MYO-INOSITOL OXYGENASE (MIOX) & YES-ASSOCIATED PROTEIN (YAP) IN COMMUNITY ACQUIRED ACUTE KIDNEY INJURY

Jaskiran Kaur[1], Kajal Kamboj[2], Prabhjot Kaur[2],Jasmine Sethi[2], Vivek Kumar[2], Ashok Kumar Yadav[1]

[1]Department of Experimental Medicine and Biotechnology, Postgraduate Institute of Medical Education and Research, Chandigarh

[2]Department of Nephrology, Postgraduate Institute of Medical Education and Research, Chandigarh

Background

Community acquired acute kidney injury (CA-AKI) form a major proportion in terms of both development of progressive renal disease and high long-term mortality. MIOX exhibited a potential role in the early diagnosis of AKI. Beside MIOX, there is increased expression of YAP in diabetic nephropathy, shows its potential role in signaling responsible for renal recovery However, it remains unclear whether MIOX and YAP are suitable biomarker for the diagnosis of CA-AKI.

Aim

We investigated the association of MIOX and YAP in the urine and blood with CA-AKI.

Material and Method

Study design: This was a prospective observational study.

Study Center: Postgraduate Institute of Medical Education & Research Chandigarh, India.

Study Subjects: Subjects with CA-AKI and healthy volunteers.

Inclusion criteria: Stable patients of either sex, aged between 18-70 years and diagnosis of CA-AKI as per KDIGO criteria.

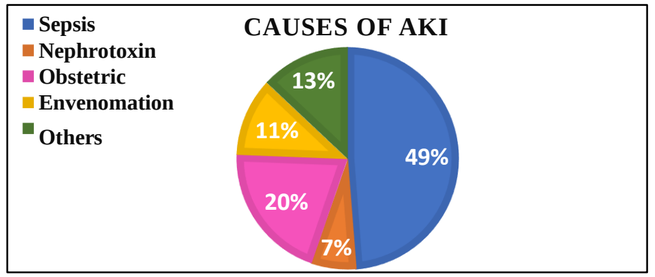
Exclusion criteria: Pre-existing CKD with baseline CKD EPI eGFR<60ml/min/1.73m2 before onset of illness, HA-AKI, patients with known malignancies, and patients with symptomatic heart failure.

*Healthy volunteers of either sex, aged ≥18 years, with stable clinical state were enrolled.

Outcomes:. Levels of urinary and serum biomarkers- MIOX, and YAP between patients with CA-AKI at discharge and healthy volunteers were compared.

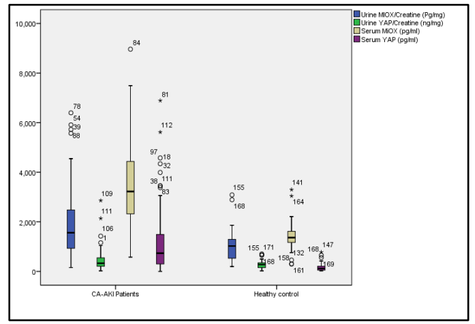
Results

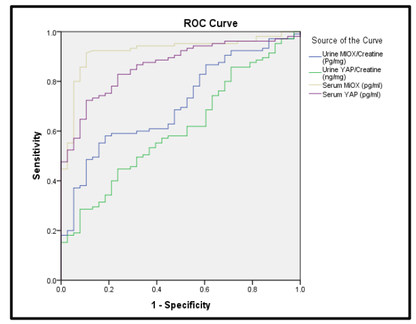
Causes of CA-AKI in the patients



Baseline demographic characteristics and clinical parameters of enrolled subjects

Characteristics	Healthy control (n=50)	Patients with CA-AKI at discharge (n= 124)	P value
Age in years	47 (41.7,56.2)	30.0 (25,44)	<0.001
Female sex (%)	40 (80%)	55 (44.4%)	<0.001
eGFR (mL/min/1.73 m^2)	104.5 (95.3,116)	36 (14.5,67.6)	<0.001
Hb (g/dL)	12.7 (11.5,13.8)	9.8 (8.6,11.4)	<0.001
Blood urea (mg/dL)	20.1 (17.4,25.5)	46.3 (25.6,82.5)	<0.001
SCr (mg/dL)	0.6 (0.5,0.7)	2.2 (1.2,4.05)	<0.001
Serum total Protein (g/dL)	7.4 (7.13,7.8)	6.7 (6.2,7.4)	<0.001
Serum albumin (g/dL)	4.1 (4.0,4.3)	3.4 (2.9,4.08)	<0.001
Uric acid (mg/dL)	4.5 (3.6,5.6)	6.2 (4.9,7.80)	<0.001
Urine creatinine (mg/dL)	4.8 (3.3,7.1)	48.2 (30.7,72.2)	<0.001
Urine total protein (mg/dL)	50.6 (35.6,85.9)	18.1 (6.1,44.0)	<0.001
uPCR (mg/g)	94.9 (74.0,128.9)	279.5 (140.9,771.5)	<0.001
Urine MIOX/Creatinine (pg/mg)	1023 (528,1311)	1560 (924,2494)	<0.001
Urine YAP/Creatinine (ng/mg)	274.5 (151.3,382.5)	326.1(204.0,553.0)	0.044
Serum MIOX (pg/mL)	1362 (1166,1619)	3224 (2304,4381)	<0.001
Serum YAP (pg/mL)	127.8 (52.1,252.5)	917 (337.2,1682.5)	<0.001





Area under the receiver-operating characteristic curve of urinary and serum biomarkers for the diagnosis of CA-AKI

	AUC	95% CI	P- value
Urine MIOX/Creatinine (pg/mg)	0.709	0.619-0.798	<0.001
Urine YAP/Creatinine (ng/mg)	0.608	0.509-0.706	0.050
Serum MIOX (pg/mL)	0.922	0.873-0.971	<0.001
Serum YAP (pg/mL)	0.864	0.804-0.925	<0.001

- Serum levels of MIOX (3224 pg/mL, versus 1362 pg/mL), and YAP (917 pg/mL, versus 127.8 pg/mL) were significantly high in CA-AKI as compared to healthy control group.
- The levels of urinary MIOX (1560 pg/mg versus 1023 pg/mg), and YAP (326.1 ng/mg, versus 274.5 ng/mg) normalized to urinary creatinine was high in CA-AKI as compared to healthy control.
- Serum MIOX serves as an excellent biomarker for the diagnosis of CA-AKI (AUC=0.922, p<0.001). Similarly, urine MIOX/Creatine and serum YAP also serve as significant biomarker for the diagnosis of CA-AKI (AUC=0.709, p<0.001) and 0.864, p<0.001) respectively).

Conclusion

The levels of MIOX and YAP are high in subjects with CA-AKI and may serve as a potential biomarker for the diagnosis of CA-AKI. Further, Multicentric, longitudinal observational studies are required to evaluate the potential use of MIOX and YAP as a specific biomarker for the early diagnosis of AKI.