Evaluation Of Incidence Of Acute Kidney Injury Cases And Their Renal Biopsies Results In Beni-Suef University Hospital. A Single Center Study

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Abstract:

Background: RIFLE, KDIGO and AKIN has been used for diagnosis and grading of AKI (acute kidney injury). The introduction of renal biopsy transformed the landscape for diagnosis and management of glomerular diseases. While the clinical classifications described above provide clinicians with a working-diagnosis, renal biopsy is typically required for definitive diagnosis. Objectives: Evaluation of incidence of acute kidney injury cases and their renal biopsies results in Beni-Suef university hospital. Patients and Methods: Our study include 63 Egyptian patients developed acute kidney injury presenting to internal medicine outpatient clinic and in patient of Beni-Suef University Hospital through one year from October 2018 to October 2019. Results: On histopathological examination renal biopsies, generally the most common pathological finding in renal biopsies of patients with AKI in the study was focal segmental glomerulosclerosis 13(20%) these result was approved by followed by global glomerulosclerosis9(14%), Lupus nephritis IV 8(13%), acute tubular injury, diabetic nodular glomerulosclerosis, Membranous N each one 4(6%). In diabetic group (7) the commonest pathology detected was Diabetic nodular glomerulosclerosis 4(36%) with marked Interstitial fibrosis and tubular atrophy (IFTA). In hypertensive patients(29) the commonest pathology detected was Global GS 8(28%) then Focal segmental glomerulosclerosis6(20%). In SLE group (12) Lupus nephritis class VI 6(50%) followed by Lupus nephritis class III 4(33%). In apparent healthy patients the predominant pathology was Focal segmental glomerulosclerosis26% followed by Global GS 18.5 % followed by membranous nephropathy (14.8%).

Keywords: Renal biopsy, Acute kidney injury, RIFLE, Histopathology.

1. Introduction

Acute kidney injury (AKI) is increasingly prevalent in developing and developed countries and is associated with severe morbidity and mortality[1]. Over 30 AKI definitions have been published effectively all are based on absolute or delta changes in serum creatinine [2].
Three dominant AKI definition;

- **RIFLE**
- **AKIN**
- **KDIGO** (*Kathleen D, et al., 2012*)

Recent definition of acute kidney injury mean sudden and temporary loss of kidney function depending on serum creatinine and urine output [3].

Acute kidney injury (AKI) is a clinical syndrome that complicates the course and worsens the outcome in a significant number of patients [4].

| Classification | Definition for AKI | Stage | Serum Creatinine Criteria for AKI Staging$^a$ |
|----------------|--------------------|-------|--------------------------------------------|
| RIFLE          | Increase in SCr $\geq$ 50% within 7 d | Risk | To $\geq$ 1.5 times baseline                |
|                |                    | Injury| To $\geq$ 2 times baseline                 |
|                |                    | Failure| To $\geq$ 3 times baseline or $\leq$ 0.5 mg/dl increase to at least 4.0 mg/dl |
| AKIN           | Increase in SCr $\geq$ 0.3 mg/dl or $\geq$ 50% within 48 h | 1 | Increase of $\leq$ 0.5 mg/dl or to 1.5–1.9 times baseline |
|                |                    | 2 | To 2–2.9 times baseline                     |
|                |                    | 3 | To $\geq$ 3 times baseline or $\leq$ 0.5 mg/dl increase to at least 4.0 mg/dl or initiation of RRT |
| KDIGO          | Increase in SCr $\geq$ 0.3 mg/dl within 48 h or $\geq$ 50% within 7 d | 1 | Increase in SCr $\geq$ 0.3 mg/dl within 48 h or to 1.5–1.9 times baseline |
|                |                    | 2 | To 2.0–2.9 times baseline                    |
|                |                    | 3 | To 3.0 times baseline or to at least 4.0 mg/dl or initiation of RRT |
| CK             | Increase in SCr $\geq$ 0.3 mg/dl within 24 h or $\geq$ 0.5 mg/dl within 48 h | 1 | Increase in SCr $\geq$ 0.3 mg/dl within 24 h or $\geq$ 0.5 mg/dl within 48 h |
|                |                    | 2 | Increase in SCr $\geq$ 0.5 mg/dl within 24 h or $\geq$ 1.0 mg/dl within 48 h |
|                |                    | 3 | Increase in SCr $\geq$ 1.0 mg/dl within 24 h or $\geq$ 1.5 mg/dl within 48 h |

For patients meeting diagnosis criteria for AKI according to RIFLE, AKIN, or KDIGO, the stages based on percentage increase were determined by the ratio of peak SCr value obtained during hospitalization to baseline. RIFLE: Risk Injury Failure Loss ESRD; AKIN: Acute Kidney Injury Network; KDIGO, Kidney Disease Improving Global Outcomes; CK, creatinine kinetics; SCr, serum creatinine; RRT, renal replacement therapy.

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2. Patients And Methods:

Our study include 63 egyptian patients developed acute kidney injury presenting to internal medicine out patient clinic and inpatient of Beni-Suef university hospital through one year from October 2018 to October 2019. We selected the patients depending on the following inclusion and exclusion criteria.

**Inclusion criteria:**

a) Patients with AKI rising creatinine 1.5 from basal creatinine.

b) Diabetic or hypertensive with AKI.

c) Systemic Lupuseryth Ematosus patients (SLE) with AKI.

d) Chronic kidney disease (CKD) with AKI.

**Exclusion criteria:**

a) Obstructive nephropathy.

b) End stage renal disease by ultrasound.

c) Sepsis or obvious prerenal element by clinical and laboratory evaluation.

Then the following were done:

a) Identification data as age, sex and weight.

b) Clinical evaluation.
**Complete history taking:**
(Presenting complaint, present history, family history, past history, history of previous operations and medical history). Complete physical examination, evaluation of urine output.

**Laboratory evaluation:**
Complete blood count (CBC)
Renal function tests (serum creatinine, urea, Na and K)
Urinary albumin/creatinine ratio
Liver function tests (albumin, ALT, AST, bilirubin) C-reactive protein.
Erythrocyte sedimentation rate (ESR). Urine analysis.

**Renal biopsy:** Histopathological examination to assess pathological changes of renal biopsy with immunostaining when required. Renal biopsy is further evaluated by immune-peroxidase staining to identify immune reactants that may be responsible for glomerular injury. These immune-reactants include IgG, IgM, IgA, C3, C1q, fibrinogen, and kappa and lambda lightchains.

There are several patterns of injury that can be observed by light microscopy evaluation of the renal biopsy, electron microscopy, or immune-fluorescence.

**Two cores for light microscope:** After preserving it in 10% concentrated formaldehyde.

The classic stains used in light microscopy include hematoxylin and eosin and periodic acid-Schiff reaction (PAS), Jones silver-methenamine, and Masson’s trichromestaining.

**Ethics:**
The study was performed after approval of local ethical committee of Beni-Suef university hospital. Written informed consent was taken from every patient before being included in the study.

**Statistical analysis:**
Data will be statistically described in terms of mean standard deviation (SD), or frequencies (number of cases) and percentages when appropriate. P values less than 0.05 will be considered statistically significant. All statistical calculations will be done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 15 for Microsoft Windows (2007).

**The aim of the study:**
To evaluate the incidence of acute kidney injury among our patients (Beni-Suef University hospital) and try to identify the underlying etiology by different investigations including mainly renal biopsy.

3. **Results:**
This single center study was conducted in nephrology unit of Beni-Suef University hospital.
Figure (1) Distribution of co-morbidities of medical importance among the studied patients:

Categorical data was presented as number and percent.

Figure (1) showed that there were only 11% of the participants diabetic but 46% of them were hypertensive. There were 19% had SLE, and 42.9% were apparent healthy with no detectable co-morbidities. Considering patients have more than comorbidities.

Table (1) Baseline serum creatinine level of the studied patients regarding their risk factors:

| Groups      | S.creat | P-value (group Vs healthy) | GFR     | P-value (group Vs healthy) |
|-------------|---------|---------------------------|---------|---------------------------|
| Diabetic    | 6.4 ±2.9| 0.235                     | 18.9 ±15.7| 0.061                    |
| Hypertension| 5.9±3.0 | 0.526                     | 23.2±15.6| 0.087                    |
| SLE         | 4.9±2.26| 0.917                     | 26.6±20.5| 0.098                    |
| Apparent healthy | 4.3±3.3 | ------                    | 32±18.3  | ----                     |

*median creat is significantly different from the apparent healthy.

Table (1) showed that creatinine of diabetic, hypertensive patients was significantly larger than the creatinine of apparent healthy patients (P-value is <0.05).

Table (1) showed that the serum creatinine level was the highest among the diabetic patients (6.4 ±2.9) followed by hypertensive patients (5.9±3.0) then, SLE patients (4.9±2.26) lastly the apparently healthy patients (4.3±3.3).

The GFR of diabetic and hypertensive patients was significantly lower than the GFR of apparent healthy patients (P-value is <0.05).
Table (2) Baseline serum hemoglobin of the studied patients regarding their risk factors:

| Groups      | HB      | P-value (group Vs healthy) | S.cal   | P-value (group Vs healthy) |
|-------------|---------|----------------------------|---------|----------------------------|
| Diabetic    | 8.3 ±2.4 | 0.736                      | 7.7 ±0.5| 0.543                      |
| Hypertension| 9.5±1.8  | 0.452                      | 7.9±1   | 0.624                      |
| SLE         | 4.4±2*   | 0.001**                    | 7.5±0.9 | 0421                       |
| Apparent healthy | 9.6±4.2 | ----                       | 8.3±0.7 | ----                       |

*mean hemoglobin is significantly different from the apparent healthy.

Table (2) showed that patient hemoglobin of SLE patients was significantly different lower than the hemoglobin of apparent healthy patients (P-value is <0.05). There was no significantly difference between the serum calcium of different patient groups (P-value is >0.05).
Figure (2) Frequency distribution of the pathological diagnosis of the studied renal biopsies
Table (3) Results of renal biopsy of the diabetic patients:

| Biopsy                                                   | Number (7) | Percent (11.11%) |
|----------------------------------------------------------|------------|-------------------|
| Acute tubular necrosis                                   | 1          | 14.3              |
| Lupus nephritis class 3                                  | 1          | 14.3              |
| Diabetic nodular glomerulosclerosis                       | 4          | 36.4              |
| Membranoproliferative GN                                 | 1          | 14.3              |
| Other pathological findings                              |            |                   |
| Interstitial fibrosis and tubular atrophy (IFTA)         |            |                   |
| -Mild                                                    | 1          | 14.1              |
| -Moderate                                                | 2          | 18.2              |
| -Marked                                                  | 4          | 36.4              |

*Data was presented as number and percent*

Table (3) showed that the most common pathologies among diabetic patients were nodular glomerulosclerosis and interstitial fibrosis and marked tubular atrophy (36.4%).

Table (4) Results of renal biopsy of the hypertensive patients:

| Biopsy                                                   | Number (29) | Percent (44.44%) |
|----------------------------------------------------------|-------------|-------------------|
| Acute tubular necrosis                                   | 4           | 13.8              |
| Lupus nephritis class III                                | 2           | 6.9               |
| Lupus nephritis class IV                                 | 3           | 10.3              |
| Focal segmental glomerulosclerosis                       | 6           | 20.6              |
| Global GS                                                | 8           | 27.6              |
| Focal necrotizing GN                                     | 2           | 6.9               |
| Membranous GN                                            | 1           | 3.4               |
| Amyloidosis                                              | 1           | 3.4               |
| TMA                                                      | 1           | 3.4               |
| No significant pathology                                 | 1           | 3.4               |
| Other pathological findings                              |             |                   |
| arterio sclerosis                                         | 8           | 27.6              |
| arteriolo- hyalnosis                                     | 1           | 3.4               |
| Interstitial nephritis                                   | 11          | 37.9              |
Table (4) Showed that the most common glomerular pathology found in hypertensive patients was Global GS (27.6%) followed by Focal segmental glomerulosclerosis (20.6%).

Table (5) Results of renal biopsy of the SLE patients:

| Biopsy                          | Number (12) | Percent (17.5%) |
|---------------------------------|-------------|-----------------|
| Lupus nephritis class III       | 4           | 33.3            |
| Lupus nephritis class IV        | 6           | 50              |
| Lupus nephritis class V         | 1           | 8.3             |
| Global GS                       | 1           | 8.3             |
| Other pathological findings     |             |                 |
| TMA                             | 3           | 25              |
| arterio sclerosis               | 4           | 33.3            |
| Interstitial nephritis          | 5           | 41.7            |
| Tubular fibrosis and Tubular atrophy: |         |                 |
| - Mild                          | 4           | 33.3            |
| - Moderate                      | 4           | 33.3            |
| - Marked                        | 3           | 25              |

Data was presented as number and percent

Table (5) Showed that Glomerular lupus nephritis grade IV (50%) was the commonest glomerular pathology followed by class III (33.3%).

Table (6) Results of renal biopsy of the apparent healthy patients (interstitium Tubules, vessels, crescent):

| Biopsy                        | Number (27) | Percent (42.9%) |
|-------------------------------|-------------|-----------------|

Data was presented as number and percent
Table (6) showed that the most common pathology was found among the apparent theal thypatients was Focal segmental glomerulosclerosis (26%) followed by Global GS (18.5%) followed by membranous nephropathy (14.8%).

Table (7) Relation between the presence of proteinuria and the glomerular pathological findings:

| Biopsy                      | SUBNEPHROTIC<3500 (n=33) | NEPHROTIC>3500 (n=30) |
|-----------------------------|--------------------------|-----------------------|
| Global glomerulosclerosis   | 10                       | 4                     |
|                             | 30.3%                    | 13.3%                 |
| FSGS                        | 5                        | 8                     |
|                             | 15.2%                    | 26.7%                 |
| Acute tubular injury        | 3                        | 1                     |
|                             | 9.1%                     | 3.3%                  |
| Membranous N                | 3                        | 2                     |

Data was presented as number and percent
Table (7) showed that there was no significant relation between the glomerular pathology and the proteinuria (P-value=0.120). The focal segmental GS was the most prevalent pathology among the nephrotic proteinuria (28.6%).

Table (8) relation between the echogenicity of the kidney detected by ultrasound and grades of interstitial fibrosis detected in some biopsies:

| Ultrasound                  | Interstitial fibrosis | Total |
|-----------------------------|-----------------------|-------|
| mild                        | Moderate | Severe |       |
|                             |          |        |       |
Data was presented as number and percent  P-value is insignificant at >0.05

Table (8) showed that there was no significant relation between the echogenicity of the kidney detected by ultrasound and grades of interstitial fibrosis detected in some biopsies (P-value=0.283).

4. Discussion:

Acute kidney injury (AKI) is increasingly prevalent in developing and developed countries and is associated with severe morbidity and mortality [6]. Recent definition of acute kidney injury mean sudden and temporary loss of kidney function depending on serum creatinine and urine outputv[7].

Understanding an individual patient’s susceptibility and risk profile is essential to prevent or ameliorate AKI through modification and avoidance of nonessential potentially nephrotoxic exposures. [8].

Renal diseases that affect the kidney itself, predominantly affecting the renal glomeruli or the renal tubules, which is associated with release of renal afferent vasoconstrictors; ischemic renal injury is the most common cause of intrinsic renal failure  [9]. Disorders of the small intrarenal vasculature can result in AKI (e.g., vasculitis, thrombotic microangiopathy [TMA], malignant hypertension, eclampsia, postpartum states, disseminated intravascular coagulation [DIC], scleroderma, all forms of acute glomerulonephritis (GN) can present as AKI, also acute inflammation and space-occupying processes of the renal interstitium (e.g., drug induced, infectious, and autoimmune disorders, leukemia, lymphoma, sarcoidosis) [10].

The three most common causes of AKI are ischaemia-reperfusion injury, systemic or localised Sepsis, surgery and (some) nephrotoxicant drugs are more prominent in hospital acquired AKI than community-acquired AKI obstruction and hypovolaemia are more prominent in community acquired AKI [11].

| Bilateral grade 1 | 14 | 5 | 4 | 23 |
|------------------|----|---|---|----|
|                  | 77.8% | 55.6% | 50.0% | 65.7% |
| Bilateral grade 2 | 4 | 2 | 3 | 9 |
|                  | 22.2% | 22.2% | 37.5% | 25.7% |
| Bilateral grade 3 | 0 | 2 | 1 | 3 |
|                  | 0.0% | 22.2% | 12.5% | 8.6% |
| Total            | 18 | 9 | 8 | 35 |
|                  | 100.0% | 100.0% | 100.0% | 100.0% |
| P-value          | 0.283 |
Acute GN can be due to a primary renal disease such as an idiopathic rapidly progressive GN or as part of a systemic disease such as systemic lupus erythematosus, bacterial endocarditis, or Wegener’s granulomatosis [12].

The introduction of renal biopsy transformed the landscape for diagnosis and management of glomerular diseases. While the clinical classifications described above provide clinicians with a working-diagnosis, renal biopsy is typically required for definitive diagnosis [13].

This report is a rare opportunity to document the causes of AKI in a selected biopsy population. However, what this study cannot answer, how many patients clinically thought to have ATN actually don’t, and have a different renal disease instead? We may know less than we think we do. In other words, how many patients have treatable forms of AKI that are being missed as a result of current biopsy practice?

This study included 63 patients that diagnosed acute kidney injury at Beni-Suef University hospital through one year duration were male 29 and female 34 with mean age 36. Our patients were divided into four groups according to their comorbidities into diabetic(11%), hypertensive(46%), SLE(19%) and patients apparent healthy (34%) and there were patients have more than comorbidities and there was no significant difference between males and females regarding the distribution of different co morbidities. The study showed that patient age of diabetic, hypertensive patients was significantly higher than the age of apparent healthy patients group as approved by [14].

Also showed that creatinine level of diabetic, hypertensive patients was significantly higher than the creatinine of apparent healthy patients as approved by [15]. The serum creatinine level was the highest among the diabetic patients (6.4 ±2.9) followed by hypertensive patients (5.9±3.0), then, SLE patients (4.9±2.26) lastly the apparently healthy patients (4.3±3.3). The GFR of diabetic and hypertensive patients was significantly lower than the GFR of apparent healthy patients group (P-value is <0.05). The study showed that patient hemoglobin of SLE patients was significantly lower than the hemoglobin of apparent healthy patients (P-value is 0.001) this may be associated haemolysis in SLE. There was no significantly difference between the serum calcium of different patient groups (P-value is >0.05). This study that no significant relation between comorbidities and echogenicity by ultrasound but grade I kidney disease was abundant in diabetic, hypertensive, SLE and apparent healthy patients with (71.4%, 62.1%, 54.5% and 85.2%; respectively). Also proteinuria (nephrotic 30 and subnephrotic 33) was the most potent presentation in our study and indication for renal biopsy with rising creatinine, there was no significant relation between the glomerular pathology and the proteinuria (P-value=0.120). The focal segmental GS was the most prevalent pathology among the nephrotic proteinuria (28.6%) meanwhile [16].

This study report that MPGN then IgA nephropathy then FSGN may be due to this study include large number through ten years (retrospective study).
regarding SLE patients lupus G.N class 4 5 (16.7%) patients in nephrotic range and 3 (9.1%) subnephrotic, Lupus nephritis class 3 2 (6.7%) nephrotic range and 3 (9.1%) subnephrotic and lupus GN class 5 1 (3.3%) in nephrotic as reported in this study [17]. On histopathological examination, the most common pathological finding in of AKI in all group (63) was focal segmental glomerulosclerosis 13 (20%) these result was approved by [18] followed by global glomerulosclerosis 9 (14%), Lupus nephritis IV 8 (13%), acute tubular injury, diabetic nodular glomerulosclerosis, Membranous N each one 4 (6%).

On the other hand these result was different from the result of [19] report that ATN the commonest pathology may be due to the Contributing factors to the development of AKI encompassed a wide spectrum. 20 patients had septicemia, Among other causes of AKI, three patients had developed post-partum AKI reported also in [20] that IgA nephropathy the commonest cause this may be due to this study include higher number including SLE patients. Other pathological findings also can be detected in this group as arteriosclerosis, Interstitial nephritis, Interstitial fibrosis and Marked tubular atrophy. In this group one patient diagnosed as SLE not known before.

In SLE group (12) Lupus nephritis class IV 6 (50%) followed by Lupus nephritis class III 4 (33%) this agreed with [25]. And [26], TMA, Interstitial nephritis and mild interstitial fibrosis and Tubular atrophy predominant.

In apparent healthy patients the predominant pathology was Focal segmental glomerulosclerosis (26%) followed by Global GS (18.5%) followed by membranous nephropathy (14.8%).

5. Conclusion:

The patient population in our study is not truly representative of the overall population who develop acute kidney injury because many patients with strong suspicion or evidence of ischemic or toxic ATN, obstructive nephropathy, acute pyelonephritis, and drug induced interstitial nephritis, do not undergo a renal biopsy and are treated on the basis of the clinical
diagnosis. Yet, our study of 63 cases carried out in a healthcare center in Beni-suef University hospital proves that renal biopsy can be an adjuvant diagnostic modality in identifying the underlying renal lesions and aiding the diagnosis and treatment of acute kidney injury. On comparing clinical and biopsy diagnoses we found that a renal biopsy is needed for accurate diagnosis of the renal lesions present in a considerable number of AKI cases and in severe yet potentially treatable causes which would aid in provision of appropriate treatment to restore and preserve renal function and decrease the risk for dialysis dependence and death in patients with AKI. Immunofluorescence (in some biopsies) and electron microscopic examination could not be done which is the lacuna of this study.

**Ethics Approval And Consent To Participate**
This study was approved by the local research ethical committee in Beni-Suef University hospital, Egypt.

**Human And Animal Rights**
All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

**Consent For Publication**
Informed consent was obtained from all patients for being included in the study.

**Availability Of Data And Materials**
The data used to support the findings of this study are included within the supplementary information file.

**Funding**
None.

**Conflict Of Interest**
The authors declare no conflict of interest, financial or otherwise.

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**Recommendation:**
1. Understanding an individual patient’s susceptibility and risk profile is essential to prevent or ameliorate AKI through modification and avoidance of nonessential potentially nephrotoxic exposures.

2. The introduction of renal biopsy transformed the landscape for diagnosis and management of glomerular diseases. While the clinical classifications described above provide clinicians with a working diagnosis, renal biopsy is typically required for definitivediagnosis.

3. RIFLE criteria were shown to be important for early AKI risk patients detection, so that, with its use, earlier diagnosis will imply more careful and less delayed therapy, which in long term will lead to reduction in this disease related morbidity and mortality.

Further studies with large number of patients should be done for more detection of pathology of renal biopsy of AKI and how to manage it.
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