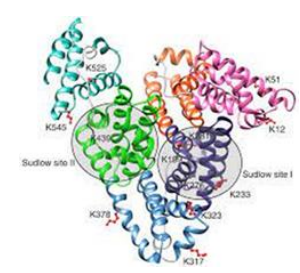
Glycated albumin levels predict the type of kidney damage in diabetic patients

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INTRODUCTION

- The main determinant of the onset of nephropathy in diabetes is **hyperglycemia** that finally leads to fibrosis, inflammation and albuminuria.
- **Glycated Albumin (GA)** measures specifically the glycation product of albumin;
- Is a more useful glycemic index in diabetic patients with CKD since it is not influenced by anemia and associated treatments;
- GA may also reflect the status of blood glucose more rapidly(2–3 weeks) than HbA1c (2–3 months).



- **Kidney disease in diabetic patients** can include different kind of renal damage. Only in 39% of the cases, renal biopsy demonstrated the presence of **real Diabetic Nephropathy (DN)** with the typical histological features, in the other cases kidney impairment in diabetic patients can be due to a **non-diabetic renal disease (NDRD)** in the presence or absence of real DN and novel biomarkers should help us to discriminate different kind of patients.

AIM: To evaluate the clinical utility of the GA dosage as non-invasive biomarker to predict the progression and type of kidney damage in diabetic patients.

METHODS:



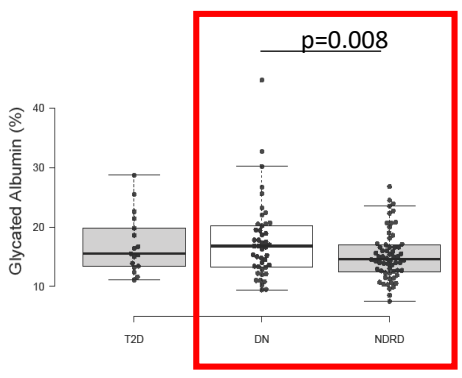
- **Glycated albumin** was evaluated by an enzymatic method coupled to a colorimetric output with the Ilab Aries instrument (Instrumentation Laboratory SpA - A Werfen® Company).
- **qPCR** (on Light Cycler 96, Roche Life Sciences) was used to evaluate urinary levels of **miR-27b-3p**, a biomarker able to discriminate the different kind of renal damage in diabetic patients (Conserva F. et al. Sci Rep, 2019).
- **Glomerular and tubulointerstitial fibrosis** in kidney biopsies was quantified on Sirius Red staining using digitalized slides and the Aperio Imagescope software
- **Statistical analysis** was performed using "SPSS Statistical Software".

Patients enrolled in the study (n=124)

	DN (45)	NDRD (62)	T1D/T2D (17)
Age	60 ± 11	64± 9	54±10
Diabetes duration	14.51 ± 9.95	10.5 ± 8.85	13.96 ± 10.02
Basal Glycemia (mg/dl)	134.8 ± 52.91	119.60 ± 50.41	143.64± 65.15
sCr (mg/dl)	2.035 ± 1.61	1.92 ±1.56	0.71± 0.17
sUrea - azotemia (mg/dl)	86.51±46.39	71.43 ± 43.63	39.58 ± 11.24
albumin (g/dl)	3.32 ±0.43	3.31 ± 0.59	-
eGFR (ml/min)	46.2± 25.40	55.70±30.20	-
Systolic pressure	139±22	138 ±20	126±15
Diastolic pressure	75±12	78±13	77±10
Proteinuria (mg/24h)	3288±3290	2424±3778	-

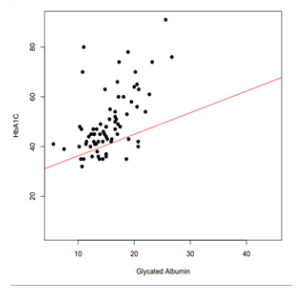
RESULTS

- GA values had a significantly different distribution among DN, NDRD and diabetic patients without renal dysfunction



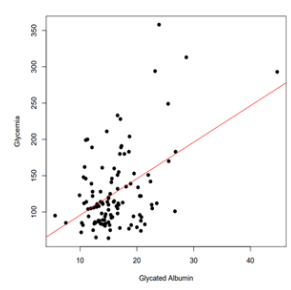
n=124
p=0.032

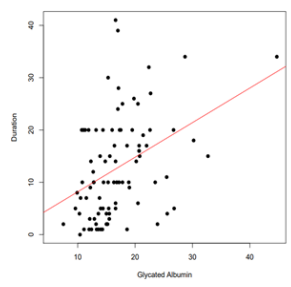
- GA values correlated with Hb1Ac levels, glicemia and diabetes duration in DN patients



GA vs Hb1Ac:
Whole cohort: R=0.522; p<0.001
DN: R=0.539; p<0.001
NDRD: R=0.374; p=0,01

GA vs Glycemia:
Whole cohort: R=0.253; p<0.07
DN: R=0.507; p=0.01
NDRD: n.s.





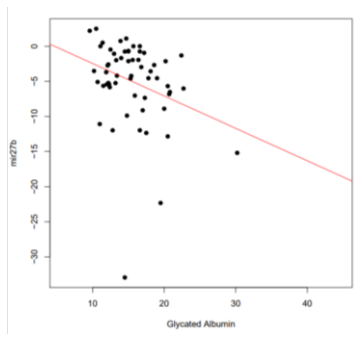
GA vs Diabetes duration:
Whole cohort: R=0.383; p=0.001
DN: R=0.442; p=0.008
NDRD: p=n.s.

- GA values correlated with different clinical and histological parameters

GA correlations	p-value vs glomerular fibrosis	p-value vs % sclerotic glomeruli	p-value vs triglyceride	p-value vs resistive index	p-value vs sCr	P-value vs sUrea	P-value vs eGFR
Whole cohort	0.04	0.02	0.04	<0.001	0.001	0.001	0.001

- GA, but not Hb1Ac, correlated with **miR-27b-3p**, thus suggesting that a deep glucose control is foundamental to prevent the down regulation of this miRNA, that regulates specific pathogenetic mechanisms involved in the progression of diabetic nephropathy.

Pontrelli P at al. FASEB J, 2017
Pontrelli P et al. J Mol Med, 2018
Conserva F. et al. Sci Rep, 2019
Pontrelli P. et al, Int J Mol Sci 2021



Hb1Ac vs miR-27b-3p: p=n.s.

GA vs miR-27b-3p:
All cohort: R=-0,345; p=0.011
DN: R=-0,37; p=0.049
NDRD: R=-0.439; p=0.01

- Finally we applied a multivariate logistic regression model to discriminate real DN and NDRD. We demonstrated that **GA is the only significant predictor of real DN** in a model corrected for sex, age and serum creatinine.

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Glycated Albumin	-,136	,058	5,544	1	,019	,873	,780	,978
	Age	,034	,024	2,000	1	,157	1,035	,987	1,085
	Sex	-,397	,539	,541	1	,462	,672	,234	1,936
	sCr	,017	,142	,015	1	,903	1,017	,771	1,343
	Constant	,366	1,691	,047	1	,828	1,443		

a. Variable(s) entered on step 1: Glycated Albumin, Age, Sex, sCr.

CONCLUSIONS

Our study described for the first time the role played by **GA as a diagnostic marker in the identification of the different kind of renal damage in diabetic patients,** thus supporting the need to introduce GA as an index of glycaemic control in diabetic patients with renal damage.

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