/h**	31.49 ± 25.99	32.19 ± 21.80	184.66 ± 67.08	48.26 ± 3.35	134.18 ± 62.05	105.76 ± 29.35	NR
				MAFLD (+steatohepatitis)	89	56.64 ± 9.79	25/64	**89.51 ± 77.39 pmol/ punch/h**	36.11 ± 18.08	43.81 ± 25.62	174.18 ± 42.19	43.0 ± 9.4	154.33 ± 73.84	115.15 ± 37.67	NR
2	Ferri et.al, (2020)	Italy	Cross sectional study	NAFLD	118	58.09 ± 12	70/48	**0.60 ± 0.27**	NR	44.36 ± 25.51	NR	NR	NR	NR	Non-Cir -Statins 14 (21) NASH-Cir- Statins 2 (4)
				Alcoholic	116	54.5 ± 9.7	112/4	**0.85 ± 0.42**	NR	24.6 ± 13.51	NR	NR	NR	NR	ALC-Non-Cir - statins 2 (4) Cir-ALD - statins 3 (5)
				HCV	49	63.5 ± 14.5	33/16	**NR**	NR	33.27 ± 22.53	NR	NR	NR	NR	Non-Cir HCV- statins (0) Cir-HCV- Statins (0)
				Control (Normal)	103	49.83 ± 27.81	47/56	**1.15 ± 0.77**	NR	16 ± 6.01	NR	NR	NR	NR	Statins 26 (25)
3	Baratta et.al, (2019)	Italy	Cross sectional study	NAFL	454	57.4 ± 11.3	274/180	**0.93 ±0.37**	21.20 ± 6.69	26.75 ± 14.13	197.9 ± 39.8	48.3 ± 12.9	141.74 ± 58.52	105.9 ± 26.6	Statins 196 (43.2)
				NASH	61	49.5 ± 12.9	38/23	**0.8 ± 0.3**	38 ± 18.6	67.71 ± 47.83	190.7 ± 38.0	49.4 ± 19.8	126.08 ± 58.84	100.0 ± 18.0	Statins 13 (21.7)
				Cryptogenic cirrhosis	60	68.6 ± 10.6	43/17	**0.5 ± 0.15**	39.55 ± 22.78	32.0 ± 15.95	153.1 ± 41.7	45.7 ± 15.6	95.76 ± 35.70	118.9 ± 40.5	Statins 4 (7.0)
				Patients without fatty liver	68	59.3 ± 13.9	34/34	**0.96 ± 0.37**	18.05 ± 3.78	17.35 ± 6.81	194.6 ± 41.0	58.2 ± 12.2	95.58 ± 7.46	95.2 ± 19.2	Statins 32 (47.7)
4	Gomaraschi et.al, (2019)	Italy	Cohort	NAFLD	164	52.8 ± 13	116/48	**0.71 ± 0.29**	37.6 ± 24	55 ± 33	194.3 ± 43	48.9 ± 13	143.5 ± 69	104.3 ± 32	On dietary recommendations 96 (58.53) On statins 28 (17.07) On fibrates 20 (12.19 On statins and fibrates in combination 36 (21.95)
				Control (Dyslipidemia)	180	56.5 ± 13.2	144/44	**1.20 ± 0.44**	25 ± 8.0	32 ± 17	223 ± 45	46.9 ± 14	195.7 ± 118	93.4 ± 25.3	NA
5	Polimeni et.al, (2017)	Italy	Cross sectional study	NAFLD	315	56.2 ± 11.3	189/126	**0.89 ± 0.08**	21.13 ± 1.94)	27.69 ± 4.04	198.6 ± 40.1	49.0 ± 14.6	138.12 ± 14.40	105.8 ± 28.2	Statins 128 (40.6)
				Control (non-NAFLD)	110	57.4 ± 14.4	65/50	**NR**	17.60 ± 0.98	15.15 ± 1.38	204.1 ± 43.3	57.3 ± 14.8	115.5 ± 60.6	94.1 ± 20.1	Statins 43 (39.8)
6	Tovoli et.al, (2017)	Italy	Cohort	NAFLD	81	58.90 ± 13.82	53/28	**0.53 ± 0.08**	36.90 ± 26.82	43.25 ± 36.72	174.48 ± 53.23	46.03 ± 18.15	97.54 ± 53.44	NR	Metformin 16 (19.8) Insulin 12 (14.8) Statins 18 (22.2)
				Control (HCV related CLD)	78	62.66 ± 10.58	41/37	**0.7 ± 0.08**	45.71 ± 45.65	58.61 ± 69.71	156.88 ± 39.84	50.47 ± 25.73	79.05 ± 44.20	NR	Metformin 2 (2.6) Insulin 5 (6.4) Statins 2 (2.6)
7	Selvakumar et.al (2016)	Italy	Prospective cohort	NAFLD	168	12.6 ± 8.5	101/67	**1.3 ± 0.70**	26.0 (22.0, 32.0)	26.70 ± 7.47	160.6 ± 37.4	44.0 ± 8.97	NR	86.93 ± 114.94	NR
8	Shteyer et.al, (2016)	Israel	Cohort	NAFLD (Low risk LAL-D)	9	54.3 ± 17.1	4/5	**0.74 ± 0.28 nmol/ punch/h**	NR	NR	NR	NR	NR	NR	NR
				Control (high risk LAL-D)	13	17.2 ± 12.3	8/5	**0.74 ± 0.28 nmol/ punch/h**	NR	NR	NR	NR	NR	NR	NR
9	Baratta et.al, (2015)	Italy	Cross sectional study	NAFLD	240	55.4 ± 11.0	145/ 95	**0.80 ± 0.29**	24.10 ± 10.44	31.75 ± 17.15	198.3 ± 38.8	48.4 ± 15.6	146.5 ± 61.15	99.64 ± 14.17	Statins 86 (35.7)
				Control	100	53.0 ± 11.3	55/45	**1.28 ± 0.57**	NR	NR	NR	NR	NR	NR	NR

Reference: Bashir A, Duseja A, Verma A, De A, Tiwari P, Lysosomal acid lipase activity in non-alcoholic fatty liver disease as a novel diagnostic and therapeutic target: A systematic literature review of current evidence and future directions, Journal of Clinical and Experimental Hepatology, https://doi.org/10.1016/j.jceh.2022.04.011.

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