# Audit of adult patients with renal dysfunction presenting to the Charlotte Maxeke Johannesburg Academic Hospital Emergency Department

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**1477847**

A research report submitted to the Faculty of Health of the University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in Emergency Medicine.

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**DECLARATION**

I, John Masina, hereby declare that this research report is my own work and has not been submitted or presented for any other degree or professional qualification at this or any other Institute. This research was undertaken in the Division of Emergency Medicine, University of the Witwatersrand, Johannesburg.

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## CONFLICT OF INTEREST

The author hereby certifies that this submission is not under publication consideration elsewhere and that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

## AUTHOR CONTRIBUTIONS

John Masina – Primary author, study design, data collection, data analysis, manuscript write up and approval of the final manuscript.

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Muhammed Moolla– Assisted with study design, data analysis, interpretation of results, preparation of manuscript, approval of the final manuscript.

**SUBMISSION LETTER TO THE EDITOR**

**Dear Editor – The Emergency Medicine Journal.**

Thank you for considering our article entitled: Audit of adult patients presenting with renal dysfunction to the CharlotteMaxeke Johannesburg Academic Hospital Emergency Department.

Renal dysfunction is a potentially life-threatening condition that is commonly encountered in the Emergency Department (ED). Specific data on the epidemiology of renal dysfunction in the ED scant.In view of the increase in the prevalence of Human Immunodeficiency Virus (HIV), diabetes mellitus (DM), cardiac disease, hypertension (HTN) and sepsis in South Africa, it is suspected that the prevalence of renal dysfunction would be relatively high in the ED. This coupled with burden of care of patients with renal dysfunction makes the study appealing to readers.We are certain that this article will appeal to the leadership of the "**Emergency Medicine Journal"**

**Presentation with abnormal renal function to a tertiary level Emergency Department**


## ABSTRACT

**Introduction**: Renal dysfunction is a potentially life-threatening condition that is commonly encountered in the Emergency Department (ED). This study aimed at describing the demographics, clinical characteristics, ultrasonographic features and disposition of patients with renal dysfunction presenting to an academic hospital ED.

**Methods**: Medical records of patients presenting to the ED with renal dysfunction were prospectively reviewed over a 6-month period (July – December 2017). Descriptive analysis of the data was performed.

**Results**: Of the 18 349 ED presentations over the study period, 219 (2.9%) patients were identified with renal dysfunction with 192 of these being enrolled in the study. The mean age of study subjects was 50.5 years (SD 16.5 years). Majority of patients 159 (82.8%) were of African race. More patients (n=90, 46.9%) presented with acute kidney injury compared to chronic kidney disease (n=53, 27.6%) and acute on chronic kidney disease (n=49, 25.5%). Hypertension was the commonest co-morbidity (n=95, 49.5%) followed by HIV (n=72, 37.5%) with sepsis being the commonest precipitating factor (n=66, 34%).

**Conclusion**: ED clinicians should adopt a low threshold to screen patients with hypertension, HIV, sepsis and other risk factors for the presence of underlying renal dysfunction.



## KEY WORDS

renal dysfunction, acute kidney injury, chronic kidney disease, emergency department

## INTRODUCTION

Abnormal renal function is frequently encountered in the emergency department (ED) and may be associated with significant morbidity and mortality (1). Presentation with abnormal renal function may be categorised into i) acute kidney injury (AKI) (2), ii) chronic kidney disease (CKD) (3) and iii) acute on chronic kidney disease (AOCKD) (4). Estimates of the global prevalence ranges from <1% to 66% for AKI (5) and 11% to 13% for CKD (6). Specific data on the epidemiology of renal dysfunction presentation to the ED is scant.

AKI can be defined as an abrupt deterioration in kidney function that is potentially reversible. The Kidney Disease: Improving Global Outcomes (KDIGO) AKI working group have defined 3 stages of AKI severity based either on the degree of acute rise in serum creatinine or on a time-based deterioration in the urine output (2).There are notable differences and regional discrepancies between developed and developing countries with regards to the incidence and risk factors for AKI. In developed countries AKI, is a hospital acquired complication arising from a multitude of factors, affecting predominantly older critically ill patients. Whereas, in developing countries sepsis, malaria, diarrheal diseases with dehydration and herbal medications are more common causes of AKI (7,8).

Comparatively, CKD is described as an abnormality of kidney structure or function that persists for >3 months. The KDIGO CKD working group has classified CKD based on the underlying aetiology, degree of deterioration in glomerular filtration rate (GFR) and severity of albuminuria (3). Risk factors for CKD include diabetes mellitus, hypertension, non-steroidal inflammatory drugs (NSAIDs), other nephrotoxic drugs, advanced age, HIV and cardiac failure (9). AOCKD is more common in patients with underlying CKD (4), with the adjusted odds ratio for developing AKI being significantly higher in patients with a lower GFR (10).

With the increasing prevalence of HIV infection, diabetes mellitus, cardiac diseases, hypertension and sepsis in South Africa it is suspected that the prevalence of renal dysfunction would be relatively higher than 18% (11,12). Most studies on renal dysfunction have been conducted in intensive care unit (ICU) and in-hospital patient settings (13). No data currently exist on the incidence and prevalence of renal dysfunction at EDs in South Africa or internationally. According to our knowledge, this is the first study to profile renal dysfunction in the ED setting. We aimed to determine the demographic characteristics, presenting features, renal ultrasonographic findings, initiation of renal replacement therapy, disposition (transfer of patients from the ED to different departments within the hospital) and in-hospital mortality of patients presenting to our emergency department with abnormal renal function.

**METHODS**

Medical records of consecutive adult patients (>18 years) that presented to the Charlotte Maxeke Johannesburg Academic Hospital Emergency Department (CMJAH ED) from 01 July 2017 to 31 December 2017 with abnormal renal function were prospectively reviewed. CMJAH is a tertiary care public hospital that is affiliated to the University of Witwatersrand and services a major portion of the Johannesburg inner-city region, as well as surrounding suburban areas.

For the purposes of this study, renal dysfunction was defined as the presence of either AKI, CKD or AOCKD. Normal serum creatinine and GFR for age was calculated as per the modification of diet in renal disease (MDRD) formula. Categorisation of subjects into the AKI and CKD groups were based on the KDIGO clinical practice guidelines definitions (3). The following subjects were placed in the AOCKD group: i) subjects with underlying CKD

who displayed a >10% fluctuation in their serum creatinine level during their hospital stay and had not received renal replacement therapy and ii) subjects that had received renal replacement therapy and were deemed to have presented with acute on chronic kidney disease by the attending nephrologist.

Before initiation of data collection, the primary investigator underwent informal training on the methodology and principles of data abstraction from medical records. After ethical clearance to commence the study (University of Witwatersrand certificate no. M 170716) was obtained; the principle investigator daily reviewed the laboratory results of all patients attending the ED over the study period to identify potential study subjects. Subjects with abnormal serum creatinine / GFR were identified and approached for study participation. Relevant data was abstracted from the medical records of consenting subjects and entered into data collection sheets. Patients whose medical records could not be accessed and subjects not consenting to study participation were excluded from the study. Patient records were followed-up until data collection was completed. The process of data collection was monitored periodically by the study supervisors. Data collected included demographic data, clinical presentation, risk factors/ co-morbidities, laboratory results, ultrasonographic findings and patient disposition information.

To assess for inter-rater reliability, an independent individual experienced in the methods of data abstraction but blinded to the study aim and objectives re-abstracted data from a sample of 20 randomly selected medical records and compared these to the ones obtained by the primary investigator. There was no difference in the two data sets collected.

Patient confidentially was strictly adhered to at all times. Patient's identifying information was blocked out and replaced with a unique code for each patient. Reporting of study

findings was in conformance with STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (14).

Data was analysed using STATA 14 (Stata Corp.2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP). Analysis of the data was conducted using summary descriptive statistics. Categorical variables (gender, race, HIV status, etc) are described and illustrated by making use of frequency and percentage tables/ graphs whereas, continues data (age, renal functions, CD4 count, etc) are described using mean, standard deviation, median and inter-quartile range.

**RESULTS**

There were 18 349 presentations to the ED over the study period, with 10642 (58.0%) patients that were triaged in to the ED. The serum urea and creatinine levels were deranged in 219 (2.1%) of the 7 449 (70.0%) patients in whom this was measured, giving an incidence of 2.1% of all ED presentations. A total of 192 (87.7%) subjects were included in the final study sample (figure 1). Of these 108 (56.3%) were male. The overall mean age of study subjects was 50.5years, SD 16.5 (Range 19 – 91). AKI and CKD accounted for 90 (46.9%) and 53 (27.6%) presentations respectively, whereas AOCKD accounted for 49 (25.5%) cases. Majority of subjects were of Black race (n= 159, 82.8%). Fatigue was the commonest presenting complaint in 46.4% (n=89) of subjects overall. Of the 139 (72.4%) subjects in whom urine dipsticks analysis was performed, proteinuria was demonstrated in 108 (56.3%) subjects. The presence of blood, leukocytes and nitrites was demonstrated in 96 (50.0%), 38 (19.8%) and 26 (13.5%) subjects respectively. HIV status was only documented in 115 (59.9%) subjects, of which 72 (62.6%) were positive. Patients were admitted to the renal ward (n=109; 56.8%), general ward (n=62; 32.3%) and intensive care unit/ high care unit (n=11; 5.7%). Two subjects (1.0%) were stepped down to other smaller health facilities,

whilst 8 (4.2%) were discharged home from the ED. Seventy-six (39.6%) subjects received dialysis during their hospital stay. The in-hospital mortality was 30.7% (n=59). None of these patients died in the ED. Details of the above are described in tables 1. The mean age (SD) of study subjects in each group and the entire cohort is described in table 2

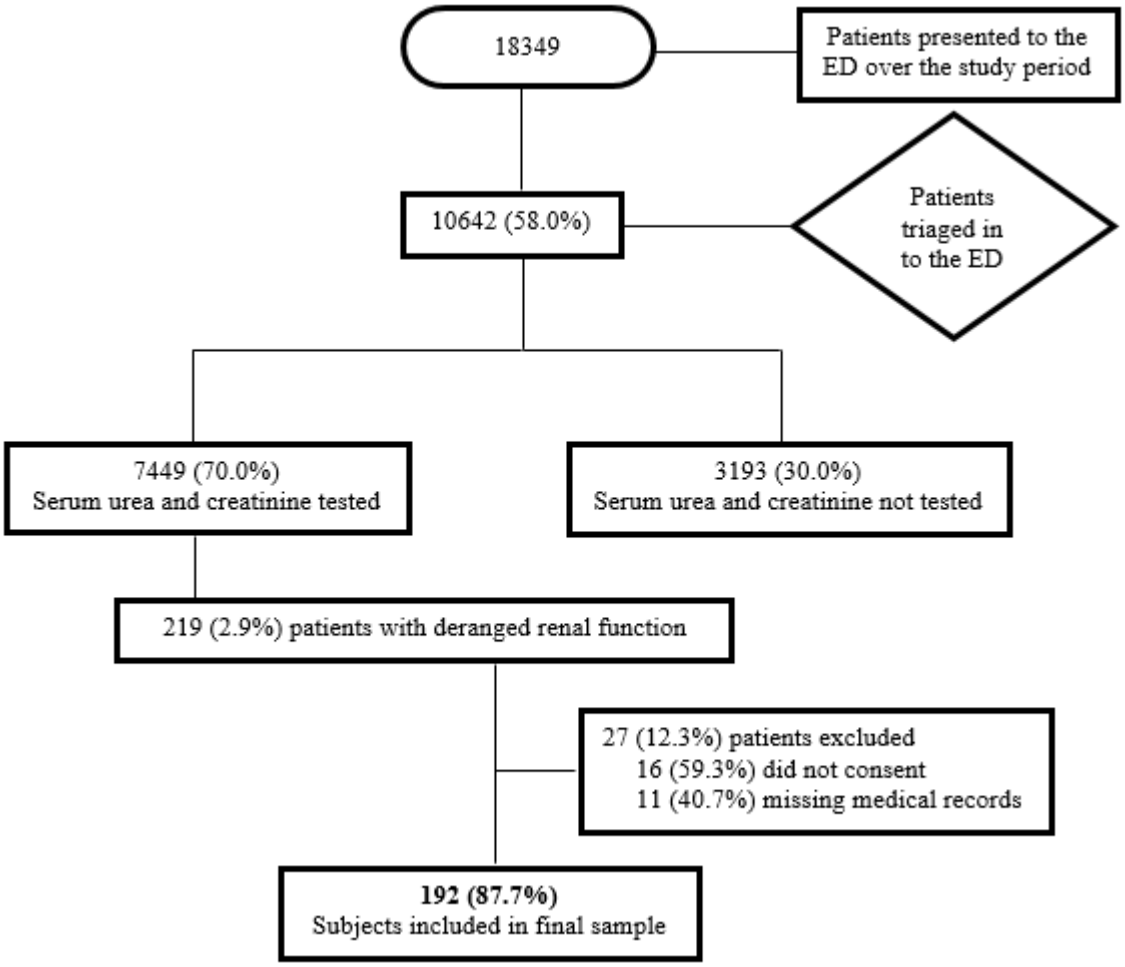



**Figure 1: Exclusion and final sample for analysis**

**Table1: Demographic details of subjects with renal dysfunction**

| | AKI (n=90) | CKD (n=53) | AOCKD (n=49) | Entire Cohort (n=192) |
|---|---|---|---|---|
| **Gender** | | | | |
| Male | 58 (64.4) | 25 (47.2) | 25 (51.0) | 108 (56.3) |
| Female | 32 (35.6) | 28 (52.8) | 24 (49.0) | 84 (43.7) |
| **Age in years** | | | | |
| <40 | 25 (27.8) | 16 (30.2) | 19 (38.8) | 60 (31.3) |
| 40 – 54 | 25 (27.8) | 14 (26.4) | 15 (30.6) | 54 (28.1) |
| 55 – 69 | 22 (24.4) | 20 (37.8) | 5 (10.2) | 47 (24.5) |
| ≥70 | 18 (20.0) | 3 (5.6) | 10 (20.4) | 31 (16.1) |
| **Race** | | | | |
| Black | 75 (83.3) | 25 (47.2) | 39 (80.0) | 139 (72.4) |
| White | 13 (14.4) | 28 (52.8) | 9 (18.4) | 50 (26.0) |
| Asian | 2 (2.2) | 0 (0.0) | 1 (2.0) | 3 (1.6) |
| **Clinical features** | | | | |
| Nausea | 36 (40.0) | 14 (26.4) | 13 (26.5) | 63 (32.8) |
| Oedema | 16 (17.8) | 24 (45.3) | 28 (57.1) | 68 (35.4) |
| Dyspnoea | 44 (48.9) | 11 (20.8) | 12 (24.5) | 67 (33.3) |
| Fatigue | 33 (36.7) | 29 (54.7) | 27 (55.1) | 89 (46.4) |
| Confusion | 24 (26.7) | 4 (7.5) | 12 (24.5 | 40 (20.8) |
| **Urine dipstick findings** | | | | |
| Proteinuria | 39 (43.3) | 36 (67.9) | 33 (67.3) | 108 (56.3) |
| Haematuria | 40 (44.4) | 28 (52.8) | 28 (57.1) | 96 (50.0) |
| Leukocytes | 17 (18.9) | 11 (20.8) | 10 (20.4) | 38 (19.8) |
| Nitrites | 10 (11.1) | 8 (15.1) | 8 (16.3) | 26 (13.5) |
| No abnormalities | 14 (15.6) | 2 (3.8) | 4 (8.2) | 20 (10.4) |
| Urinalysis not done | 28 (31.1) | 14 (26.4) | 11 (22.4) | 53 (27.6) |
| **HIV status** | | | | |
| Positive | 29 (32.2) | 22 (41.5) | 21 (42.9) | 72 (37.5) |
| Negative | 15 (16.7) | 19 (35.8) | 9 (18.4) | 43 (22.4) |
| Unknown | 46 (51.1) | 12 (22.6) | 19 (38.8) | 77 (40.1) |
| **Disposition From the ED** | | | | |
| Intensive care unit | 5 (5.5) | 3 (6.7) | 3 (6.1) | 11 (5.7) |
| General ward | 52 (57.8) | 5 (9.4) | 5 (10.3) | 62 (32.3) |
| Renal ward | 26 (28.9) | 44 (83.0) | 39 (79.6) | 109 (56.8) |
| Step down facility | 1 (1.1) | 0 (0) | 1 (2.0) | 2 (1.0) |
| Discharge home | 6 (6.7) | 1 (1.9) | 1 (2.0) | 8 (4.2) |
| **Renal Replacement Therapy** | | | | |
| Dialysed | 44 (48.9) | 9 (17.0) | 23 (46.9) | 76 (39.6) |
| Not dialysed | 46 (51.1) | 44 (83.0) | 26 (53.1) | 116 (60.4) |
| **Mortality** | | | | |
| Died | 32 (35.6) | 12 (22.6) | 15 (30.6) | 59 (30.7) |
| Survived to hospital discharge | 58 (64.4) | 41 (77.4) | 34 (69.4) | 133 (69.3) |

**Table 2: Mean (SD) age of study subjects in each group and the entire cohort**

| | AKI (n=90) | | CKD (n=53) | | AOCKD (n=49) | | Entire cohort (n=192) | |
|---|---|---|---|---|---|---|---|---|
| | **Male (n=58)** | **Female (n=32)** | **Male (n=25)** | **Female (n=28)** | **Male (n=25)** | **Female (n=24)** | **Male (n=108)** | **Female (n=84)** |
| Mean age in years (SD) | 50.3 (16.5) | 50.4 (16.4) | 49.5 (16.3) | 50.5 (16.5) | 50.3 (16.4) | 50.4 (16.4) | 50.4 (16.5) | 50.5 (16.5) |
| Overall mean age (SD) | 50.3 (16.4) | | 50.1 (16.5) | | 50.4 (16.4) | | 50.5 (16.5) | |

SD = Standard Deviation

Table 3 describes the aetiology and risk factors for renal dysfunction amongst study patients. Sepsis was the commonest precipitating factor for AKI (n=38, 42.2%) and AOCKD (n=18, 36.7%). Urosepsis was the commonest source of sepsis in both the AKI group (n=18, 47.4%) and the AOCKD group (n=9, 50.0%). Chronic hypertension (n=12, 22.6%), diabetes mellitus (n=11, 20.8%) and HIV associated nephropathy (n=8, 15.1%) were the commonest aetiologies in the CKD group.

Table 4 summarizes the spectrum of clinical and laboratory findings amongst study subjects. Of the 72 HIV positive subjects, the CD4 cell count and HIV viral load was measured in 60 (83.3%) and 56 (77%) subjects respectively. The median CD4 cell count was 168 (IQR 10 – 1178) cells/μL whilst the median viral load was 160 (IQR 20 – 24900) copies/mL.

**Table 3: Aetiology and risk factors for renal dysfunction amongst study patients**

| **AKI** | **n=90** |
|---|---|
| Sepsis | 38 (42.2) |
| Urosepsis | 18 (47.4) |
| Abdominal sepsis | 3 (7.9) |
| Pneumonia | 9 (23.7) |
| Skin and soft tissue infections | 7 (18.4) |
| Infective endocarditis | 1 (2.6) |
| [1]Urinary tract obstruction | 25 (27.8) |
| Gastroenteritis | 12 (13.3) |
| Herbal medication | 9 (10.0) |
| [2]Other | 6 (6.7) |
| **CKD** | **n=53** |
| Chronic hypertension | 12 (22.6) |
| Diabetes mellitus | 11 (20.8) |
| HIV associated nephropathy | 8 (15.1) |
| Chronic hypertension and diabetes mellitus | 7 (13.2) |
| Non-steroidal anti-inflammatory drugs | 6 (11.3) |
| Idiopathic | 5 (9.4) |
| [3]Other | 4 (7.5) |
| **AOCKD** | **n=49** |
| Sepsis | 18 (36.7) |
| Urosepsis | 9 (50.0) |
| Pneumonia | 4 (22.2) |
| Skin and soft tissue infections | 3 (16.7) |
| Bacteraemia | 2 (11.1) |
| Congestive cardiac failure | 15 (30.6) |
| [4]Urinary tract obstruction | 8 (16.3) |
| Gastroenteritis | 5 (10.2) |
| Herbal medication | 3 (6.1) |

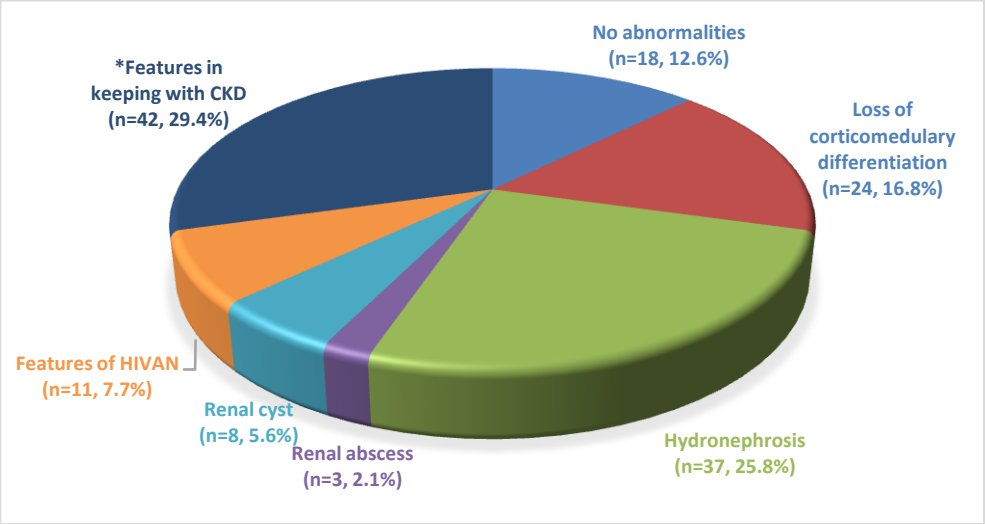
[1]carcinoma of the cervix (n=8, 32.0%), urolithiasis (n=7, 28.0%), prostate carcinoma (n=5, 20.0%), urethral stricture (n=3, 12.0%), ovarian cancer (n=2, 8.0%)
[2]one case each of acute pancreatitis, upper gastrointestinal bleed, perforated peptic ulcer, intestinal intussusception, malaria and recent surgery
[3]one case each of renal cell carcinoma, Alport syndrome, systemic lupus erythematosus and rapidly progressing glomerular nephritis
[4]prostate carcinoma (n=4, 50.0%), benign prostate enlargement (n=3, 37.5%), carcinoma of the bladder (n=1, 12.5%)

**Table 4: Median clinical and laboratory findings amongst study subjects**

| | Median (IQR) | Median (SD) | | |
|---|---|---|---|---|
| | | AKI (n=90) | CKD (n=53) | AOCKD (n=49) |
| **SBP (mmHg)** | 132 (112-179) | 131 (31.8) | 134 (32.3) | 130 (32.7) |
| **DBP (mmHg)** | 80 (66.5-94) | 79.5 (22.2) | 82 (23.3) | 80 (22.6) |
| **RR (breaths/min)** | 18 (16-20) | 18 (4.1) | 18 (4.2) | 18 (4.2) |
| **Potassium (mmol/L)** | 4.9 (4.1-5.8) | 4.9 (1.3) | 4.8 (1.3) | 4.8 (1.3) |
| **Bicarbonate (mmol/L)** | 16 (10-20) | 15 (5.6) | 16 (5.7) | 16 (5.6) |
| **Urea (mmol/L)** | 22.4 (12.5-39.4) | 22.4 (22.0) | 22.4 (22.0) | 22.4 (22.1) |
| **Creatinine (mmol/L)** | 342.5 (176.5-921.5) | 342 (810) | 349 (810) | 336 (819) |
| **eGFR (ml/min/1.73m²)** | 14 (5-31.5) | 14 (16.7) | 14 (16.6) | 14 (16.6) |
| **CRP (mmol/L)** | 61 (15-202.5) | 60 (116.3) | 62 (116.1) | 60 (116.3) |
| **WCC ($\times 10^9$ /L)** | 9 (6.2-13.9) | 8.9 (135.6) | 8.9 (135.6) | 8.9 (135.9) |
| **Haemoglobin (g/dL)** | 9.4 (7.2-12.5) | 9.5 (3.6) | 9.4 (3.5) | 9.5 (3.5) |
| **CD4 count, cells/µL (n=60)** | 168 (59 – 353) | 21 (35.0) | 19 (31.7) | 20 (33.3) |
| **<100** | | 6 (28.6) | 4 (21.1) | 10 (50.0) |
| **100 – 250** | | 5 (23.8) | 9 (47.4) | 3 (15.0) |
| **>250** | | 10 (47.6) | 6 (31.6) | 7 (35.0) |
| **HIV viral load, copies/mL (n=56)** | 160.5 (20 – 24900) | 20 (35.7) | 17 (30.4) | 19 (33.9) |
| **Undetectable** | | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| **1 – 1 000** | | 10 (50.0) | 12 (70.6) | 15 (78.9) |
| **1 000 – 1 000 000** | | 6 (30.0) | 4 (23.5) | 3 (15.8) |
| **>1 000 000** | | 4 (20.0) | 1 (5.9) | 1 (5.3) |

SBP-systolic blood pressure; DBP- diastolic blood pressure; RR- respiratory rate; eGFR-estimated glomerular filtration rate; CRP- c reactive protein; WCC- white cell count, CD4-cluster of differentiation

Renal ultrasonography was performed in 143 (74.5%) subjects with 125 (87.4%) displaying abnormal sonographic feature. Figure 2 illustrates the various ultrasonographic findings.




*small or hyperechoic kidneys

**Figure 2: Findings of the 143 subjects in whom renal ultrasonography was performed**

## DISCUSSION

Renal dysfunction, especially AKI in patients admitted to the intensive care unit and adult acute renal unit has been widely studied in multiple small and large scale studies (11,13). However, it's incidence in the ED is poorly defined, largely due to differences in case definition and case mix (15). To our knowledge, this is the first study describing the presentation of patients with renal dysfunction presenting to a tertiary academic hospital ED in Johannesburg.

The incidence of renal dysfunction of 2.4% in this study was low compared to other studies (7,16). A South African study by Dlamini at el. reported an incidence of 3.4% in patients admitted to the renal unit (15). Higher incidence of 22.7% to 32.9% have been reported in other studies (7,16). Compared to our study findings, these three studies were conducted amongst hospitalised patients and had only enrolled patients with AKI. The low figure in our study may reflect low renal dysfunction pick up rates in the ED, especially in patients with early stages of renal impairment. However, factors such as class of medication prescribed, mechanical ventilatory support, intravenous fluid administration, ionotropic support and contrast administration all predispose hospitalised patients to developing AKI, as compared to ED patients, potentially explaining the higher figures in hospital acquired AKI studies. A multi-centre study that was conducted in Australian ICUs reported a crude cumulative incidence of AKI of 5.2% over a 10-year review period from 1$^{st}$ January 1996 to 31$^{st}$ December 2005 (17).

Demographic features of patient with renal dysfunction in this study were in keeping with previous studies. A male predominance was noted in this study (56.3%). Kaze et al. in Yaunde, Cameroon and Dlamini et al. in Cape Town, South Africa reported rates of 60% and 58.5% in males respectively (15,18). The proportion of patients with AKI (46.9% vs 56%)

CKD (27.6% vs 23%) and AOCKD (25.5% vs 21%) was very similar to the findings of Vachiat et al. in 101 HIV positive hospitalised patients with renal dysfunction in Johannesburg, South Africa (11).

The mean age of study subjects (50.5 ±16.5) was similar to that reported in other studies (50 ± 14.5) (19,20). The racial dominance of Black Africans (82.8%) in this study was similar to the study by Vachiat et al. (11). This figure closely mirrors the population of people of African race residing in Johannesburg (89.6%), as well as that presenting to the CMJAH ED (approximately 85%, per hospital records department) (21–23). Low rates of medical insurance coverage among Black Africans could also account for the higher proportion attending public hospitals (24).

Chronic hypertension as a cause of CKD was documented in a large proportion of study subjects with CKD (35.8%). This was similar to what was found by Dlamini at el, in 41.5% of patients (15). Almost two-thirds (62.6%) of patients in whom the HIV status was known were positive, which is much higher than the reported national incidence of 19% (25). Comparatively Dlamini et al. and Vachiat et al. reported the prevalence of HIV as 20.5% and 14.8% respectively (11,15). HIV infected individuals are more prone to renal dysfunction due to various factors that include higher rates of sepsis (primarily related to opportunistic infections), diarrhoea and direct infection of the kidney with HIV itself (HIV Associated Nephropathy, HIVAN). Other mechanisms or causes of renal dysfunction in HIV infected individuals include immune- complex kidney disease, non- collapsing focal segmental glomerulosclerosis and prolonged exposure to highly active antiretroviral therapy (26,27).

Sepsis was the commonest aetiology of renal dysfunction overall (n=56, 29.2%). This figure was lower compared to other South African studies that reported rates of 59.4% and 60.7%

(11,15). Sepsis as an aetiology ranged between 20.8% to 52% in other studies (12,13,28–30). Compared to urosepsis (14.0%), which was the commonest source of sepsis in our study, a study by Brown et al. in the United States of America reported pneumonia (11.5%) as the commonest source of sepsis (28). Pneumonia was only documented in 6.8% of subjects in this study.

Similar to a Sudanese study (17%) (31), post renal obstruction was responsible for 33 (17.2%) cases in this study. However, in the study by Dlamini et al., only 4.6% of subjects presented with an obstructive cause of renal dysfunction (15). This difference may be attributed to the fact that patient with obstructive uropathy are more likely to be admitted to the urology unit rather than the renal unit (18).

Urinalysis was performed in 72.4% compared to 2.8% in a study done in Poland (32) and 65.5% in a study in Cameroon (33), with proteinuria being the commonest finding in 56.3% of subjects. Renal sonography was performed in 74.5% of subjects with 87.4% having abnormal sonographic features of renal disease. Ultrasound is important in the assessment of: i) intrinsic causes of AKI, ii) distinguishing acute from chronic kidney disease and iii) detection of acute obstructive causes of renal dysfunction (34).

An overall mortality of 30.7% was found in our study which was lower to what Dlamini et al. and Vachiat et al. had reported (40.1% and 42.0% respectively) (11,15), whereas, dialysis was performed in 39.6% subjects which was similar to a study conducted in Tanzania, 42% (20).

The extremely higher proportion of patients who presented with AKI (46.9%) compared to CKD (27.6%) and AOCKD (25.5%) and the high HIV rate (62.6%) among renal dysfunction

subjects are significant findings of our study. Factors such as cultural practices, local healthcare protocols, private versus publicfacility and local HIV prevalence limit the generalization of our data. Despite the above limitations, our study is valuable in that it highlights the various risk factors that should make the clinician adopt a low threshold to screen patients for renal dysfunction.

## CONCLUSION

Patients presenting to the ED with sepsis, urinary tract obstruction, hypertension, diabetes mellitus, HIV and congestive cardiac failure are at risk of renal dysfunction. It is therefore crucial that the attending physician actively pursues renal function tests, urine analysis and renal ultrasonography in these patients.

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**RESEARCH PROTOCOL**

**Audit of adult patients with renal dysfunction presenting to the Charlotte Maxeke Johannesburg Academic Hospital Emergency Department**

Research protocol in partial fulfillment of the degree for master's in medicine (Emergency Medicine)

**John Masina (1477847)**

**Supervisors: Prof Abdullah Laher**

**Dr Muhammed Moolla**

## INTRODUCTION

The global incidence of Acute Kidney Injury (AKI) is poorly known because of underreporting, regional disparities, and differences in definition and case mix. Knowledge of incidence and risk factors is crucial because it drives local and international efforts on prevention and treatment. Notable differences exist in the incidence and risk factors of AKI between developing and developed countries (35). The burden of treatment of patients with renal failure is exponentially increasing with increased prevalence of HIV infection, diabetes mellitus, cardiac diseases and sepsis. Therefore, it can be expected that the burden of both AKI and chronic kidney disease (CKD) in South Africa would be high (36). However, no data currently exist on the incidence and prevalence of AKI at ED's in South Africa.

Historically, there have been more than 50 definitions of AKI, which has posed significant problems for comparative epidemiology and clinical research (37). Efforts have been made to

standardize the definition of AKI by multitude of societies. In 2004, the Risk- Injury- Failure-Loss- End stage (RIFLE) criterion was published, followed by the revised AKI Network (AKIN) classification in 2007.

Recently the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines (38) define AKI by the presence of any of the following:

a. increase in serum creatinine by ≥0.3mg/dL (>26.5$\mu$mol/L) within 48 hours;
b. increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within prior 7 days; or
c. urine volume <0.5mL/kg/h for 6 hours.

AKI carries a significant, independent risk of mortality among hospitalized patients. Recent studies have demonstrated increase mortality among patients with small increase in serum creatinine concentration (39).

Major risk factors for development of AKI include advanced age, diabetes mellitus, heart failure, liver failure, chronic kidney disease, hypotension, HIV infection and sepsis. Patients who undergo cardiac/vascular surgery, organ transplantation, and mechanical ventilation or who are exposed to contrast media, non-steroidal-inflammatory drugs (NSAIDs), antimicrobial drugs, nephrotoxic agents (herbal medication) or chemotherapeutic agents commonly experience AKI as a complicating condition (40). It is well known that many patients present to the emergency department (ED) with the above conditions. The incidence of the above risk factors in patients with AKI, is however undetermined (35). Using the KDIGO definition, 1 in 5 adults and 1 in 3 children worldwide experience AKI during a hospital episode care (41). Seedat at el; reported in 1978 that medical cases were the dominant cause of AKI, occurring in 65% of patients in Durban. Nephrotoxins (herbal remedies) being the most common. A recent survey of patients presenting to acute renal

services at CMJAH, over one-year period November 2005 to October 2006 showed 122 of 700 patients (17.5%) were HIV positive. Mortality occurred in 25 of the 122 patients (20%) of HIV positive patients (35). An incidence of 60.2% was found in a study done in Sri Lanka among patients admitted to Intensive care unit (ICU) with a mortality of 38.9% (42).

Early identification and treatment of patients with renal failure is critical. The potential role of biomarkers in this area is growing. Biomarkers such as Neutrophil gelatinase- associated lipocalin (NGAL) and cystatin C can be used to identify patients earlier, which potentially may reduce the severity of AKI(43). Parikh and colleagues showed that a cost savings can be realized by utilizing NGAL to identify AKI in the emergency department. Biomarkers can potentially allow earlier detection of AKI and implementation of renoprotective mechanisms and early initiation of Renal Replacement Therapy (RRT). Biomarkers may predict whether a patient will realize renal recovery or not. This would improve disposition planning and may reduce the inpatient resources currently utilized. The application of these and other biomarkers in the ED setting have not been fully evaluated and lends to potential areas of research (43,44). At this time the use of biomarkers is highly speculative.

Determining whether the renal function is improving, or deteriorating is done by monitoring serum creatinine and urine output. Like creatinine clearance, the serum creatinine will not be an accurate reflection of Glomerular Filtration Rate (GFR) in the non- steady- state condition of AKI. Nonetheless, the degree to which serum creatinine changes from baseline will reflect the changes in GFR. Serum creatinine is readily and easily measured and it is specific to renal function, while urea (or blood urea nitrogen, BUN) is a nonspecific maker of renal function, making it a poor maker relatively to creatinine (45). Urine output is far less specific, except when it is severely decreased or absent. Severe AKI can exist despite normal urine output (e.g. no oliguric) but changes in urine output can occur long before biochemical changes are

present (45). Patients may present with AKI without a known baseline measure of renal function. This presents a problem for a system that considers the change from baseline. The theoretical baseline serum creatinine value for a given patient can be calculated assuming a normal GFR. By normalizing the GFR to the body surface area, estimated GFR (eGFR) of approximately 75 to 100 ml/min per 1.73 $m^2$ can be assumed and thus a change from baseline can be estimated for a patient. The simplified modification of diet in renal disease (MDRD) formula provides a robust estimate of GFR relative to serum creatinine based on age, race and gender. Thus, given a patient without renal disease but in whom a baseline creatinine is unknown one can estimate the baseline creatinine (45).

International guidelines for the treatment of AKI emphasize appropriate adjustments of drug dosing, avoiding nephrotoxic exposures, and careful attention to fluid and electrolyte balance in patients at risk for and with established AKI (46). This audit will evaluate the demographics and the clinical characteristics of patients presenting with AKI to a South African Hospital ED and allow improvement in management and disposition of patients. The potential use of biomarkers for early detection of AKI in patients presenting to an ED may be evaluated in subsequent study.

**STUDY AIM**

To conduct an audit of adult patients presenting with renal dysfunction to CMJAH, ED

**STUDY OBJECTIVES**

1. To describe the demographics of adult patients with renal dysfunction.
2. To describe the clinical characteristics of adult patients with renal dysfunction.
3. To describe the disposition of adult patients with renal dysfunction.
4. To describe the renal ultrasonographic features of adult patients with renal

dysfunction.

## METHODOLOGY

### Study design

This study is a hospital-based, descriptive, prospective audit of medical records.

### Study population

The study population will consist of consecutive adult patients that present to CMJAH ED and renal function tests (Blood Urea and Creatinine) performed.

### Study site

The study will be conducted at the Charlotte Maxeke Johannesburg Academic Hospital, Emergency Department.

### Inclusion criteria

All consecutive adult patients (>18 years) that present to the Charlotte Maxeke Johannesburg Academic Hospital, Emergency Department with abnormal renal function tests (measured serum creatinine more than 1.5 the calculated baseline according to MDRD formula).

### Exclusion criteria

- All adult patients with normal renal function tests (measured serum creatinine not more than 1.5 the calculated baseline according to MDRD formula).
- Patients with no renal function tests performed.

### Sample size calculation

A sample of convenience will be used in the study. As per review of the CMJAH, ED daily patient register, on average 4 patients are seen with renal dysfunction per day. A sample size of 200 patients will be the target for the study. Data collection will be conducted over a period of 4 months with an average of 3 patients per day recruited in the study.

### Data Collection

- Data collection will commence once the protocol has been approved and ethical clearance obtained.
- The researcher will review the CMJAH ED daily patient register five times weekly outside working hours from the date of initiation of data collection.
- Hospital numbers (patients file number) of all patients who had the renal function tests carried out will be selected.
- All the renal function tests done will be reviewed and patient's eGFR and assumed baseline serum creatinine calculated. Patients with serum creatinine rise of more than 1.5 times the baseline will be selected for the study (Renal dysfunction as defined by the KDIGO classification).
- Patients with renal dysfunction will be followed up in the wards or ED (if still present)
- Data collection sheet (see below) will be completed and ultrasound performed on patients after informed consent.
- Medical records of these patients will be requested and obtained from the hospital records department.
- Patients whose medical records can still not be accessed will be excluded from the study.
- For ease of later reference, all medical records that meet study criteria will be scanned and stored in a password-protected folder in a password-protected computer only accessible to the researcher.
- Patient identifying information will be blocked out and replaced with a unique PIN number for each patient prior to scanning. This folder will be deleted at the end of the study.
- Data from available medical records meeting the study criteria will be abstracted and

entered into a specifically designed data collection sheet.

- Data collected will include demographic data, admission information, clinical presentation, risk factors/ co-morbidities, lab results, radiological imaging (ultrasound) findings if available and disposition information.

**Data Analysis**

- Specific data from the data collection sheet pertinent to this leg of the study will be analyzed using STATA 14, (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP).
- A descriptive analysis of the data will be conducted.
- Summary descriptive statistics such as frequencies and percentages for categorical variables (gender, race, HIV status, etc.) will be conducted and illustrated by pie and bar charts.
- Continuous data (age, renal functional tests results and kidney size) will be described by the mean, standard deviation, median and inter-quartile range, and the distribution of data will be analyzed by histogram.

## ETHICS

Permission to conduct the study will be sought from the CEO of CMJAH and the HOD of CMJAH ED (appendix 2). Ethical approval for this study will be obtained from the University of the Witwatersrand Human Research Ethics Committee (medical) (HREC (medical)). In accordance with patient confidentiality, patient-identifying information will not be recorded and a unique patient identification number (PIN) will be assigned to all patients studied, starting from 001. Only the researcher will know the PIN. The information gathered will be stored in a password-protected computer that will only be accessible to theresearchers.

**TIMING**

As per the CMJAH ED patient register, an average of 5 patients with renal dysfunction are seen daily. Therefore, it is estimated that data collection will be completed within 4 months from the date of initiation of data collection.

| | Feb | Mar | Apr | May | June | Jul | Aug | Sep | Oct | Nov | Dec | Jan |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Literature review | | | | | | | | | | | | |
| Preparing protocol | | | | | | | | | | | | |
| Protocol assessment | | | | | | | | | | | | |
| Ethics application | | | | | | | | | | | | |
| Data collection | | | | | | | | | | | | |
| Data analysis | | | | | | | | | | | | |
| Writing up-thesis | | | | | | | | | | | | |
| Writing up-paper | | | | | | | | | | | | |

**FUNDING**

This research project will be self-funded with an estimated cost as follows:

| **Activity** | **Amount** |
|---|---|
| Stationary and printing | R500 |
| Travel Expenses (petrol) | R1000 |
| Internet costs | R1000 |
| **Total** | **R2500** |

**LIMITATIONS**

- Patients with renal dysfunction presenting to the Emergency Department who do not have the renal function tests carried out on them hence excluding them from the study. We estimate these to be very few.
- Patients may be discharged before the researcher sees the patient
- Patient may have been transferred to another hospital before the researcher sees the patient

- Patients refusing consent (Appendix 7,8 and 9)

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**DATA COLLECTION SHEET**

**Participant serial number: _____**

**1) Demographics**

| **Gender:** | Male | Female |
|---|---|---|

| **Race:** | African | White | Indian | Coloured | Others |
|---|---|---|---|---|---|

**Age:** _____ years **D.O.A: _____D.OD: _____**

**2) Vitals**

**BP: _____ mmHgTemperature: _____ °C RR _____ bpmHR: _____ bpm**

**3) Clinical presentation**

| | Y | N |
|---|---|---|
| Nausea | | |
| Vomiting | | |
| Abdominal pains | | |
| Oedema (Any part of the body) | | |
| Dysuria | | |

**4) Risk factors/ Co-morbidities**

| | Yes | No | Comments |
|---|---|---|---|
| DM | | | |
| Heart problems | | | |
| Known HTN | | | |
| Use of NSAID | | | |
| Chronic Medication/chemotherapy Specify: _____ _____ _____ _____ | | | YES: Specify (eg. ARVs) |
| History of recent surgery | | | |
| Herbal medication use | | | |
| Other (specify): | | | |

**5) Urine dipstix / analysis**

Blood: _____

Protein: _____

Leucocytes: ____

**6) Lab results**

| **Laboratory findings on admission (where indicated)** | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Blood:** | | | | | | | | | | | | | | | | | | | | | | | | |
| **HIV** | | | **CD4 count** | | | **HIV-1 viral load** | | | **CRP** | | | | | | | | | | | | | | | |
| **ABG** | pH | | | $FiO_2$ | | | $PaO_2$ | | | $PaCO_2$ | | | | | | | | | | | | | | |
| | BE | | | Gluc | | | Lactate | | | Osmolality | | | | | | | | | | | | | | |
| **U+E** | Na | | K | | Cl | | $HCO_3$ | | Urea | | Cr | | GFR | | | | | | | | | | | |
| **FBC** | WCC | | | | Hb | | | | Plt | | | | | | | | | | | | | | | |
| | MCV | | | | MCH | | | | RPI | | | | | | | | | | | | | | | |
| **LFT** | Bili(tot) | | Bili(conj) | | | Prot | | | Alb | | ALP | | | GGT | | | | | | | | | | |
| | Ammonia | | Amylase | | | Lipase | | | | | AST | | | ALT | | | | | | | | | | |
| **Coag** | INR | | PTT(c) | | | PTT(p) | | | **CMP** | Ca | | Mg | | | P | | | | | | | | | |
| **Urine** | MCS | | | | | | | | Cells / other | | | | | | | | | | | | | | | |
| | WCC | | RCC | | | Albumin | | | Prot:Cr | | | | | | | | | | | | | | | |

**Serial U+E**

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Date** | Na | | K | | Cl | | $HCO_3$ | | Urea | | Cr | | GFR | |
| **Date** | Na | | K | | Cl | | $HCO_3$ | | Urea | | Cr | | GFR | |
| **Date** | Na | | K | | Cl | | $HCO_3$ | | Urea | | Cr | | GFR | |
| **Date** | Na | | K | | Cl | | $HCO_3$ | | Urea | | Cr | | GFR | |

**7) Renal sonography / radiology**

**Kidney size** Right: _____ Left: _____

**Hydronephrosis** Right: Y / N, Grade: _____ Left: Y / N, Grade: _____

**Echogenicity** Right: _____ Left: _____

**Other significant findings / radiological investigations:**

_____

_____

_____

**8) Disposition/ Admission information**

| Referring institution | Self-referral | | Local clinic / hospital | |
|---|---|---|---|---|
| Patient disposition | ICU/ high care | General Ward | Step-down | D/C Home |

## APPENDIX 1: ETHICS CLEARANCE CERTIFICATE

R14/49 Dr J Masina

**HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)**
**CLEARANCE CERTIFICATE NO. M170716**

| | |
|---|---|
| **NAME:** (Principal Investigator) | Dr J Masina |
| **DEPARTMENT:** | School of Clinical Medicine<br>Department of Emergency Medicine<br>Charlotte Maxeke Johannesburg Academic Hospital |
| **PROJECT TITLE:** | An audit of adult patients with renal dysfunction presenting to Charlotte Maxege Academic Hospital Emergency Department |
| **DATE CONSIDERED:** | 28/07/2017 |
| **DECISION:** | Approved unconditionally |
| **CONDITIONS:** | |
| **SUPERVISOR:** | Drs A Laher and M Moolla |
| **APPROVED BY:** | Professor PE Cleaton-Jones, Chairperson, HREC (Medical) |
| **DATE OF APPROVAL:** | 06/11/2017 |

**This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.**

**DECLARATION OF INVESTIGATORS**

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on 3rd floor, Phillip V Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

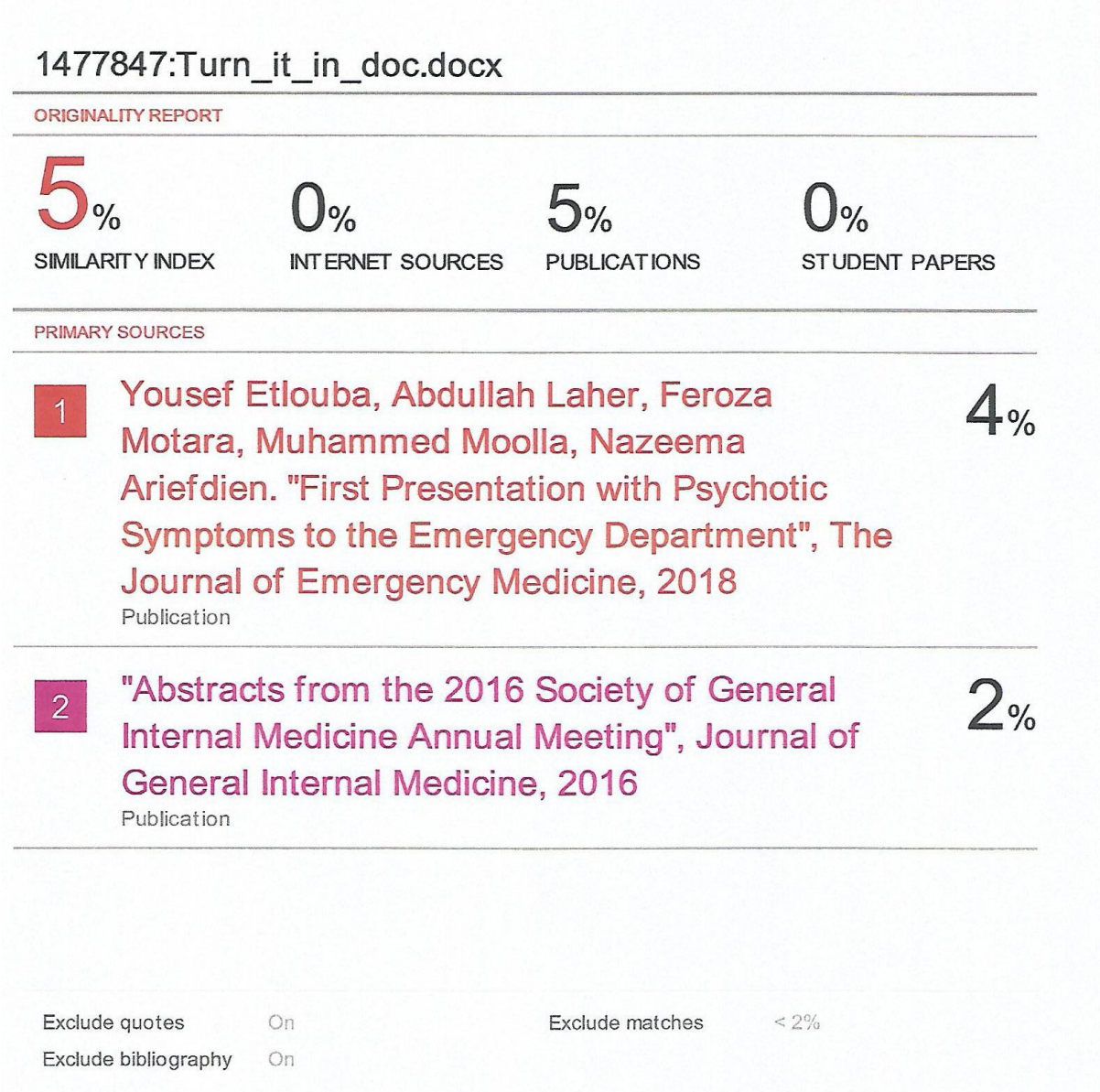
I/We fully understand the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially reviewed in **July** and will therefore be due in the month of **July** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

09TH NOVEMBER, 2017.
Date

**PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES**

**APPENDIX 2: TURN-IT-IN-REPORT**



1477847:Turn_it_in_doc.docx

ORIGINALITY REPORT

| 5% | 0% | 5% | 0% |
|---|---|---|---|
| SIMILARITY INDEX | INTERNET SOURCES | PUBLICATIONS | STUDENT PAPERS |

PRIMARY SOURCES

| | | |
|---|---|---|
| 1 | Yousef Etlouba, Abdullah Laher, Feroza Motara, Muhammed Moolla, Nazeema Ariefdien. "First Presentation with Psychotic Symptoms to the Emergency Department", The Journal of Emergency Medicine, 2018<br>Publication | 4% |
| 2 | "Abstracts from the 2016 Society of General Internal Medicine Annual Meeting", Journal of General Internal Medicine, 2016<br>Publication | 2% |

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