Epidemiology of Hospital-Acquired Acute Kidney Injury(HAAKI) in Medical Hospitalized Patients in Al-Diwanyia Teaching Hospital

Alaa Abdulabbas Hamza* ,Mohamed Ali H.Hamed*
*Specialist physician of Internal Medicine, Al Diwanyia Teaching Hospital
MBchB.D.M-internal medicine

Abstract

Background: Minimum elevation of serum creatinine,even within normal reference range are associated with worse outcome of the patients.

Objective: The application of the most recent definition of AKI proposed by the Acute Kidney Injury Network (AKIN),published in March 2012 to promote the earlier detection of HAAKI .

Patients&Method: Cross –sectional observational study conducted in the medical ward in Al-Diwanyia Teaching Hospital for a period 9 months from 1st of January to 30 of September 2013 . All adolescents & adults patients who fulfill the criteria of the study included. Data about demographics ,co-morbidities of patients & serial measurement of (S.Cr) were directly collected . The definition of AKI according to Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Acute Kidney Injury -2012,based on AKIN criteria.

Result :
Out of 522 patients included in the study(the mean age of them 59 ± 23) ,HAAKI (stage1)were recorded in 79 (15.13%) patients , elderly patients aged ≥ 65 represent 50.63% of all cases of HAAKI(without significant gender variation). About 19 patients(24.05%) morbidities HAAKI due to intermingle co morbidities. The most 3 prevalent co morbidities were reported either independent or in association with other co morbidities in patients with HAAKI,1stone diabetes mellitus , 51 diabetic patients which represent 64.5% of total 79 patients with HAAKI & 37.22% of total diabetic patients studied . The 2nd was sepsis which reported in about 37 patients (46.83%).About 36 patients (45.56%) had HAAKI due to nephrotoxic drugs which represent the 3rd more frequent co morbidities.

Limitations: Single-medical ward study of limited period .Classification of the diseases according to conventional method.
Conclusions: Our results suggest that HAAKI is a common complication . Our efforts should be focused to prevent or minimize the risk factors of HAAKI (particularly in advanced age).

Introduction

Acute renal failure (ARF) is a complex disorder that occurs in a variety of settings with clinical manifestations ranging from a minimal elevation in serum creatinine to anuric renal failure.[1] In a recent review, Eknoyan notes that the first description of ARF, then termed ischuria renalis, was by William Heberden in 1802.[2] A recent survey revealed the use of at least 35 definitions for ARF in the literatures, this state of confusion has given rise to wide variation in reported incidence and clinical significance of ARF. [3] Acute kidney injury (AKI) has now replaced the term acute renal failure and an universal definition and staging system has been proposed to allow earlier detection and management of AKI and the term ARF preferably should be restricted to patients who have AKI and need renal replacement

therapy (RRT).[4] The incidence of hospital-acquired AKI is about 5-10 times higher than that of community-acquired cases, despite the fact that all surveys of hospital-acquired AKI underestimate its true incidence.[5] When one searches for data from developing countries,no nationwide collection systems are available, and data from isolated centers are not based on the current AKI definition.[6] Mounting evidences suggests that acute, relatively mild injury to the kidney or impairment of kidney function, manifest by changes in urine output and blood chemistries, portend serious clinical consequences.[7] Recent analysis strongly suggests that the renal prognosis of AKI is not "an all or none" phenomenon, recovery of kidney function is often suboptimal and may lead to progression to severe CKD and even ESRD.[8 [

The Acute Dialysis Quality Initiative (ADQI) group developed a system for diagnosis and classification of a broad range of acute impairment of kidney function in 2004,the acronym RIFLE stands for the increasing severity classes: Risk, Injury, and Failure; and the two outcome classes, Loss and End-Stage Renal Disease (ESRD).[9] In 2007 the AKI Network(AKIN) proposed the following changes to the RIFLE criteria: proposed that stages 1, 2 and 3 be used instead of R, I and F; L and E are discarded, broadening of the 'risk' category of RIFLE to include increase in serum creatinine of at least 0.3 mg/dl within 48 hours, even if this does not reach 1.5x the baseline creatinine.[10] The substance creatiine was first named in 1847 by Liebig.[11] Jaffe described its reaction with alkaline picrate in1886, and this reaction utilized for assay of creatinine in urine in 1904 and later in blood , this method remains dominant in clinical laboratories today.[12] Numerous endogenous substances are known to interfere with different Jaffe reaction based assays, either positive interferents such as protein, ascorbate, pyruvate, glucose and cephalosporin and negative interferents such as bilirubin.[13] The structural changes that occur with aging contribute to functional alterations .[14],[15] Based on longitudinal studies of healthy patients without hypertension, diabetes, heart disease, or clinically apparent atherosclerosis, a progressive decline in GFR of 0.75 ml/min/1.73m2 per year was observed after the age of 30. [16] [17]

Patients & Method

:Study design

The study was approved by the Institute Ethics Committee in Al-Diwanyia Teaching . Hospital

This cross-sectional study was carried out in the 4th medical ward , Al-Diwanyia Teaching Hospital during the period from 1st of January 2013 – 30th of September .2013

:Patients

All patients aged ≥14 admitted to the medical ward in Al-Diwanyia Teaching Hospital during the period of study were included, except the following patients were excluded: (i)Serum creatinine >1.5 mg/dl on admission(ii) Pregnant patients,(iii) postoperative patients referred from surgical wards& intensive care unit(ICU) & (iv)hospital stay for less than48 hours . Clinical data was collected directly for all patients including gender, age, provisional diagnosis, co-morbidities, current medications, progression of AKI during the course of hospital stay. The primary disease classified according to conventional method into diabetes mellitus(diabetic foot & acute complications without evidences of other systemic disease),cardiovascular diseases , hepatobiliary diseases, malignancy, respiratory diseases, gastro-intestinal diseases, haematological diseases,& .miscellanies category

Definition of AKI: according to Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Acute Kidney Injury (AKI)-2012:AKI is defined as any of the following (Not Graded): Increase in SCr by ≥0.3 mg/dl (≥26.5 mol/l) within 48 hours; or Increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the

prior 7 days; or Urine volume 0.5 ml/kg/h for 6 hours. [18]The variant for diagnosis of HAAKI was serum creatnine (S.Cr) level only. Baseline serum creatinine values at the time of admission were collected & consecutive values on 48 hours intervals were recorded. Serum levels of creatinine were estimated on Abbott/C4000 autoanalyzer by modified Jaffe reaction (Reference range for s.creatinine:0.5 - 0.9mg/dl for women & 0.6 – 1.1mg/dl for men, according to Randox laboratories limited, Abbot/C400) . The tests made by the hands of the most expert biochemistry laboratory staff. Modification of diet of the patients, just restriction of cooked meat was .applied

Classification of co morbidities :Co morbidities were classified as following:

[(a)Sepsis: Criteria of diagnosis.[18

[b) Nephrotoxicity.[18)

(c) Exposure to contrast media during hospital stay or up to one week prior to admission to hospital.

[d) Hypotension: according to definition[18)

[e) Volume loss: definition.[18)

[f) Sepsis and drugs. [19)

g)Volume loss and sepsis: When there was) [volume loss as well as septicemia.[19

h)Sepsis-drugs – hypotension: If there was) septicemia, use of drugs which are potentially nephrotoxic as well as hypotension, because of cardiovascular [cause.[19

Data analysis: Variables were reported as mean±SD.Statistical calculation was done using analysis of variance(ANO VA) &Chi –square test.P.value<0.05 was considered significant. All the calculations were carried .out with help of software SPSS16 version

:Result

A total 0f 522 patients were admitted to the 4th floor medical ward-Al-Diwaniah Teaching Hospital who fulfill the criteria of the study , 79 patients of them (15.13%) had AKI stage 1 during hospitalization .according to AKIN criteria

.Figure 1

Flow diagram describing the derivation of the study cohort.

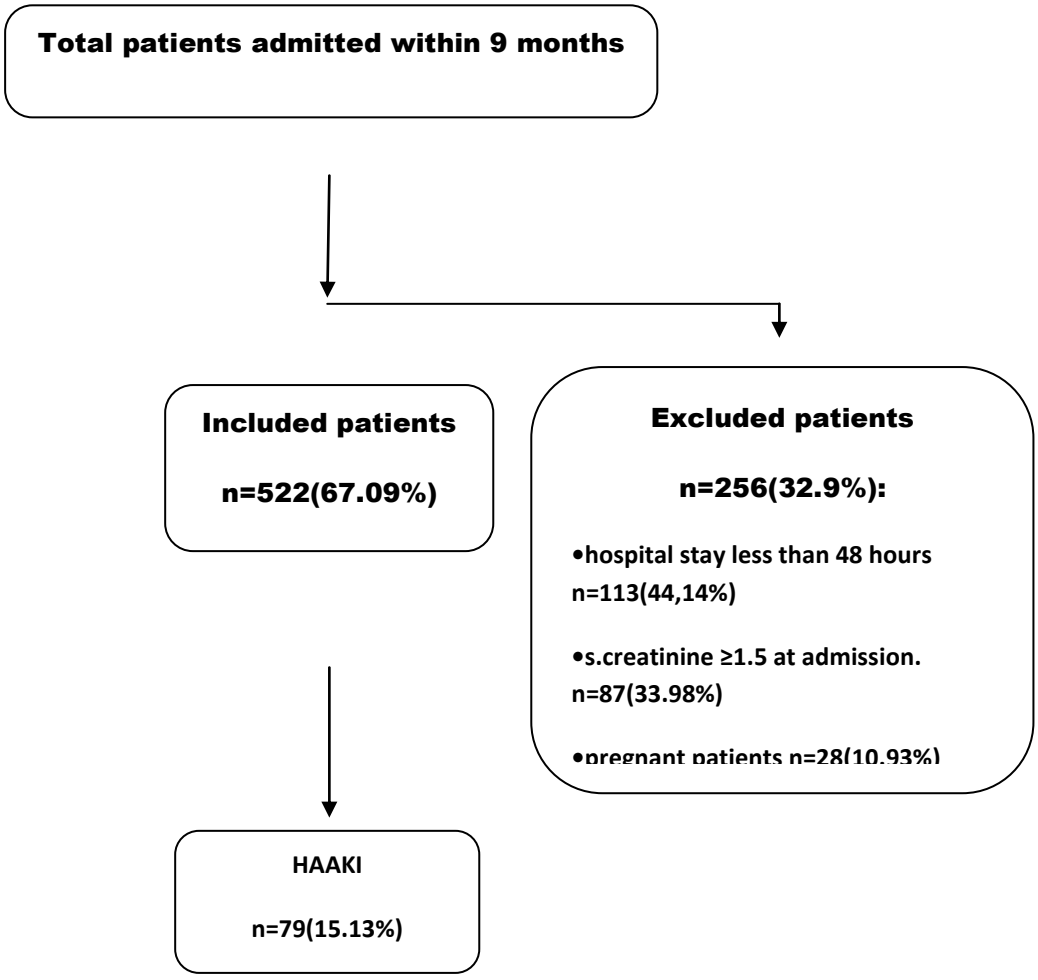

Table 1.Demographic distribution of 522 patients including 79patients with HAAKI.

Gender	Age(year) Total n=522	stage (1) HAAKI Total n=79
Female:	n=267(51.14%)	n=42(53.16%)
	14-44 n=55(20.59%)	n=6(14.28%)
	45-64 n=118(44.19%)	n=13(30.95%)
	≥65 n=94(35.20%)	n=23(54.76%)
Male	n=255(48.85%)	n=37(46.83%)
	14-44 n=68(26.66%)	n=4(10.8%)
	45-64 n=110 (43.13%)	n=16(43.24%)
	≥65 n=77(30.19%)	n=17(45.94%)

The mean age of affected patients was 59±23,without significant gender variation, But there is statistically significant association between incidence of HAAKI with advanced age of the patients ≥65 years(40 cases of HAAKI between 171 patients aged ≥ 65,represent 23.39% of them**.**

Figure 2.

Distribution 0f 552 patients according to their ages & relation to the cases of HAAKI.

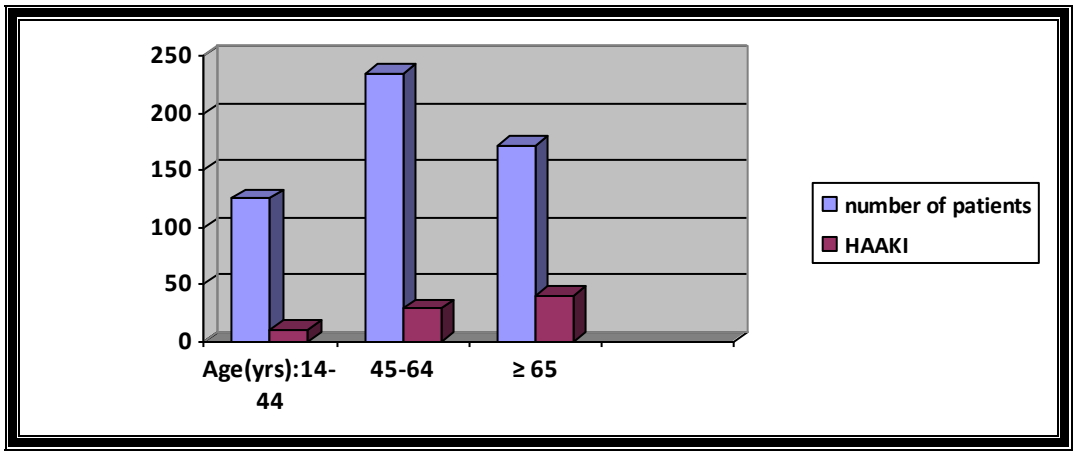

Table 2. Distribution of 79 cases of HAAKI according to the primary cause of admission to the hospital.

Primary disease at admission	No. of recorded HAAKI-stage 1 (n=79)
Diabetes mellitus & its complications:	19(24.05%)
diabetic foot	11
hyper-osmolar non-ketotic coma	5
diabetic ketoacidosis	3
Cardiovascular diseases:	18(22.78%)
coronary artery disease*	8*
heart failure	5
un controlled hypertension	3
infective endocarditis	1
pericarditis	1
Infection related diseases:	17(21.51%)
Pyrexia of un known origin	5
septicemia	4
Typhoid fever	3
Brucellosis	2
Acute pyelonephritis	1
Tuberculous pleural effusion	2
Respiratory diseases:	7(8.86%)
pneumonia	3
chronic obstructive pulmonary diseases	1
bronchial asthma	1
upper respiratory air way infection	1
restrictive lung diseases	1
Gastro-intestinal diseases:	5(6.32%)
Acute gastroenteritis	3
Inflammatory bowel diseases	1
Upper GIT bleeding	1

Haematological diseases:	**5(6.32%)**
Iron deficiency anaemia	**1**
Acute leukaemia	**1**
Chronic leukaemia	**1**
Multiple myeloma	**1**
Aplastic anaemia	**1**
Hepatobilliary diseases:	**5(6.32%)**
liver cirrhosis	**2**
obstructive jaundice	**3**
Malignant diseases:	**2(2.53%)**
Bronchogenic carcinoma	**1**
Urinary bladder carcinoma	**1**
Miscellaneous cause:	**1(1.26%)**
Hypothyroidism	**1**

*2 patients underwent coronary angioplasty 6 days prior to admission, so contrast media were blamed because initial preoperative s.creatinine was lower than the next reading & they didn't received any potential nephrotoxic drug.

Figure 3.Distribution of 522 patient according to the presence of diabetes mellitus with or without HAAKI

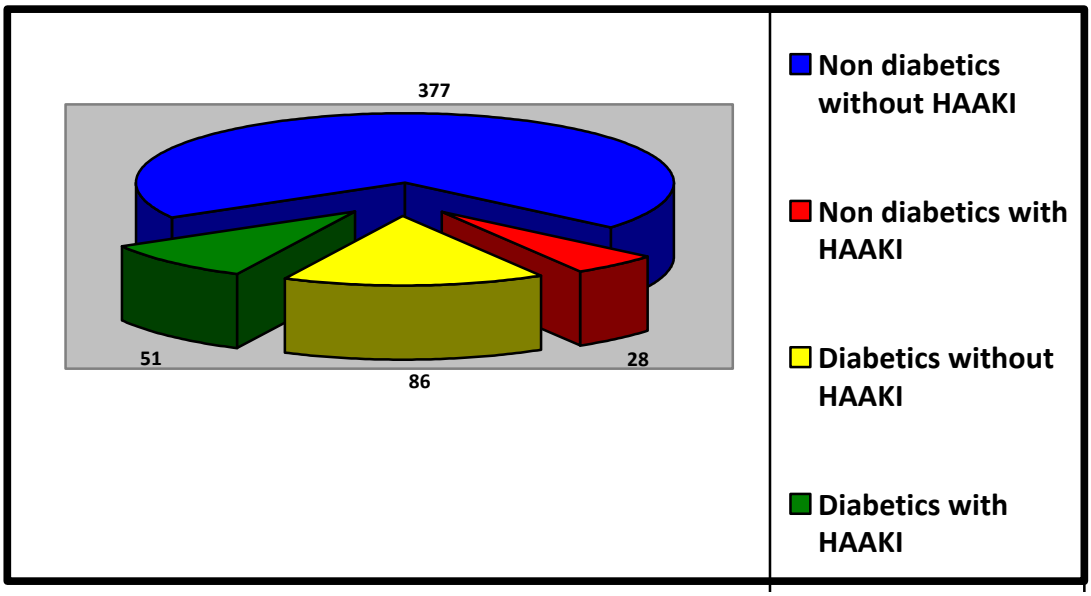

Table 3.Distribution of 79 patients with HAAKI according to the co morbidities ± diabetes mellitus(51 patients).

Co morbidities	Number of patients with HAAKI(N=79)	Number of diabetic patients with HAAKI(N=51))
Nephrotoxic drugs	25(31.64%)	5(9.80%)
Sepsis	18(22.78%)	16(31.37%)
Sepsis+ Nephrotoxic drugs+Hypotension	11(13.92%)	11(21.56%)
Volume loss	11(13.92%)	8(15.68)
Sepsis+ Volume loss	8(15.68)	8(10.12%)
Hypotension	4(5.09%)	2(3.92%)
Contrast media	2(2.53%)	1(1.96%)

Discussion:

HAAKI detected in this study mostly the classical one, because most cases of acute on chronic renal failure had been already excluded .

HAAKI detected in 79(15.13%) out of 522 patients(Fig.1), which is seems to be high .The cases of HAAKI stage 1 detected according to AKIN criteria mostly asymptomatic & usually passed un noticed by the responsible physicians. A number of studies have attempted to determine the real incidence & categorize the etiology of AKI in hospitalized patients; however, most studies were retrospective reviews of the hospital charts and only subjectively attributed a cause of AKI in patients without using properly predefined criteria , **Shusterman N** ,et al:Acute kidney injury is seen in 13–18% of all people admitted to hospital, with older adults being particularly affected .[20]

Xue JL, et al , analyzed the 2001 National Hospital Discharge Survey, identifying patients with AKI : Among the approximately 330 210 discharges included in the database, AKI was coded as a discharge diagnosis with a frequency of 19.2 per 1000 hospitalizations.[21]

Mehta KS,et al : In the tropical zone,HAAKI remains one of the most challenging problems, with reported incidence rates between 25% and 80%.[22]

Female gender reported as risk factor for development of HAAKI , inclusion of female gender as a risk factor in several validated predictive scores[23] , but in our study no significant gender variation reported as shown in table 2. This is because gynecological &obstetrical cases not included & the study conducted in the general hospital in particular for medical patients.

Table 1. revealed that HAAKI was more frequent & significantly reported in elderly patients aged ≥ 65 (50.63%) of all cases of HAAKI.Figure 2. Showed comparison between total numbers of patients of each age group with the numbers of HAAKI cases, the incidence rates were 23.39% for patients aged ≥ 65year ,12.71% for patient aged 44-64 year & 8.13% for patients aged 14-44 year. In an Italian hospital cohort(Baraldi A,et al,1998.[24]

Our study was established that the primary diseases for admission mentioned in table 2,as

diabetes mellitus, cardiovascular diseases & infection related diseases responsible for about 24.05%,22.78%&21.51% of recorded cases of HAAKI respectively.

All recent guidelines for AKI had been considered these clinical conditions as main risk factors, Druml W, et al,2010: Diabetes mellitus, hypertension, obesity and proteinuria are independent risk factors for acute kidney injury.[25]

In developing countries, "prerenal"due to obstetric cause is most common [26], infectious [27,28]. Our observation revealed that the association of hypertension with or without diabetes mellitus associated with development of HAAKI,another interesting observation noticed which is reduction of serum creatinine level following control of hypertension.

Although hypertension considered as independent risk factor for development of AKI , Lyanada,Circulation;2010:acute severe hypertension,AKI is acute target organ dysfunction.[29]

Regarding the co morbidities considered as risk factors for development of HAAKI , **diabetes** mellitus on the top of the list as shown in Figure.3:137 out 0f 522 patients(26.24%) included in the study were diabetic. HAAKI were reported in 51 out of 137 diabetic patients (37.22%),& this represents 64.5% of the total 79 patients with HAAKI. Those 51 diabetics with HAAKI were divided into 2 groups.

The 1st group ,diabetes mellitus was the primary disease for admission to the hospital without evidence of other associated disease represents 19 patients out of 79(24.05%) with HAAKI & the 2nd group include 32 patients (40.50%) out of 79 patients were diabetes mellitus is a co morbidity. Diabetes mellitus is the most significant(P.value<0.05) leading cause of HAAKI.

Un fortunately diabetes mellitus not controlled in most of the patients studied. Almost all diabetic patients admitted to the hospital due to one or more of its complications.Girman et al [30] retrospectively performed a survey of the General Practice Research Database (UK) comparing 119.966 type 2 DM patients with 1.794.516 nondiabetic individuals .The yearly AKI incidence was198 versus 27/100000subjects,& the difference remained statistically significant even after adjustment for other well-known AKI risk factors & comorbidities.

In about 19 patients(24.05%), HAAKI due to intermingle co morbidities (interaction between 2 or more co morbidities especially, Nephrotoxic drugs , Sepsis, hypotension in addition to diabetes mellitus) were one of the most significant risk factors associated with the development of HAAKI, as shown in table 3.

We noticed that the nephrotoxicity associated with the development of HAAKI either independent or in association with other co morbidities such as diabetes mellitus&/or sepsis . Fournier,2012:Nephrotoxic effects, either alone or more commonly associated with ischemia, have been a factor in the development of AKI in almost one-half of the cases. In particular, the triple combination of NSAIDs, ACE inhibitors (or ARBs) and diuretics can cause acute renal injury by interfering with homeostatic mechanisms. [31],this finding agreed to great extent with our finding ,45.56% of cases of HAAKI due to nephrotoxic drugs.

Perazella;2003:Patient-related risk factors vary somewhat depending on the offending drug

,however, some risk factors are common to all nephrotoxins and include age older than 60 years, underlying renal insufficiency, intravascular volume depletion, exposure to multiple nephrotoxins, diabetes, heart failure, and sepsis[32].

Exposure to radio contrast material is well established cause of AKI in most of the studies . but in our study this co morbidity was documented in 2 cases(2.53%) only as mentioned in table 2. Although we stressed about contrast media as important co morbidity in our study, this percentage(2.53%) considered low when compared with other international studies, McCullough PA,2008:The estimated general incidence of contrast induced AKI is approximately 7%.[33] This disparity mostly explained by 1st the contrast induced AKI usually underestimated & 2nd because most patients who underwent cardiac catheterization followed in outpatients clinic. The strength of this study is not ideally stems , but this is the 1st study in our hospital to apply recent definition**, using AKIN criteria**. The cohort of this study is limited & not a fully representative, because patients in isolation wards , coronary care units & neurological wards were not included & it was done within 9 months.

Conclusion:

Acute kidney injury (AKI) is a well suspected complication in hospitalized patients.

Efforts should be focused on minimizing causes of AKI & early detection &

instant therapeutic intervention.

Recommendations:

1- A large, prospective epidemiological or cohort study is needed to investigate all aspect of acute kidney injury (incidence, co morbidity &outcome) in Iraq.

2- Application of recent AKI management guidelines in Iraqi hospitals e.g.

KDIGO CLINICAL PRACTICE GUIDELINE FOR ACUTE KIDNEY INJURY-2012

3- Development of Iraqi clinical team or network , comprising healthcare professionals (including consultants, GPs and technical staff) for AKI researches .

4 - Judicious use of nephrotoxic drugs especially in elderly patients and awareness of potential drug interactions.

Acknowledgements:

I wish to express my appreciation to the persons who assisted me during the preparation of this research. Dr.Hayder Jiham (assistant professor of statistics/department of community medicine) , Colleagues ,biochemistry laboratory staff, residents &staggers.

References:

[1]Ympa YP, Sakr Y, Reinhart K, Vincent JL: Has mortality from

acute renal failure decreased? A systematic review of the

literature. Am J Med 2005, 118:827-832

[2]Eknoyan G. Emergence of the concept of acute renal failure. Am.Nephrol 2002 22: 225–230 .

[3]Kellum JA, Levin N, Bouman C, et al. Developing a consensus classification system for acute renal failure. Curr Opin Crit Care 2002; 8: 509–514.

[4]Mehta RL, Chertow GM: Acute renal failure definitions and classification: Time for change? J Am Soc Nephrol14 :2178– 2187,2003

[5]Hoste EA, Clermont G, Kersten A, et al. RIFLE criteria for acute kidneyinjury are associated with hospital mortality in critically ill patients: acohort analysis. Crit Care 2006; 10: R73.

[6] Cerda J, Bagga A, Kehr V, Chakravarthi RM: The contrasting characteristics of acute kidney injury in developed and developing countries. *Nat Clin Pract Nephrol*2008 , in press. [7] Praught ML, Shlipak MG. Are small changes in serum creatinine an important risk factor? Curr Opin Nephrol Hypertens 2005; 14, 265-270

[8]Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW:

Acute kidney injury, mortality, length of stay, and costs in hospitalized

patients. J Am Soc Nephrol 2005, 16:3365-3370

[9]Bellomo R, Ronco C, Kellum JA, et al. Acute renal failure – definition,outcome measures, animal models, fluid therapy and informationtechnology needs: the Second International Consensus Conference of theAcute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004; 8:R204–212.

[10]Cruz DN, Ricci Z, Ronco C. Clinical review: RIFLE and AKIN–time for reappraisal. Crit Care. 2009;13(3):211. doi: 10.1186/cc7759

[11]Liebig J. Kreatin und Kreatinin, Bestandtheile des Harris der

Menschen. J Prakt Chem 1847;40:288-92.

[12]Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, *et al*. Acute Kidney Injury Network: Report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:R31. Available from: [Last accessed 2011 Oct 23].

[13] Peake M, Whiting M. Measurement of serum creatinine – current status and future goals. Clin Biochem Rev 2006;27:173-184 .

[14] Hollenberg NK, Adams DF, Solomon HS, Rashid A, Abrams HL, Merrill JP. Senescence and the renal vasculature in normal man. Circ Res. 1974 Mar;34(3):309–316. [PubMed]

[15] Fliser D, Zeier M, Nowack R, Ritz E. Renal functional reserve in healthy elderly subjects. J Am Soc Nephrol. 1993 Jan;3(7):1371–1377. [PubMed]

[16]. Lindeman RD, Tobin J, Shock NW. Longitudinal studies on the rate of decline in renal function with age. J Am Geriatr Soc. 1985 Apr;33(4):278–285. [PubMed]

[17]. Rowe JW, Andres R, Tobin JD, Norris AH, Shock NW. The effect of age on creatinine clearance in men: a cross-sectional and longitudinal study. J Gerontol. 1976 Mar;31(2):155–163. [PubMed]

[18] **to Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Acute Kidney Injury(KDIGO) guideline-2012: Chapter 2.1: Definition and classification of AKI:**

table 2:Staging of AKI;p 19

Chapter 2.2: Risk assessment:p 23

Chapter 4.1: Contrast-induced AKI: definition, epidemiology, and prognosis ; p 69

[19]Nice clinical guideline 169 ,August-2013.Prevention,detection & management of acute kidney injury up to the point of renal replacement therapy.

[20] Shusterman N, Strom BL, Murray TG, Morrison G, West SL, Maislin G. Risk factors and outcome of hospital-acquired acute renal failure. Clinical epidemiologic study. Am J

Med. 1987;83:65–71. [PubMed]

[21]Xue JL, Daniels F, Star RA, et al. Incidence and mortality of acute renal failure in Medicare beneficiaries, 1992 to 2001. J Am Soc Nephrol 2006; 17: 1135-1142

[22]Mehta KS, Halankar AR, Makwana PD, Torane PP, Satija PS, Shah VB: Severe acute renal failure in malaria. *J Postgrad Med***47** :24– 26,2001.

[23] Nash K, Hafeez A, Hou S. Hospital-acquired renal insufficiency. Am J Kidney Dis 2002; 39: 930-936.

[24] Baraldi A, Ballestri M, Rapana R, et al. Acute renal failure of medical type in an elderly population. Nephrol Dial Transplant. 1998;13(Suppl 7):25–29. [PubMed

[25] Druml W, Metnitz B, Schaden E, et al. Impact of body mass on incidence and prognosis of acute kidney injury requiring renal replacement therapy. Intens Care Med 2010;36(7):1221–8.87.

[26]Ujah IA, Aisien OA, Mutihir JT, Vanderjagt DJ, Glew RH, Uguru VE: Factors contributing to maternal mortality in north-central Nigeria: A seventeen-year review. *Afr J Reprod Health***9** :27– 40,2005

[27]Gokalp AS, Oguz A, Gultekin A: Acute renal failure related to infectious disease . *Ann Trop Paediatr***11** :119–121,1991

[28]Prakash J, Gupta A, Kumar O, Rout SB, Malhotra V, Srivastava PK: Acute renal failure in falciparum malaria: Increasing prevalence in some areas of India—A need for awareness. *Nephrol Dial Transplant***11** :2414– 2416,1996

[29] Lyanada Szeczch, MD, MSCE; the Studying the Treatment of Acute Hypertension Investigators :Circulation.2010; 121: 2183-219136.

[30]Girman C.J.,Kou T.D.,Brodovics K.,et al .Risk of acute renal failure patients with typre 2 diabetes mellitus. *Diabetic Medicine*.2012;29(5):614-621.doi:10.1111/j.1464-5491.2011.03498.x.[PudMed][Gross Ref]

[31]Fournier J-P, Lapeyre-Mestre M, Sommet A, et al. Laboratory monitoring of patients treated with antihypertensive drugs and newly exposed to non steroidal anti-inflammatory

drugs: a cohort study. PLoS ONE 2012;7(3):e341

[32]Perazella MA. Drug-induced renal failure: update on new medications and unique mechanisms of nephrotoxicity. *Am J Med Sci*.

[33]McCullough PA.Contrast-induced acute kidney injury.J Am Coll Cardiol.2008;51:1419-1428. .[PudMed]