Non-alcoholic fatty liver disease in psoriasis and psoriatic arthritis

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Introduction

- Psoriasis (PsO) is a chronic immune-mediated inflammatory disease
- Cardiometabolic co-morbidities, viz. the metabolic syndrome (MetS) and its components are increasingly recognised in PsO
- Non-alcoholic fatty liver disease (NAFLD) is considered to be a hepatic manifestation of the MetS [1]
- No SA data on NAFLD and PsO

Psoriasis Vulgaris

[1] KOTRONEN, A. & YKI-JARVINEN, H. 2008. *Arterioscler Thromb Vasc Biol,* 28**,** 27-38.

Relationship of mild and severe psoriasis with cardiometabolic diseases in South Africans[1] (n-201)

Psoriasis Severity *	Metabolic syndrome	Type 2 diabetes	Hypertension
Mild disease	0.49 (0.16, 1.49) 0.20	3.27 (0.72, 14.9) 0.12	1.39 (0.50, 3.85) 0.53
Severe disease	4.42 (1.72, 11 4) 0.002	11.3 (3.07, 41.3) 0.0002	2.48 (0.97, 6.32) 0.05

Data expressed as OR (95% CI), p value

***Adjusted for age, body mass index, hsCRP, smoking, education and socio-economic status; p values relative to the reference group (non-psoriatic)**

GOOLAM MAHYOODEEN, N., CROWTHER, N. J., SNYMAN, T., *ET AL* 2018. *Int J Dermatol*.

Studies examining the relationship between NALFLD and psoriasis			
Study	**N Number**	**Diagnosis**	**Prevalence in PsO vs Controls**
Gisondi, 2009	130 patients vs 260 controls	Ultrasound	47% vs 28 %, P < 0.001
Van der Voort, 2015	Population cohort of 2292 particpants	Ultrasound and transient elastography	44% vs 34 %, P <0.05
Roberts, 2015	103 patients	Ultrasonography and biopsy (selected patients)	NAFLD : 47% NASH: 22% (in biopsy group)

MANTOVANI, A., GISONDI, P., LONARDO, ET AL 2016. *Int J Mol Sci,* 17

NAFLD Diagnosis	
ALT:AST > 1	Differentiates from ethanol associated liver dysfunction
Ultrasound	User-dependent. Only detects >25-30% hepatic fat
Transient elastography (Fibroscan)	Measures liver stiffness and therefore detects liver fibrosis
CT scan	Various quantitative measures can be applied Most commonly: Liver-spleen attenuation ratio < 1
Liver biopsy	Gold standard to detect steatosis, steatohepatitis and fibrosis Invasive and may have sampling error

SATTAR, N., FORREST, E. & PREISS, D. 2014. Non-alcoholic fatty liver disease. *BMJ,* 349**,** g4596.
BENEDICT, M. & ZHANG, X. 2017. *World J Hepatol,* 9**,** 715-732.

Aims and Methods

- **Aims**
  - To determine the prevalence and predictors of NAFLD in patients with PsO and PsA
- **Design**
  - Cross sectional case-control study
- **Inclusion Criteria**
  - Consenting, adult patients
    - PsO
    - HIV negative
- **Controls**
  - Matched for:
    - Sex
    - Ethnicity
    - BMI
- **Patient Groups**
  - Cutaneous PsO (PsC)
  - Psoriatic arthritis (PsA)
  - Further classified based on methotrexate therapy

Methods

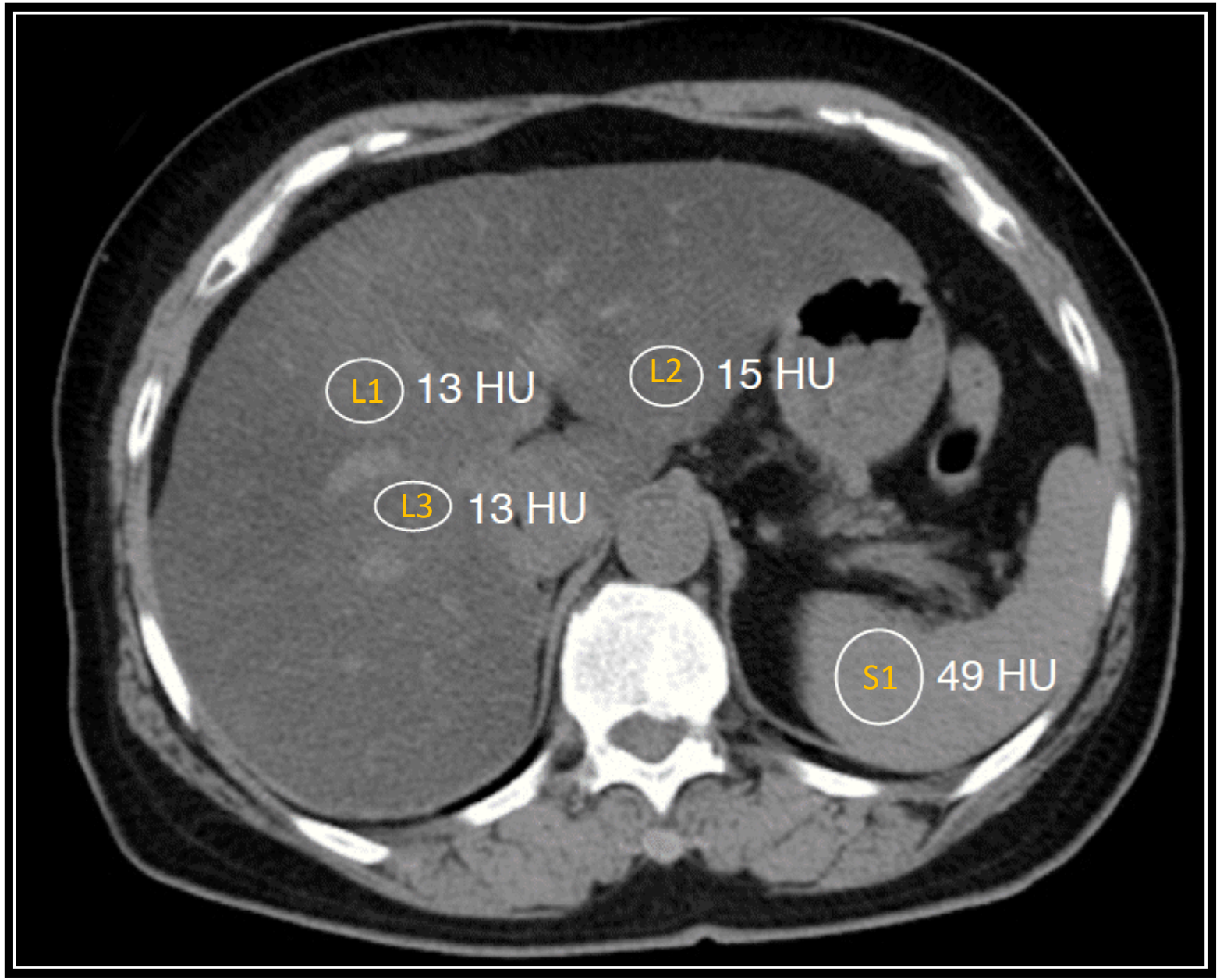
- **Data Collection**
  - Demographic: age, sex, ethnicity
  - Anthropometry
  - Patient characteristics
  - Co-morbidities
  - Patient characteristics
    - Disease duration
- **Investigations**
  - **Biochemical**
    - Fasting plasma glucose
    - Fasting insulin, HOMA Index
    - hsCRP
    - Adipokines: TNF, IL6, leptin, adiponectin
  - **Radiological**
    - CT abdomen
      - Limited, non-contrast scan
      - Visceral, subcutaneous fat and hepatic measurement
      - Reported quantitatively by radiologist

Definitions

- Psoriasis
  - Clinically and/or histologically based on the opinion of a dermatologist
- Psoriatic arthritis
  - Clinically based on the opinion of a rheumatologist
- Metabolic syndrome:
  - Harmonised guidelines[1]
- Non-alcoholic fatty liver disease
  - Based on CT measure liver-to-spleen attenuation ratio[2]

[1]ALBERTI, K. G., ECKEL, R. H., GRUNDY, S. M., *ET AL.* 2009. *Circulation,* 120**,** 1640-5.

[2]DAVIDSON, L. E., KUK, J. L., CHURCH, T. S. *ET AL*, R. 2006. *J Appl Physiol (1985),* 100**,** 864-8.



Average liver density

= (L1 + L2+ L3)/3

= (13+13+15)HU/3

= 13.7 HU

Splenic density

= 49 HU

Attenuation Ratio

= Average liver density / Splenic density

= 13.7/49 HU

= 0.28

Participant Characteristics		
Variable	**PsO**	**Controls**
▪ ***n***	103	98
▪ ***Female***	61 (62.2)	55 (53.3)
▪ ***Race: Black*** ***White*** ***Indian*** ***Mixed Race***	15 (14.5) 12 (11.7) 44 (42.7) 32 (31.1)	16 (19.3) 14 (14.3) 42 (42.9) 26 (26.6)
▪ ***Age (years)***	53.3 ± 14.5	47.4 ± 14.0 *
▪ ***Disease duration (years)***	18.9 ± 13.3	-
▪ ***Systemic therapy*** ***(excl. corticosteroids)***	43 (41.7)	-

Data expressed as mean ± SD, median (interquartile range) or n (%)
***p <0.05, **p<0.005, ***p < 0.005 versus controls**

Biochemical and radiological measures of liver function in psoriasis patients and control subjects				
Variable	**PsA (n=27)**	**PsC (n=58)**	**All PsO (n-85)**	**Controls (n=97)**
AST (IU/L)	23.0 (19.0,26.0)	23.0 (19.0, 26.0)	23.0 (19.0, 26.0)	23.0 (20.0, 28.0)
ALT (IU/L)	23.0 (19.0, 33.0)	22.5 (17.0, 30.0)	23.0 (18.0 ,31.0)	23.0 (18.0,29.5)
ALT:AST	1.06 (0.94, 1.27)	1.00 (0.86, 1.32)	1.02 (0.98, 1.32)	0.94 (0.77, 1.22)
GGT (IU/L)	25.0 (14.0, 36.0)	24.5 (14.0, 37.0)	25.0 (17.0, 36.0)	23.5 (11.5, 36.5)
ALP (IU/L)	85.0 (73.0, 115)	91.0 * (66.0, 118)	91 (68.0,116)	76.0 (68.0, 92.0)
Albumin (g/L)	45.0 ** (41.0,48.0)	46.0 (44.0, 49.0)	46.0 (43.0, 48.0))	47.0 (44.0, 50.0)
Liver attenuation ratio	1.24 (0.80, 1.41)	1.24 (1.04,1.38)	1.25 (1.04, 1.39)	1.24 (1.12, 1.35)
NAFLD (%)	7 (30.4)	8 (17.3)	15 (21.7)	13 (16.2)

Data expressed as median (IQ)
***p <0.05 **p<0.005 vs controls**

Clinical and anthropometric differences between subjects with/without NAFLD		
Variable	No NAFLD (n=121)	NAFLD (n=28)
Psoriasis (%)	54 (45.0)	15 (53.6)
Psoriatic arthritis (%)	16 (13.3)	7 (25.0)
Body mass index (kg/m2)	29.8 ± 7.71	36.2 ± 8.47 ***
Obesity (%)	47 (39.2)	21 (75.0) *
Waist circumference (cm)	95.7 ± 16.0	110 ± 13.8 ***
Hypertension	69 (57.5)	24 (85.7) *
Subcutaneous fat (cm^3)	396 (268, 552)	604 (431, 839) **
Visceral fat (cm^3)	154 (87.0, 212)	280 (195, 356) ***

Data expressed as mean ± SD, median (interquartile range) or n (%)
***p <0.05, **p<0.005, ***p < 0.005 versus controls**

Biochemical and metabolic differences between subjects with/without NAFLD		
Variable	**No NAFLD (n=121)**	**NAFLD (n=28)**
Type 2 diabetes (%)	12 (10.0)	7 (25.0) *
Hypertriglyceridaemia (%)	24 (20.0)	15 (53.6) **
HDL-C (mmol/L)	1.34 (1.10, 1.62)	1.21 (1.01, 1.46) *
Low HDL-C levels	27 (22.5)	13 (46.4)
Metabolic syndrome (%)	45 (37.5)	23 (82.1) ***
HOMA	1.97 (1.57, 2.89)	3.89 (3.05, 7.00) ***
hsCRP	.00 (1.30, 7.20)	4.05 (1.60, 11.5)
Leptin (ng/mL)	16.3 (7.90, 33.2)	29.3 (12.1, 49.2) *
Adiponectin (µg/mL)	5.98 (3.68, 9.50)	4.59 (2.94, 6.33) *
TNF (pg/mL)	6.30 (4.60, 9.30)	7.65 (5.65, 8.70)
IL-6 (pg/mL)	2.25 (1.50, 4.40)*	3.30 (1.85, 7.90)

Data expressed as mean ± SD, median (interquartile range) or n (%)
***p <0.05, **p<0.005, ***p < 0.005 versus controls**

Prevalence of NAFLD, liver attenuation ratio and serum albumin levels in relation to methotrexate therapy and presence of psoriatic arthritis				
Variables	Subject groups (n)			
	Non-PsA, no MTX (116)	PsA, no MTX (13)	PsC, on MTX (9)	PsA, on MTX (10)
NAFLD (%)	19 (16.1)	2 (15.4)	1 (11.1)	5 (50) OR=5.1 (1.35-19.37)*
LAR - mean (SD)	1.19 (0.24)	1.25 (0.32)	1.16 (0.16)	1.08 (0.37)
Albumin (g/L) - mean (SD)	46.8 (4.39)	44.8 (4.44)	47.3 (2.28)	43.1 (7.04)*

* vs non-PSA, $p<0.05$

Multvariable logistic regression model showing predictors of NAFLD			
Categorical variable	Independent variable	OR (95% CI)	P value
Non-alcoholic fatty liver disease	Triglycerides	1.63 (1.05, 2.52)	0.03
	HOMA	1.98 (1.44, 2.72)	<0.0001
	PsA on methotrexate	2.77 (1.31, 5.87)	0.007

Limitations

- Cross-sectional study
- Small sample size

Strengths

- Analysis of a large number of relevant variables
- Hepatic fat measurements obtained by CT scan
- First analysis of NAFLD in a South African cohort of patients with PsO

Conclusions

- Subjects with NAFLD have increased visceral fat volume and a higher prevalence of cardiometabolic diseases.
- There was no increase in NAFLD in psoriatic patients, except in those with PsA receiving methotrexate.
- Hypertriglyceridaemia, insulin resistance and therapy with methotrexate in PsA are predictors of NAFLD.
- This data suggests that this particular sub-group may warrant screening for NAFLD.

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