Study Protocol

Scientific title	**Clinical characteristics and CRI-defined high-risk presentation among adults evaluated for anti-glomerular basement membrane antibodies: a retrospective cross-sectional analytical study at Baoding No.1 Central Hospital**
Public title	Which clinical features are linked with severe presentation in people tested for anti-GBM antibodies?
Protocol version/date	Version 1.0 - 28 September 2026
Study design	Retrospective cross-sectional analytical study
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Ethics	Medical Ethics Committee of Baoding First Central Hospital; IRB-A27N5-2026; approved 15 January 2026
Funding	Medical Science Research Project of Hebei Province (Project No. 20251434).
Conflict of interest	None

1. Background and rationale

Anti-glomerular basement membrane disease is a rare autoimmune pulmonary-renal syndrome with substantial heterogeneity at initial presentation. Severe renal dysfunction, dialysis dependence, pulmonary hemorrhage, ANCA overlap, antibody burden, and destructive renal histopathology may occur in different combinations. Existing prognostic studies are often kidney-dominant and focus on longitudinal outcomes. This study uses Clinical Risk Integration (CRI) as a rule-based descriptive framework to organize multidomain severity at index presentation among anti-GBM-positive patients.

2. Objectives

1. Describe baseline demographic, clinical, laboratory, serologic, imaging, and histopathologic characteristics among adults evaluated for anti-GBM antibodies.

2. Compare anti-GBM-positive and anti-GBM-negative patients at index presentation.

3. Within the anti-GBM-positive cohort, describe CRI high-risk and lower-risk presentation and compare non-defining clinical and histopathologic features between the two groups.

4. Describe CRI risk distribution across prespecified symptom, serology, and antibody-titer subgroups and explore univariable associations of non-defining severity markers with CRI risk class.

3. Study design and setting

This is a single-center retrospective cross-sectional analytical study conducted at Baoding No.1 Central Hospital, Baoding, Hebei, China. Historical clinical records cover 1 January 2021 to 31 December 2025.

Retrospective record retrieval and abstraction took place from 1 February to 30 April 2026, and analysis was completed on 31 August 2026. The unit of analysis is the individual patient at the first eligible index presentation.

4. Ethics and consent

The Medical Ethics Committee of Baoding First Central Hospital approved the study on 15 January 2026 under reference IRB-A27N5-2026. The requirement for written informed consent was waived because the study uses existing de-identified clinical records, involves no direct participant contact, and adds no clinical procedures. Confidentiality is protected through de-identification, restricted access, and aggregate reporting.

5. Population and record identification

Potentially eligible records are identified consecutively from the hospital anti-GBM laboratory registry and linked to nephrology, laboratory, urinalysis, imaging, dialysis, and renal pathology records. Only the first eligible index presentation for each patient is retained. The retrieval target is 130 records; 138 records are screened and 91 unique index records form the final analytical dataset.

5.1 Inclusion criteria

1. Age 18 years or older at index evaluation.
2. Documented anti-GBM antibody test within routine clinical care during the source-record period.
3. Serum creatinine available at index presentation to calculate eGFR using the 2021 CKD-EPI creatinine equation.
4. Sufficient chart detail to determine renal and pulmonary involvement at index presentation.

5.2 Exclusion criteria

1. Age younger than 18 years.
2. Repeat encounters after the first eligible presentation.
3. Records lacking core CRI variables required for classification: antibody status, renal-function data, or organ-involvement documentation.
4. Irretrievable records in which serologic or clinical source documents cannot be verified.

6. CRI classification

CRI is applied only within the anti-GBM-positive cohort. Anti-GBM positivity is defined as >=20 RU/mL. High-risk presentation is assigned when at least one major criterion is present at index evaluation: eGFR <15 mL/min/1.73 m², dialysis dependence, pulmonary hemorrhage, or concurrent anti-GBM and ANCA positivity. Anti-GBM-positive patients without any major criterion are classified as lower risk. Low anti-GBM titer is 20 to <100 RU/mL and high titer is >=100 RU/mL. CRI is a descriptive rule-based classification and is not treated as a validated prognostic score.

7. Data sources and variables

The data linkage sequence begins with the anti-GBM laboratory registry and proceeds to inpatient or outpatient records, serum chemistry, full blood count, urinalysis, chest imaging, dialysis documentation, and renal biopsy reports. Data are entered into a standardized abstraction form with predefined coding and missing-data checks. Uncertain CRI assignments are reviewed by two assessors. Categorical abstraction quality is assessed using Cohen kappa with a target agreement of at least 0.80.

8. Outcomes

8.1 Primary outcome

Outcome name	CRI-defined high-risk presentation
Metric or method of measurement	Binary classification among anti-GBM-positive patients. High risk requires at least one of: eGFR <15 mL/min/1.73 m², dialysis dependence, pulmonary hemorrhage, or anti-GBM/ANCA co-positivity; lower risk requires none of these criteria.
Timepoint(s)	Index presentation; measured once from the first eligible record.

8.2 Key secondary outcomes

Outcome name	Renal status
Metric or method of measurement	Serum creatinine, eGFR, blood urea nitrogen, serum albumin, dialysis dependence, proteinuria, hematuria, red cell casts, and active urinary sediment extracted from the index clinical/laboratory record.
Timepoint(s)	Index presentation; measured once.
Outcome name	Pulmonary status
Metric or method of measurement	Hemoptysis, dyspnea, diffuse alveolar infiltrates, and pulmonary hemorrhage determined from respiratory review and chest-imaging records.
Timepoint(s)	Index presentation; measured once.
Outcome name	Serologic profile
Metric or method of measurement	Anti-GBM titer, ANCA status, single-positive versus double-positive serology, and anti-GBM titer category (20 to <100 RU/mL versus >=100 RU/mL) extracted from the index immunology record.
Timepoint(s)	Index presentation; measured once.
Outcome name	Histopathologic status
Metric or method of measurement	Crescent burden, necrotizing lesions, glomerulosclerosis, interstitial fibrosis or tubular atrophy, and tubular injury extracted from the final renal biopsy report when biopsy data are available.
Timepoint(s)	Index presentation / diagnostic biopsy; measured once.

8.3 Exploratory analysis outcome

Outcome name	Exploratory association of non-defining severity markers with CRI risk class
Metric or method of measurement	Univariable logistic regression for non-defining features including age, blood urea nitrogen, serum albumin, high anti-GBM titer, crescent burden >=50%, glomerulosclerosis, and tubular injury. CRI-defining

Outcome name	Exploratory association of non-defining severity markers with CRI risk class
	variables are excluded from predictor modelling.
Timepoint(s)	Index presentation; analysis performed after record abstraction was complete.

9. Sample size

An a priori G*Power 3.1 calculation used a two-tailed alpha of 0.05, power of 0.80, and a medium effect size of 0.30, giving a minimum required sample of 88. The retrieval target was set at 130 records to accommodate ineligible records and subgroup description. The final analytical sample contains 91 unique records, exceeding the minimum threshold.

10. Statistical analysis

Analyses are conducted using IBM SPSS Statistics 29.0. Continuous variables are summarized using mean and standard deviation or median and interquartile range, and categorical variables using frequency and percentage. Shapiro-Wilk and Levene tests are used to assess distributional and variance assumptions as appropriate. Anti-GBM-positive and anti-GBM-negative groups, and CRI high-risk and lower-risk groups within the positive cohort, are compared using independent-samples t tests, Mann-Whitney U tests, Pearson chi-square tests, or Fisher exact tests according to data type and assumptions.

The four constitutive CRI criteria are descriptive components of the primary outcome and are not entered as predictors of CRI risk class. Exploratory univariable logistic regression is limited to non-defining variables including age, blood urea nitrogen, serum albumin, high anti-GBM titer, crescent burden >=50%, glomerulosclerosis, and tubular injury. Effect estimates are reported with 95% confidence intervals. Tests are two-tailed with $p<0.05$; no multiplicity adjustment is applied because the exploratory analyses are hypothesis-generating.

11. Data management and confidentiality

Study data are de-identified before analysis. The analytic dataset is held within controlled institutional research systems and is accessible only to authorized study personnel. Direct identifiers are not included in registry or publication outputs. Any external sharing of de-identified data requires institutional approval and compliance with applicable privacy and research-governance requirements.

12. Dissemination

Results will be submitted to the ISRCTN registry and may be disseminated through peer-reviewed publication and scientific presentation. CRI will be described as a presentation-classification framework requiring external prospective validation, not as an established prognostic or treatment-decision tool.

13. Funding and conflicts of interest

Funding: Medical Science Research Project of Hebei Province (Project No. 20251434).

Conflict of interest: None.