1/ 🚨Tweetorial Alert🚨
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2/ 🚨Our topic🚨:
Time-Updated Hematuria and Kidney Disease Progression in IgAN - Kidney International Reports
https://www.kireports.org/article/S2468-0249%2826%2902885-8/fulltext
There are no conflicts of interest. #MedTwitter #nephtwitter @ISNkidneycare


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Time-Updated Hematuria and Kidney Disease Progression in IgAN

Check for updates

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3/ How about a quick quiz-
What percentage of hematuria, whether macroscopic or asymptomatic microscopic occurs in IgA nephropathy?

a) 25-30%
b) 30-40%
c) 60-80%
d) 70-100%

4/ 💡💥 The correct answer is D. Previous studies have demonstrated that both the severity & persistence of hematuria are independent predictors of poor renal outcomes in IgAN.
Remission status highlighting therapeutic benefits and better renal survival.

5/ However, despite previous reports highlighting the importance of 💥hematuria💥 🩸🧋
⬇️It remains underutilized in clinical practice
🧶It has been excluded from multicenter clinical trials
📓It is insufficiently incorporated into clinical guidelines
6/ Why does this occur⁉️

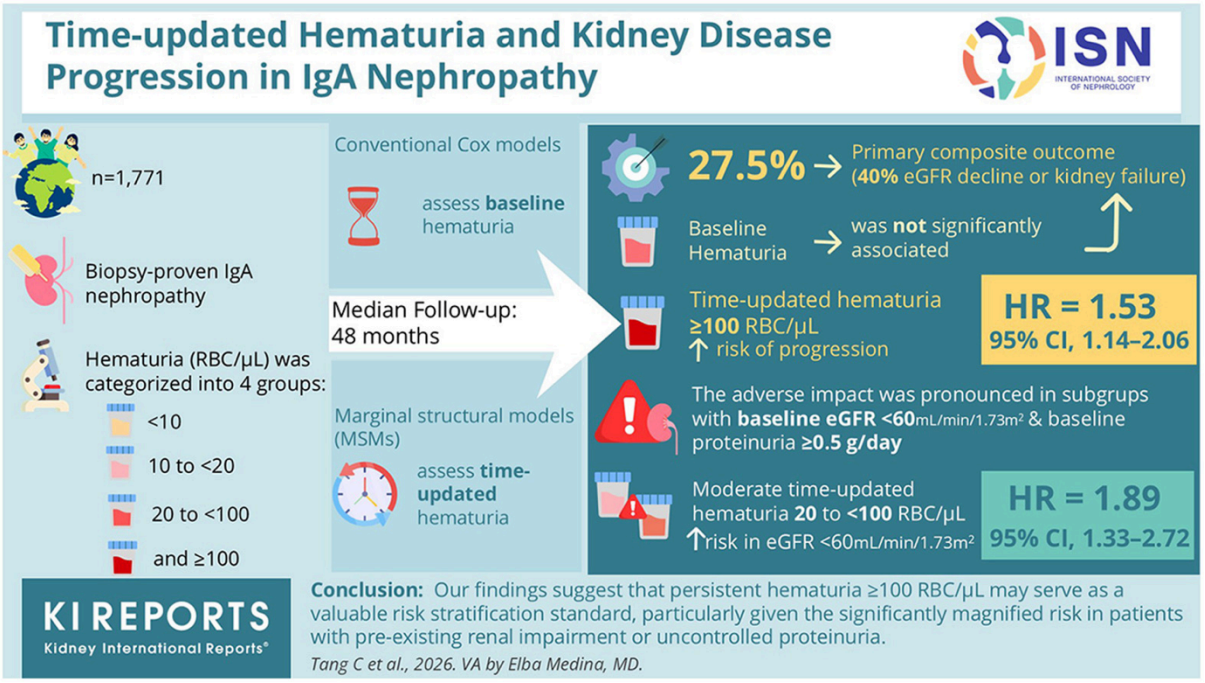
📏The absence of standardization

🗓️Daily variability in hematuria

😵‍💫Time-dependent confounders

Because of this, Tang et al https://www.kireports.org/article/S2468-0249%2826%2902885-8/fulltext sought to evaluate the association between hematuria and kidney outcomes in IgAN✨

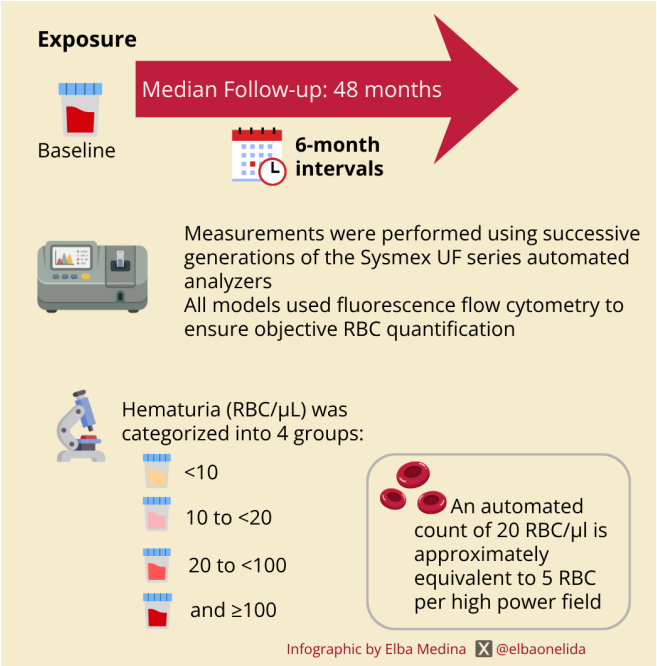
Check out this visual abstract 🔥🔥 VA by @elbaonelida



7a/ Methods
🕶️Prospective observational cohort study
🇨🇳Peking University First Hospital
1,771 patients
Jan 2024-June 2024

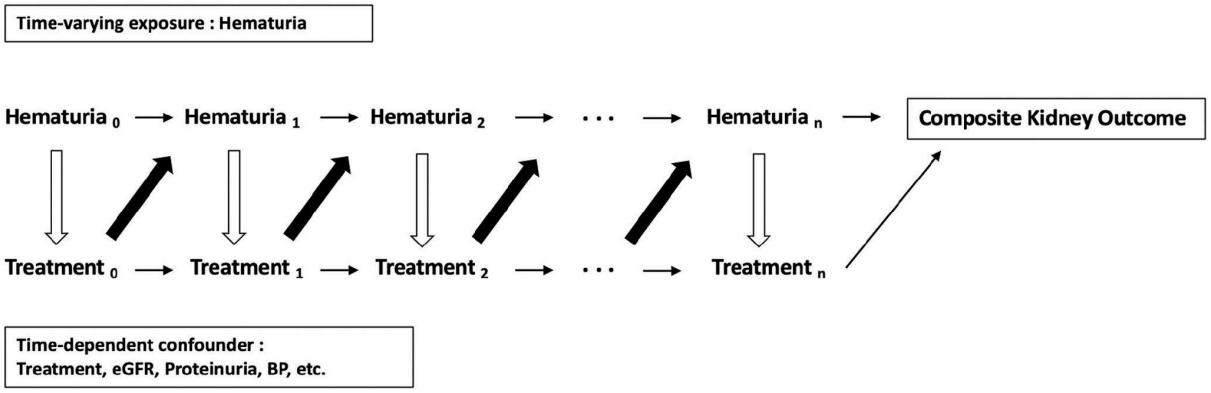
7b/
Inclusion:
🧑Adult patient with biopsy-proven IgAN
🚷 Exclusion criteria:
2️⃣secondary forms of IgAN
🫘eGFR <20 ml/min per 1.73m2
🔬Missing baseline histopathological data

08/Exposure



9/ Outcome
🫘Composite kidney disease progression :
📉40% decline in eGFR from baseline or
the onset of ESKD (defined as eGFR <15mL/min/1.73m², dialysis initiation, or kidney transplantation)
👫Covariates:
Age, sex, BMI, albumin, proteinuria, eGFR, MAP, diabetes and MEST/C

10/Statistical Analyses
Risk disease progression: Cox proportional hazards models
Marginal Structural Models: Causal effect of time-updated hematuria on the primary outcome
Examined causal relationships among time-updated hematuria, time-dependent confounders, & kidney outcomes



11/💥Results (4 groups by baseline hematuria)
🎂Mdn age: 36
🫘Mdn eGFR:74.2
🥃 proteinuria:1.28
👤 Patients with higher baseline hematuria: were ⬇️Age⬆️eGFR & baseline proteinuria⬆️ Crescent prevalence⬆️ Corticosteroid & immunosuppressant use

Table 1. Baseline characteristics of participants according to baseline hematuria categories

Variables	Total	Baseline hematuria, RBC/µl				*P*-value
		< 10	10 to < 20	20 to < 100	≥ 100	
N	1771	131	160	608	872	
Age, yrs	36 (29–45)	39 (33–48)	36 (30–43)	36 (30–45)	35 (29–45)	0.008
Male, *n* (%)	888 (50.1%)	68 (51.9%)	92 (57.5%)	320 (52.6%)	408 (46.8%)	0.029
BMI, kg/m^2	24.2 (21.6–27.0)	25.6 (23.6–27.8)	25.0 (22.0–27.7)	24.2 (21.6–26.5)	24.0 (21.4–26.7)	< 0.001
Diabetes, *n* (%)	59 (3.3%)	4 (3.1%)	6 (3.8%)	18 (3.0%)	31 (3.6%)	0.901
Albumin, g/l	39.2 (35.7–41.8)	40.4 (38.1–42.0)	40.0 (37.2–42.4)	39.5 (36.4–42.3)	38.5 (34.8–41.3)	< 0.001
MAP, mmHg	93.3 (86.7–102)	96.7 (90.8–103)	94.7 (89.3–103)	93.3 (87.3–102)	93.3 (86.3–101)	0.001
Proteinuria, g/d	1.28 (0.66–2.34)	1.03 (0.51–1.89)	1.18 (0.62–2.19)	1.21 (0.63–2.21)	1.35 (0.72–2.66)	0.001
eGFR, ml/min per 1.73 m^2	74.2 (49.8–99.0)	68.4 (43.2–92.1)	72.0 (44.3–98.6)	69.2 (48.8–94.2)	78.0 (52.4–102.0)	0.001
CKD stage (%)						0.005
1-2	1138 (64.3%)	76 (58.0%)	99 (61.9%)	370 (60.9%)	593 (68.0%)	
3a	276 (15.6%)	21 (16.0%)	20 (12.5%)	109 (17.9%)	126 (14.4%)	
3b	260 (14.6%)	19 (14.5%)	28 (17.5%)	99 (16.3%)	114 (13.1%)	
4	97 (5.5%)	15 (11.5%)	13 (8.1%)	30 (4.9%)	39 (4.5%)	
Time from biopsy to baseline, mos	3.2 (17.2)	9.7 (32.2)	4.5 (22.2)	3.0 (15.3)	2.0 (13.6)	
Oxford classification						
M 0/1	973/798	81/50	94/66	305/303	493/379	0.019
E 0/1	1063/708	91/40	102/58	367/241	503/369	0.050
S 0/1	543/1228	39/92	46/114	167/441	291/581	0.100
T 0/1/2	1154/468/149	84/32/15	96/47/17	373/173/62	601/216/55	0.015
C 0/1/2	615/980/176	75/50/6	66/83/11	204/350/54	270/497/105	< 0.001
Medications during follow-up, *n* (%)						
RAS inhibitors	1672 (94.4%)	123 (93.9%)	148 (92.5%)	578 (95.1%)	823 (94.4%)	
α-Blockers	175 (9.8%)	20 (15.3%)	24 (15.0%)	48 (7.9%)	83 (9.5%)	
β-Blockers	359 (20.3%)	32 (24.4%)	34 (21.2%)	124 (20.4%)	169 (19.4%)	
Calcium channel blockers	583 (32.9%)	54 (41.2%)	60 (37.5%)	196 (32.2%)	273 (31.3%)	
Diuretics	758 (42.8%)	62 (47.3%)	66 (41.2%)	267 (43.9%)	363 (41.6%)	
Corticosteroids	724 (40.9%)	39 (29.8%)	62 (38.8%)	238 (39.1%)	385 (44.2%)	
Other immunosuppressants	690 (39.0%)	49 (37.4%)	63 (39.4%)	212 (34.9%)	366 (42.0%)	
Hydroxychloroquine	590 (33.3%)	40 (30.5%)	49 (30.6%)	207 (34.0%)	294 (33.7%)	
SGLT-2 inhibitors	432 (24.4%)	42 (32.1%)	51 (31.9%)	154 (25.3%)	185 (21.2%)	

BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; RAS inhibitors, renin angiotensin system inhibitors; SGLT-2, sodium-glucose cotransporter 2. Data are expressed as mean (SD), median (interquartile range), or count (%).

12/🫘 Adverse Kidney Event
👤🗓️n= 8932 person-year of follow-up (median 48 mo)
💥Primary composite kidney outcome in 487 (27.5%)
🥃The estimated cumulative incidence of composite kidney outcome was similar across baseline hematuria categories (P =0.8)

Table 2. Adverse kidney event rates according to baseline hematuria categories

Outcome	Overall	Baseline hematuria, RBC/µl			
		< 10	10 to < 20	20 to < 100	≥ 100
No. of participants	1771	131	160	608	872
Composite kidney outcome					
Person-yr	8932.1	690.6	882.5	3173.8	4245.2
Events	487	33	46	174	234
Events per 1000 person-yr	54.5	47.8	55.9	54.8	55.1

Composite kidney outcome was defined as a decline in eGFR ≥ 40% or end-stage kidney disease.

Supplementary Table 2. Cumulative incidence of the composite kidney outcome and competing risk of death according to baseline hematuria categories

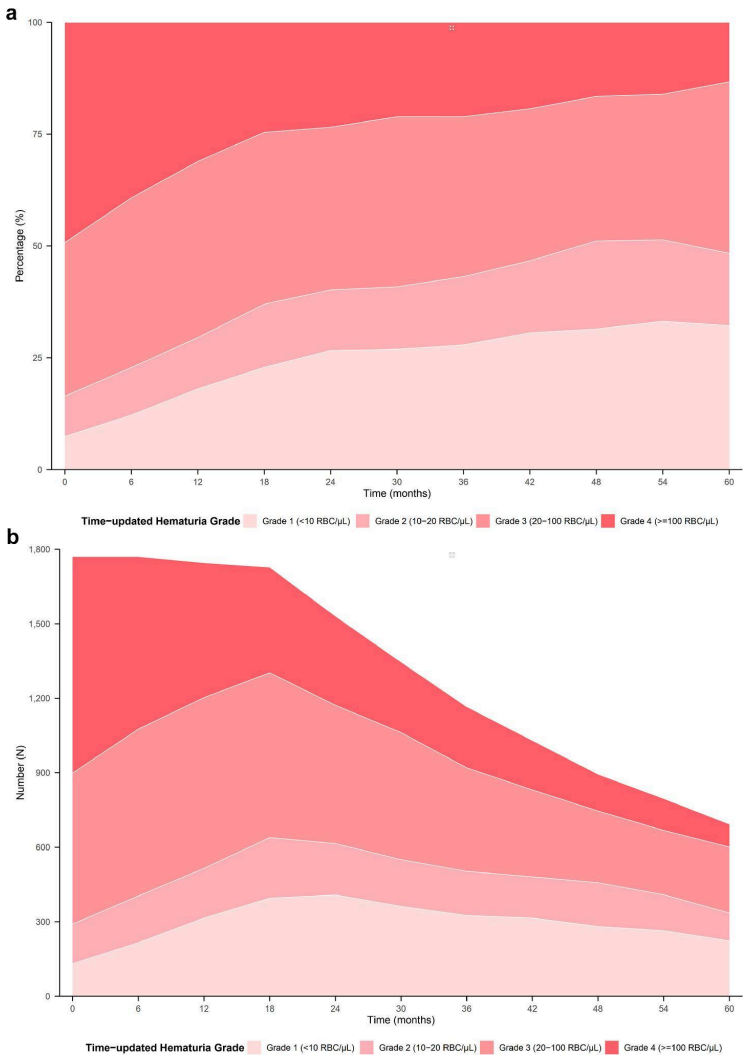
Outcome	Cumulative incidence (HR, 95%CI)					
	1 Year	2 Year	3 Year	4 Year	5 Year	P value[1]
Death before composite kidney outcome						
Overall (n=1771)	—	—	0.15 (0.03, 0.51)	0.15 (0.03, 0.51)	0.15 (0.03, 0.51)	
Composite kidney outcome						
Overall (n=1771)	2.4 (1.8 3.2)	6.2 (5.2, 7.5)	11 (9.9, 13)	17(15, 19)	21 (19, 24)	
Baseline hematuria (/ul)						0.8
< 20 (n=131)	1.5 (0.3, 4.9)	4.9 (2.0, 9.7)	9.0 (4.6, 15)	14 (7.8, 21)	18 (11, 27)	
10 to < 20 (n=160)	3.8 (1.5, 7.6)	6.3 (3.2, 11)	11 (6.1, 16)	17 (11, 24)	23 (15, 32)	
20 to < 100 (n=608)	1.6 (0.85, 2.9)	5.6 (3.9, 7.6)	12 (9.7, 15)	19 (15, 22)	22 (19, 27)	
≥ 100 (n=872)	2.9 (1.9, 4.1)	6.9 (5.3, 8.7)	11 (9.1, 14)	16 (13, 19)	21 (17, 24)	

[1] Gray's Test

Abbreviations: HR, hazard ratio

13/

❌No graded association between baseline hematuria & primary outcome risk
⚖️Compared to reference (<10 RBC/μL), HRs (95% CI) were:
10–19 /μL: 1.14 (0.73–1.79)
20–99 /μL: 1.09 (0.74–1.59)
≥100 /μL: 1.11 (0.76–1.61)
5-year longitudinal hematuria distribution.⬇️



14/ Marginal structural models (adjusting for time-dependent confounders/fluctuations):

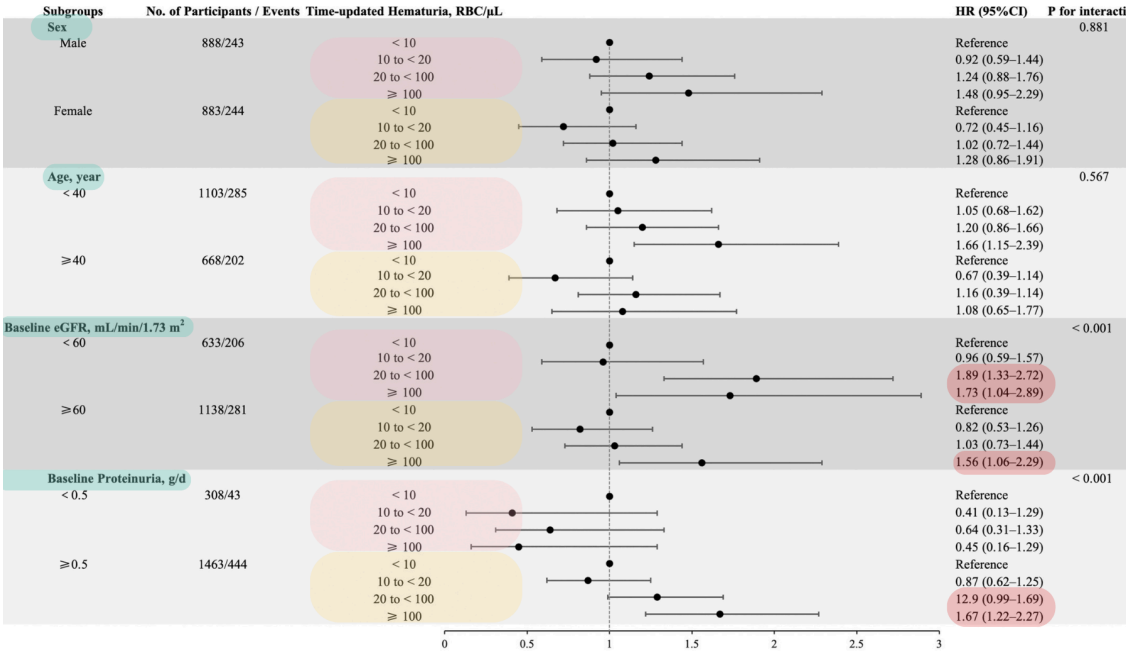
- ⬆️ ≥100 RBC/µL: Increased kidney outcome risk (HR: 1.53; 95% CI: 1.14–2.06)
- 20 to <100 RBC/µL: No significant risk increase (HR: 1.19; 95% CI: 0.93–1.53) vs reference group

Table 3. Hazard ratios for the composite kidney outcome according to baseline and time-updated hematuria

	HR (95% CI)	*P*-value
Baseline hematuria, RBC/μl		0.733[a]
< 10	Reference	
10 to < 20	1.14 (0.73–1.79)	0.559
20 to < 100	1.09 (0.74–1.59)	0.665
≥ 100	1.11 (0.76–1.61)	0.588
Time-updated hematuria, RBC/μl		0.003[a]
< 10	Reference	
10 to < 20	0.88 (0.63–1.22)	0.441
20 to < 100	1.19 (0.93–1.53)	0.154
≥ 100	1.53 (1.14–2.06)	0.004

eGFR, estimated glomerular filtration rate; MAP, mean arterial pressure; SGLT-2, sodium-glucose cotransporter 2.
[a]P for trend.
Composite kidney outcome was defined as a decline in eGFR ≥ 40% or end-stage kidney disease.
All models were adjusted for baseline covariates, including age, sex, body mass index, albumin, proteinuria, eGFR, MAP, diabetes, and MEST-C scores (Oxford classification of IgA nephropathy). Time-updated hematuria was analyzed using marginal structural models, in which albumin, proteinuria, eGFR, MAP, the usage of renin-angiotensin system inhibitors, other antihypertensive medications (α-blocker, β-blocker, calcium channel blocker, diuretic), hydroxychloroquine, SGLT-2 inhibitors, corticosteroids and other immunosuppressants during the follow-up period, were treated as time-dependent covariates.

15/ Subgroup Analyses
Significantly modified by baseline eGFR & proteinuria.
Risk pronounced in:
🥃Proteinuria ≥0.5 g/d: Time-updated hematuria 100 RBC/ul⬆️ risk HR: 1.67; 95% CI: 1.22–2.27
🫘eGFR <60 mL/min/1.73m² : Even moderate hematuria (20 to < 100RBC/uL) ⬆️risk HR: 1.89



16/ Summary

Persistent high-grade hematuria (specifically ≥ 100 RBC/μl) is a potent driver of disease progression

The results suggest that persistent hematuria acts as a critical biomarker of ongoing disease activity & a complementary target in clinical management.

17/ conclusion

⚠️Persistent high-grade hematuria ≥100 RBC/μl ➡️critical & independent predicts IgAN progression, particularly in🤦‍♂️with impaired🫘 function or uncontrolled proteinuria

🎯Target: Achieving hematuria remission

🧐Need: RCTs validation

18/ Limitations

1. Residual confounding by unobserved factors
2. Limited clinical exposure to emerging therapies
3. Equipment-related data variability (changes or upgrades in equipment)
4. Predominantly Asian study population

19/💥 Follow-up hematuria monitoring in this population is required; standard urinalysis is easily performed.

20/ Please share this #tweetorial with your followers and friends! Thanks to & for great feedback!

Thanks for reading! ✨ tweetorial by @elbaonelida (adult nephrologist)