



5-year Change in Urinary Albumin Excretion Rate (AER) in the Insulin Resistance and Atherosclerosis Study (IRAS)

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Insulin Resistance Atherosclerosis Study

IRAS is a large multicenter, observational epidemiological study designed to explore the cross-sectional relationships among insulin resistance, cardiovascular disease risk factors and behaviors, and disease in African-American, Hispanic, and non-Hispanic white men and women, aged 40-69 years, selected to represent a broad range of glucose tolerance.

BACKGROUND

Urinary Albumin Excretion Rate = AER

- Elevated AER is a strong predictor of cardiovascular risk.
- Elevated AER may be an early indicator of diabetic nephropathy.
- AER screening is routinely conducted in diabetes care, although not in non-diabetic subjects.
- The natural history of AER, particularly in non-diabetic subjects with normal glucose tolerance (NGT) or impaired glucose tolerance (IGT), is poorly understood.

AER and Diabetic Nephropathy

- Microalbuminuria (MA)** in the diabetic patient may be the first indication of "incipient nephropathy"; but MA may be reversible and has low specificity for diabetic nephropathy
- Proteinuria** in the diabetic patient is a reliable marker of nephropathy
- Diabetic nephropathy** is a leading cause of End-Stage Renal Disease (ESRD)

METHODS

- We studied 5-year changes in AER status in African American, Hispanic and non-Hispanic white subjects
- Subjects were classified by glycemic status at baseline
- AER status was assessed through single tests at baseline (1992-94; n= 1624) and follow-up (1998-99; n=1338) (83% retention)

LABORATORY ASSAYS

AER assessed in central IRAS laboratory using random morning spot sample stored at -20°C

Urinary albumin assessed using immunoprecipitation assay (Incstar SPQ test system); urinary creatinine assessed using modified Jaffe method.

AER status was categorized by urinary albumin:creatinine ratio:

- Normal or normoalbuminuric (N) if <30 mg/g,**
- Microalbuminuria (MA) if 30-299 mg/g and**
- Proteinuria (P) if >300 mg/g.**

RESULTS

BASELINE	Glucose status			p-value
	Normal (n= 591)	IGT (n=292)	Type 2 DM (n=389)	
Age, yrs (SD)	53.7(8.5)	56.3(7.9)	56.8(8.2)	<0.0001
Sex male (%)	46.2%	36.6%	46.5%	0.0138
Ethnicity (%)				0.1722
Non-Hispanic white	40.8	38.0	34.4	
African American Hispanic	26.4	28.1	33.2	
Hypertension (%)	32.8	33.9	32.4	
Hypertension (%)	26.1	40.4	51.7	<0.0001
Smoker (%)	14.6	13.0	15.2	0.164
HDL (mg/dL)	15.3	14.7	11.4	<0.0001
Waist (cm)	88.0	94.8	99.2	<0.0001
BMI (kg/m ²)	27.4	30.5	31.63	<0.0001

BASELINE	AER status		
	Normo-albuminuria N (%)	Micro-albuminuria N (%)	Proteinuria N (%)
Normoglycose tolerance (NGT)	555 (94%)	34 (6%)	2 (0%)
Impaired glucose tolerance (IGT)	275 (94%)	15 (5%)	2 (1%)
Type 2 Diabetes new (DM-new)	119 (84%)	20 (14%)	3 (2%)
Type 2 diabetes prevalent (DM-prev)	190 (77%)	48 (19%)	9 (4%)

RESULTS

	Change in AER among subjects who were NORMOALBUMINURIC at baseline		
	5-year AER change		
Glycemic status	Stable (stay N)	Progress (to MA)	Progress (to P)
NGT (n=555)	94%	6%	0%
IGT (n=275)	93%	7%	0%
DM-new (n=119)	85%	14%	1%
DM-prev (n=190)	77%	19%	4%

	Change in AER among subjects who were MICROALBUMINURIC at baseline		
	5-year AER change		
Glycemic status	Regress (to N)	Stable (stay MA)	Progress (to P)
NGT (n=34)	68%	29%	3%
IGT (n=15)	47%	40%	13%
DM-new (n=20)	45%	55%	0%
DM-prev (n=48)	54%	29%	17%

	Change in AER among subjects who were PROTEINURIC at baseline		
	5-year AER change		
Glycemic status	Regress (to N)	Regress (to MA)	Stable (stay P)
NGT (n=2)	0%	50%	50%
IGT (n=2)	0%	50%	50%
DM-new (n=3)	0%	0%	100%
DM-prev (n=9)	0%	44%	56%

N = Normoalbuminuria, M = Microalbuminuria, P = Proteinuria

LIMITATIONS

AER status was based on a single test at baseline and a single test at follow-up. Because of variability in AER, multiple abnormal tests (2 of 3 tests in a 3-6 month period) are recommended (ADA Position Statement) before classifying subjects as having microalbuminuria.

IRAS is not a population-based sample of patients with type 2 diabetes. Baseline eligibility criteria (e.g., no insulin-treated patients) may account for differences in distribution of AER in our sample (e.g., low rates of proteinuria)

SUMMARY

Cross-sectional Findings

- Baseline prevalence of microalbuminuria was not greater in pre-diabetes (IGT) relative to normoglycemics.
- Baseline prevalence of microalbuminuria was low (6%) in non-diabetics, but was more common (18%) in diabetes.
- Baseline prevalence of proteinuria was rare, even among diabetic subjects.

Longitudinal Changes

- Progression of AER was equally common among NGT and IGT, but increased sharply in diabetic subjects
- Normalization of microalbuminuria was very common across levels of glucose tolerance
- Subjects with baseline proteinuria remained stable or regressed to microalbuminuria, but never normalized

CONCLUSIONS

Baseline AER and its progression was greater in diabetes relative to non-diabetes; however baseline AER and its progression did not differ between IGT and NGT.

Microalbuminuria normalized more often than it progressed, and thus may be transient and/or potentially modifiable (low specificity).