



# **The Role of urinary chitinase 3 Like Protein 1 for Early Detection of Acute Kidney Injury in Adult Critically Ill Patients**

*Thesis*

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## ABSTRACT

**Background:** AKI is a common problem in ICU patients and is mostly multifactorial. Also, it is known to increase mortality, duration of ICU and hospital stay and increase the cost of care in critically ill patients. Early diagnosis in these settings help in decreasing the outcome of AKI. Multiple biomarkers have developed concentrating on early diagnosis of acute kidney injury. urinary Chitinase 3 like protein 1 is a novel biomarker studied for early detection of acute kidney injury.

**Objectives:** The current study is aimed to assess the role of urinary chitinase 3 like protein 1 (CHI3L1) as an early biomarker for detection of acute kidney injury in adult critically ill patients.

**Patients and methods:** This is a prospective cohort study that was conducted in Ain Shams University Hospital. The study included 30 adult critically ill patients with normal kidney function and they will be observed for 48 hours. The development of Acute Kidney Injury will be based on Serum Creatinine and Urine Output criteria according to KDIGO Criteria. Urine samples, for assessment of urinary CHI3L1, urine creatinine and urine CHI3L1/Cr ratio were collected under aseptic techniques at 3 times intervals ( 0hr, 12 hrs and 24hrs).

**Results:** our results showed of these 30 patients, 15 patients developed acute kidney injury using KDIGO Criteria and 15 patients had normal kidney function. Our results showed the percentage of patient who developed AKI according to KDIGO, stage I 60.0%, stage II 33.3% and stage III 6.7%. Of these patients 80% developed AKI based on serum creatinine and 20% based on serum creatinine and urine output. Our results showed that there is statistically significant difference between AKI group and non-AKI group as regards urine chitinase 3 like protein 1(CHI3L1) at 0hour, 12 hours and 24hours ( $P \leq 0.05$ ). As the higher level of urine CHI3L1 was found in AKI group which ranges from 35-135ng/ml with mean  $94 \pm 34.02$  at 0 hour, from 70-200ng/ml with mean  $126.80 \pm 43.77$  at 12 hours and from 105-200ng/ml with mean  $160.57 \pm 28.02$  which means that urine CHI3L1 level increases with AKI. Our results showed that there is statistically significant difference as regards urine CHI3L1 between non-AKI group and the 3 stages of AKI in AKI group at 0hr, 12hrs and 24hrs ( $P \leq 0.05$ ).

**Conclusion:** Urinary chitinase 3 like protein 1 is a highly sensitive early marker in prediction of acute kidney injury in adult critically ill patients.

**Key Words:** acute kidney injury, biomarkers, chitinase 3 like protein 1, critically ill patients.



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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لَسْبَحَانَكَ لَا عِلْمَ لَنَا  
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ  
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢

## Contents

| Subjects                                                                   | Page |
|----------------------------------------------------------------------------|------|
| List of abbreviations.....                                                 | II   |
| List of figures.....                                                       | VII  |
| List of tables.....                                                        | IX   |
| • <b>Introduction</b> .....                                                | 1    |
| • <b>Aim of the work</b> .....                                             | 4    |
| • <b>Review of Literature</b>                                              |      |
| ♦ <b>Chapter (1): Acute Kidney Injury</b> .....                            | 5    |
| ♦ <b>Chapter (2): Acute Kidney Injury in Critically ill patients</b> ..... | 29   |
| ♦ <b>Chapter (3): Novel Biomarkers in Acute Kidney Injury</b> .....        | 48   |
| ♦ <b>Chapter (4): Chitinase 3 Like Protein 1</b> .....                     | 63   |
| • <b>Patients and Methods</b> .....                                        | 74   |
| • <b>Results</b> .....                                                     | 85   |
| • <b>Discussion</b> .....                                                  | 109  |
| • <b>Summary and Conclusion</b> .....                                      | 117  |
| • <b>Recommendations</b> .....                                             | 121  |
| • <b>References</b> .....                                                  | 122  |
| • <b>Arabic Summary</b>                                                    |      |

## **List of Abbreviations**

|                |   |                                                              |
|----------------|---|--------------------------------------------------------------|
| <b>ACEIs</b>   | : | Angiotensin-converting enzyme inhibitor.                     |
| <b>ACS</b>     | : | Acute coronary syndrome                                      |
| <b>AHF</b>     | : | Acute heart failure.                                         |
| <b>AIN</b>     | : | Acute interstitial nephritis.                                |
| <b>AKI</b>     | : | Acute kidney injury.                                         |
| <b>AKI-EPI</b> | : | Acute kidney injury-epidemiologic prospective investigation. |
| <b>AKIN</b>    | : | Acute kidney injury network.                                 |
| <b>AKS</b>     |   | Acute kidney stress.                                         |
| <b>AMcase</b>  | : | Acidic mammalian chitinase.                                  |
| <b>APACHE</b>  | : | Acute physiology and chronic health evaluation.              |
| <b>E</b>       |   |                                                              |
| <b>ARBs</b>    | : | Angiotensin receptor blockers.                               |
| <b>ARF</b>     | : | Acute renal failure.                                         |
| <b>ATN</b>     | : | Acute tubular necrosis.                                      |
| <b>AUC</b>     | : | Area under a curve.                                          |
| <b>BMI</b>     | : | Body mass index.                                             |
| <b>BRP-39</b>  | : | Breast regression protein 39.                                |
| <b>CAD</b>     | : | Coronary artery disease.                                     |

## *List of Abbreviations*

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|                |   |                                                             |
|----------------|---|-------------------------------------------------------------|
| <b>CBC</b>     | : | Complete blood picture.                                     |
| <b>CD</b>      | : | Cluster of differentiation.                                 |
| <b>CHF</b>     | : | Congestive heart failure.                                   |
| <b>CHI3L1</b>  | : | Chitinase 3 like protein 1                                  |
| <b>CI</b>      | : | Confidence interval.                                        |
| <b>CI-AKI</b>  | : | Contrast induced acute kidney injury                        |
| <b>CKD</b>     | : | Chronic kidney disease.                                     |
| <b>CKD-EPI</b> | : | Chronic kidney disease-epidemiology collaborative equation. |
| <b>CLP</b>     | : | Chitinase like protein.                                     |
| <b>CNI</b> s   | : | Calcineurin inhibitors.                                     |
| <b>COPD</b>    | : | Chronic obstructive pulmonary disease.                      |
| <b>CBP</b>     | : | Cardio-pulmonary bypass.                                    |
| <b>CRBSI</b>   | : | Catheter related bloodstream infection.                     |
| <b>CR.</b>     | : | Creatinine.                                                 |
| <b>CRP</b>     | : | C-reactive protein.                                         |
| <b>CRRT</b>    | : | Continuous renal replacement therapy.                       |
| <b>CRS</b>     | : | Cardio-renal syndrome.                                      |
| <b>CSA-AKI</b> | : | Cardiac surgery associated acute kidney injury.             |
| <b>CVP</b>     | : | Central venous pressure.                                    |
| <b>CVVH</b>    | : | Continuous veno-venous hemofiltration                       |

## *List of Abbreviations*

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|                        |   |                                     |
|------------------------|---|-------------------------------------|
| <b>DCL</b>             | : | Distal convoluted tubules           |
| <b>DGF</b>             | : | Delayed graft function.             |
| <b>DM</b>              | : | Diabetes mellitus.                  |
| <b>ECM</b>             | : | Extracellular matrix.               |
| <b>EDTA</b>            | : | Ethylene diamine tetra-acetate.     |
| <b>ELISA</b>           | : | Enzyme-linked immune-sorbent essay. |
| <b>ESKD</b>            | : | End stage kidney disease.           |
| <b>ESRD</b>            | : | End stage renal disease.            |
| <b>FENa</b>            | : | Fractional excretion of sodium.     |
| <b>FEUr</b>            | : | Fractional excretion of urea.       |
| <b>FiO<sub>2</sub></b> | : | Fraction of inspired oxygen.        |
| <b>GBM</b>             | : | Glioblastoma.                       |
| <b>GFR</b>             | : | Glomerular filtration rate.         |
| <b>GIT</b>             | : | Gastrointestinal tract.             |
| <b>GLc-NAc</b>         | : | N-49 acetyl glucosamine.            |
| <b>GN</b>              | : | Glomerulonephritis.                 |
| <b>HB</b>              | : | Hemoglobin.                         |
| <b>HcGP</b>            | : | Human cartilage glycoprotein.       |
| <b>HCV</b>             | : | Hepatitis C virus.                  |
| <b>HF</b>              | : | Heart failure.                      |

## *List of Abbreviations*

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|                |   |                                              |
|----------------|---|----------------------------------------------|
| <b>HRS</b>     | : | Hepato-renal syndrome.                       |
| <b>IABP</b>    | : | Intra-aortic balloon pressure.               |
| <b>IAH</b>     | : | Intra-abdominal hypertension.                |
| <b>IAP</b>     | : | Intra-abdominal pressure.                    |
| <b>IBD</b>     | : | Inflammatory bowel disease.                  |
| <b>ICU</b>     | : | Intensive care unit.                         |
| <b>IG</b>      | : | Immunoglobulin.                              |
| <b>IGF-1</b>   | : | Insulin like growth factor 1.                |
| <b>IGFBP-7</b> | : | Insulin like growth factor binding protein7. |
| <b>IHD</b>     | : | Ischemic heart disease.                      |
| <b>IL</b>      | : | Interleukin.                                 |
| <b>I/R</b>     | : | Ischemia- reperfusion                        |
| <b>KDIGO</b>   | : | Kidney disease improving global outcomes.    |
| <b>KIM-1</b>   | : | Kidney injury molecule 1                     |
| <b>LBP</b>     | : | Liver binding protein.                       |
| <b>L-FABP</b>  | : | L-type fatty acid binding protein.           |
| <b>LODS</b>    | : | Logistic organ dysfunction system.           |
| <b>LOS</b>     | : | Length of stay.                              |
| <b>MAP</b>     | : | Mean arterial pressure.                      |
| <b>MMP:</b>    | : | Matrix metalloproteinase.<br>.....           |

## *List of Abbreviations*

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|                        |                                                     |
|------------------------|-----------------------------------------------------|
| <b>MODS</b>            | : Multiple organ dysfunction system.                |
| <b>MPM</b>             | : Mortality predictive model.                       |
| <b>NAC</b>             | : N-acetyl cysteine.                                |
| <b>NAG</b>             | : N-acetyl B-d glucosamine.                         |
| <b>NGAL</b>            | : Neutrophil gelatinase associated lipoprotein.     |
| <b>NSAIDs</b>          | : Non-steroidal anti-inflammatory drugs.            |
| <b>NSBBs</b>           | : Non-selective beta blockers.                      |
| <b>PaO<sub>2</sub></b> | : Partial pressure of oxygen.                       |
| <b>PD</b>              | : Peritoneal dialysis.                              |
| <b>PIRRT</b>           | : Prolonged intermittent renal replacement therapy. |
| <b>PPI</b>             | : Proton pump inhibitors.                           |
| <b>PPV</b>             | : Positive pressure ventilation.                    |
| <b>RA</b>              | : Rheumatoid arthritis.                             |
| <b>RAAS</b>            | : Renin-angiotensin aldosterone system              |
| <b>RCT</b>             | : Randomized control trial.                         |
| <b>RIFLE</b>           | : Risk, Injury, Failure, Loss, End-stage.           |
| <b>RRT</b>             | : Renal replacement therapy.                        |
| <b>SA-AKI</b>          | : Sepsis associated acute kidney injury.            |
| <b>SAPS</b>            | : Simplified acute physiology score.                |
| <b>SIRS</b>            | : Systemic inflammatory response syndrome.          |
| <b>SLED</b>            | : Sustained low efficiency dialysis.                |

## *List of Abbreviations*

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|               |                                                    |
|---------------|----------------------------------------------------|
| <b>SOFA</b>   | : Sequential organ failure score.                  |
| <b>TECs</b>   | : Tubular epithelial cells.                        |
| <b>Th-2</b>   | : Type 2 T helper cells.                           |
| <b>TIMP-2</b> | : Tissue inhibitor metalloproteinase 2.            |
| <b>TINU</b>   | : Tubulo-interstitial nephritis and uveitis.       |
| <b>TIPS</b>   | : Trans-jugular intra-hepatic portosystemic shunt. |
| <b>TLRs</b>   | : Toll like receptors.                             |
| <b>UA</b>     | : Urine analysis.                                  |
| <b>UO/UOP</b> | : Urine output.                                    |
| <b>VSMCs</b>  | : Vascular smooth muscle cells.                    |
| <b>WBCs</b>   | : White blood cells.                               |

## List of Figures

| <b><u>No.</u></b> | <b><u>Figure</u></b>                                                            | <b><u>Page</u></b> |
|-------------------|---------------------------------------------------------------------------------|--------------------|
| <b><u>1</u></b>   | The RIFLE Criteria for AKI.                                                     | <b>6</b>           |
| <b><u>2</u></b>   | APACHE II severity of disease classification.                                   | <b>31</b>          |
| <b><u>3</u></b>   | SAPS II score.                                                                  | <b>32</b>          |
| <b><u>4</u></b>   | SOFA score.                                                                     | <b>34</b>          |
| <b><u>5</u></b>   | Summary of pathophysiologic interaction between sepsis and acute kidney injury. | <b>38</b>          |
| <b><u>6</u></b>   | Potential mechanism and specificity of urinary biomarkers of kidney damage.     | <b>50</b>          |
| <b><u>7</u></b>   | YKL-40 regulates the pathogenesis of cancer and inflammatory disorder.          | <b>73</b>          |
| <b><u>8</u></b>   | Comparison between the two studied groups according to urine CHI3L1.            | <b>97</b>          |
| <b><u>9</u></b>   | Comparison between the two studied groups according to urine CHI3L1/Cr. ratio.  | <b>99</b>          |
| <b><u>10</u></b>  | ROC Curve for urine CHI3L1 to predict AKI vs non-AKI.                           | <b>101</b>         |
| <b><u>11</u></b>  | ROC Curve for urine CHI3L1/Cr. ratio to predict AKI vs non-AKI.                 | <b>103</b>         |

## **List of Tables**

| <b><u>No.</u></b> | <b><u>Table</u></b>                                                                 | <b><u>Page</u></b> |
|-------------------|-------------------------------------------------------------------------------------|--------------------|
| <b><u>1</u></b>   | AKIN Classification of Acute Kidney Injury                                          | <b>7</b>           |
| <b><u>2</u></b>   | KDIGO Staging of Acute Kidney Injury                                                | <b>8</b>           |
| <b><u>3</u></b>   | Risk factors of Acute Kidney injury                                                 | <b>11</b>          |
| <b><u>4</u></b>   | Urinary tests in Acute Kidney Injury                                                | <b>19</b>          |
| <b><u>5</u></b>   | Comparison between the two studied groups according to demographic data             | <b>86</b>          |
| <b><u>6</u></b>   | Comparison between the two studied groups according to GFR                          | <b>87</b>          |
| <b><u>7</u></b>   | Comparison between the two studied groups according to risk factors                 | <b>88</b>          |
| <b><u>8</u></b>   | Comparison between the two studied groups according to SOFA score                   | <b>89</b>          |
| <b><u>9</u></b>   | Comparison between the two studied groups according to CBC                          | <b>90</b>          |
| <b><u>10</u></b>  | Comparison between the two studied groups according to CRP                          | <b>91</b>          |
| <b><u>11</u></b>  | Comparison between the two studied groups according to urine analysis               | <b>91</b>          |
| <b><u>12</u></b>  | Comparison between the two studied groups according to serum creatinine             | <b>92</b>          |
| <b><u>13</u></b>  | Comparison between the two studied groups according to urine output (uop)           | <b>93</b>          |
| <b><u>14</u></b>  | Distribution between the studied cases according to stage and progress in AKI group | <b>94</b>          |
| <b><u>15</u></b>  | Relation between AKI stage and progress                                             | <b>95</b>          |

## *List of Figures*

---

| <b><u>No.</u></b> | <b><u>Table</u></b>                                                                        | <b><u>Page</u></b> |
|-------------------|--------------------------------------------------------------------------------------------|--------------------|
| <b><u>16</u></b>  | Comparison between the two studied groups according to urine CHI3L1 ng/ml                  | <b>96</b>          |
| <b><u>17</u></b>  | Comparison between the two studied groups according to urine CHI3L1/Cr. ratio ng/mg        | <b>98</b>          |
| <b><u>18</u></b>  | Comparison between the two studied groups according to mortality                           | <b>100</b>         |
| <b><u>19</u></b>  | Agreement (sensitivity & specificity) for urine CHI3L1 to predict AKI vs non-AKI           | <b>102</b>         |
| <b><u>20</u></b>  | Agreement (sensitivity & specificity) for urine CHI3L1/Cr. ratio to predict AKI vs non-AKI | <b>104</b>         |
| <b><u>21a</u></b> | Relation between AKI stage and urine CHI3L1 in AKI group                                   | <b>105</b>         |
| <b><u>21b</u></b> | Relation between AKI stage and urine CHI3L1 in total sample                                | <b>106</b>         |
| <b><u>22a</u></b> | Relation between AKI stage and urine CHI3L1/Cr. ratio in AKI group                         | <b>107</b>         |
| <b><u>22b</u></b> | Relation between AKI stage and urine CHI3L1/Cr. ratio in total sample                      | <b>108</b>         |

## Introduction

Acute kidney injury (AKI) is a well-recognized clinical condition that occurs in critically ill patients. Its incidence in all hospitalized patients is about 1-7% and about 30-50% in intensive care units **(Herget-Rosenthal S et al., 2012)**.

Despite of the advancement made for understanding the pathophysiology and causal processes of acute kidney injury and the developments in critical care medicine, acute kidney injury (AKI) mortality rates are still high and account for more than 50% in ICU. Also, about 20% will develop chronic kidney disease (CKD) and end stage renal disease requiring RRT **(Herget-Rosenthal S et al., 2012)**.

The Acute Dialysis Quality Initiative first defined acute kidney injury with RIFLE criteria in 2004. Then Acute Kidney Injury Network (AKIN) put staging for acute kidney injury. Then, Kidney Disease Improving Global Outcomes (KDIGO) put a recent guideline update. Acute kidney injury is now defined as an increase in serum creatinine of 0.3mg/dl or more within 48hours of observation or 1.5 times baseline or greater, which is known or presumed to have occurred within 7 days, or a reduction in urine volume below 0.5 ml/kg/h for 6 hours **(KDIGO Working Group, 2012)**.