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The Occurrence and Risk Factors of Acute Kidney Injury Among Patients Who Undergoing Cardiac Surgery

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Abstract: **Overview: Acute kidney injury (AKI) accounts for one to five percent of all hospital admissions. The most frequent cause of AKI in the intensive care unit (ICU) following infection is AKI following heart surgery. AKI is a frequent and dangerous side effect that occurs in 30–40% of adults and kids following CPB. Up to 5% of AKI cases require dialysis, and the death rate is close to 80%. On the other hand, mortality following heart surgery without AKI is within the range of 1% to 8%.**
Methodology: Observational prospective quantitative design study, 103 participants were included, preoperative risk factors, serum creatinine, demographic data collected, AKI post-cardiac surgery identified according to KDIGO criteria based on serum creatinine and urine output, the dynamic predictive scoring system used for risk prediction of AKI post-cardiac surgery.
Results: The occurrence of acute kidney injury (AKI) among patients undergoing cardiac surgery at three large hospitals in the west bank was twenty-seven cases (26.2%) and 76 (26.2%) normal cases according to diagnostic criteria. The result showed that stage 1 (19.4%) was the highest group of patients, followed by 4.9% of cases were stage 2, and the lowest group was stage 3. Regarding sociodemographic and clinical data, the results showed no statistical significance between patients with and without AKI (P>0.05). The results showed that oliguria time was statistically significant among patients with AKI than those without (P<0.05). Also, vasopressors (Noradrenaline, Adrenaline, Dopamine, and Dobutamine) time higher statistically significant among patients with AKI compared to those without AKI (P<0.05). Serum creatinine on day 3 was statistically significantly higher among patients with AKI than those without AKI (P<0.05). In contrast, the table showed that it is not statistically significantly different between patients with and without AKI regarding other days, urine output, oliguria time, hypotension, and vasopressors such as Noradrenaline, Adrenaline, Dopamine, and Dobutamine (P>0.05).
Conclusion: The incidence of acute kidney injury (AKI) among patients undergoing cardiac surgery is (26.2%), and the highest percentage was in stage 1 (19.4%), followed by (4.9%) in stage 2, and the lowest group was stage 3. AKI on day 3 post cardiac surgery showed a higher increase in serum creatinine, The oliguria time >6hrs, and Serum creatinine on day three are associated with the incidence of AKI.
Recommendation:
Further studies must be conducted in experimental design with a control group and a larger sample. Awareness about AKI post-cardiac surgery has to be increased including protocols and policies in the therapy regimen.

Keywords: Acute kidney injury; Cardiac surgery; CABG; Risk Factor.

Introduction:

1% to 5% of hospital admissions are acute kidney Injury (AKI) cases. In perioperative period AKI has serious implications on patient outcome, like the consistent association with increased mortality, morbidity, and a more complicated hospital course with associated cost-effectiveness implications (1).

After infection, AKI following heart surgery is the most common cause of AKI in the intensive care unit (ICU) (2). Furthermore, surgery is the primary cause of AKI in

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hospitalized patients (1). Depending on the criteria employed, the incidence of AKI following heart surgery varies from 18% to 47%. AKI is a frequent and severe complication following cardiac bypass surgery that affects 30–40% of adults and adolescents. Up to 5% of these people require dialysis due to AKI, and in these circumstances, the death rate is close to 80% (2). In contrast, the mortality rate following heart surgery for patients without acute kidney injury (AKI) ranges from 1% to 8% (3).

During cardiac surgery, several associated factors for AKI: aortic clamping; time of cardiopulmonary bypass (CPB)time; quantity of erythrocytes transfusion; and administration of vasopressors that decrease renal perfusion. These factors motivate the development of AKI. The contribution can be by a number of mechanisms like induced cycles of ischemia and reperfusion, increased oxidative damage, and increased renal and systemic inflammation (4).

Consequently, AKI associated with cardiac surgery has further complications. That is, it increases the risk of acquiring infection, increases the length of the hospitalization period in the intensive care unit as this leads to an increase in the cost of treatment and consumption of resources, and independently increases the mortality rate (5).

Methodology:

Design and setting: An observational prospective quantitative design study was conducted in the north of West Bank-Palestine in cardiac surgery wards at Al-Arabi Specialized Hospital in Nablus city, Nablus Specialized Hospital in Nablus, and the governmental Palestine Medical Complex in Ramallah city. These three hospitals receive patients from all over the West Bank.

Population and sample: The population is the patients who underwent cardiac surgery including coronary artery bypass graft (CABG), valve surgery or a combination of both. Consecutive sampling used. the Sample size n=103.

Exclusion criteria is: Age below 18 years old, patients with chronic renal failure and ends stage renal disease, congenital heart disease, patients with congenital and metabolic renal disease, and patients who have urology problems.

Data collection tools: The tool is divided into four parts; the first part is demographic data, medical history, medications, risk factors, and the dynamic predictive score system preoperative. The second part is on ICU admission post-operative using intraoperative parameters, the dynamic predictive scoring system and KDIGO criteria. The third part at 24 hrs. is the dynamic predictive score system and KDIGO criteria. The fourth part is the KDIGO checklist criteria from the second to the seventh day of post-operative followed up.

Statistical analysis: For data input and analysis, the researcher utilized the statistical package of social science (SPSS-version 25) program. The frequency of particular characters was described using the frequency results. When necessary, other statistical tests were employed, including the t-test, means and standard deviation (SD), and percentage (%), to determine whether the means of two groups varied statistically. The Chi-square test was employed to ascertain whether any noteworthy distinctions exist between the groups. Eventually, a statistically significant value was defined as a probability value (P-value) smaller than 0.05.

RESULTS:

Analyzing Descriptively The sample (n = 103) had a mean age of 56.0±10.9 years, a mean BMI of 28.0±4 kg/m2, and 91 (88.3%) of the participants were men. Surgery was the most prevalent procedure, with 81 cases (78.6%) undergoing CABG, 18 cases (17.5%) undergoing valve replacement, and 4 cases (3.9%) undergoing a combination of the two procedures. The average time for cross clamp was 54.5±21.5 minutes, and the average time for CPB was 88.2±34.1 minutes. The average serum creatinine level before to surgery was 0.89±0.18 mg/dL. His preoperative hemoglobin level was 13.6±1.5 g/dL, according to laboratory tests. In the 48 hours following heart surgery, 26.2% of patients experienced any kind of AKI. Of them, 20 (19.4%) were classified as having KDIGO stage 1, 5 (4.9%) as having KGIGO stage 2, and 2 (1.9%) as having KDIGO stage 3.

Table (1): preoperative factors:

Variables	Total (n=103)	Patients undergoing cardiac surgery		Statistical test		
		With AKI (n=27)	Without AKI (n=76)	t	c2	P-value
Diagnosis n (%)						
MI	14 (13.6)	5 (18.5)	9 (11.8)		6.222	0.101
IHD	38 (36.9)	7 (25.9)	31 (40.8)			
Unstable angina	34 (33.0)	13 (48.1)	21 (27.7)			
Valve disease	17 (16.5)	2 (7.5)	15 (19.7)			
Years of having DM±SD *(Min - Max)*	2.4±1.4 (0-17)	2.4±1.5 (0-17)	2.3±1.7 (0-15)	-0.120		0.905
Type of surgery n (%)						
CABG	81 (78.6)	25 (92.6)	56 (73.7)		0.054	0.108
Valve surgery	18 (17.5)	2 (7.4)	16 (21.1)			
Both	4 (3.9)	0 (0.0)	4 (5.3)			
DM n (%)						
Yes	35 (34.0)	8 (29.6)	27 (35.5)		0.309	0.578
No	68 (66.0)	19 (70.4)	49 (64.5)			

HTN n (%)						
Yes	57 (55.3)	16 (59.3)	41 (53.9)		0.227	0.633
No	46 (44.7)	11 (40.7)	35 (46.1)			
Years of having HTN±SD	3.7±1.2	3.9±1.6	3.6±1.1	-0.257		0.798
(Min - Max)	(0-15)	(0-15)	(0-15)			
COPD n (%)						
Yes	2 (1.9)	0 (0.0)	2 (2.6)		0.725	0.395
No	101 (98.1)	27 (100.0)	74 (97.4)			
NSAIDs n (%)						
Yes	2 (1.9)	2 (7.4)	0 (0.0)		5.741	0.067
No	101 (98.1)	25 (92.6)	76 (100.0)			
Preoperative Hemoglobin (g/dl) ±SD	13.6±1.5	13.9±1.1	13.5±1.7	-1.270		0.207
(Min - Max)	(9.5-16.9)	(12-15.6)	(9.5-16.9)			
Baseline Creatinine ±SD	0.89±0.18	0.88±0.23	0.9±0.17	0.491		0.625
(Min - Max)	(0.5-1.48)	(0.5-1.26)	(0.6-1.48)			
eGFR±SD	89.2±23.2	91.1±23.8	88.5±23.1	-0.492		0.624
(Min - Max)	(24-126)	(43-126)	(24-125)			
Left ventricular ejection fraction± SD	48±8.1	47.3±7.5	48.2±8.3	0.468		0.641
(Min - Max)	(30-65)	(35-60)	(30-65)			
NYHA score n (%)						
Class 1	19 (18.4)	5 (18.5)	14 (18.4)		1.817	0.611
Class 2	47 (45.7)	10 (37.1)	37 (48.7)			
Class 3	30 (29.1)	9 (33.3)	21 (27.6)			
Class 4	7 (6.8)	3 (11.1)	4 (5.3)			

SD: standard deviation **n:** number; **c^2:** chi square test, **t:** student t test. *****P < 0.05: significant, P ≥ 0.05: not significant

As shown in Table 1. Comparison Between the Patients With and Without AKI. The patients with AKI (n=27) did not differ significantly from those without AKI (n=76) in terms of the mean age was 53.1±12.4 years vs. 57.01±10.1 years (P=0.102); the mean preoperative baseline serum creatinine was 0.88±0.23 mg/dL vs. 0.9±0.17 mg/dL (P=0.625); the mean eGFR was 91.1±23.8 vs. 88.5±23.1 (P=0.624); the mean left ventricular ejection fraction was 47.3%±7.5% vs. 48.2%±8.3% (P=0.641). the mean duration of CPB was 86±35.5 minutes vs. 88.8±33.8 minutes (P=0.733); the mean duration of cross clamp was 55.7±24.8 minutes vs. 54.1±20.4 minutes (p=0.740) ; the mean duration of mechanical ventilation duration was higher in AKI group 16.4±30.6 hours vs. 12.6±26.1 hours (P=0.539).Vasopressors administration used in 51 patient

31.37% (n=16) of them developed AKI, while 21.15% (n=11) out of 52 of whom did not receive vasopressors patients develop AKI (P=0.238), red blood cells transfusion was higher in AKI group 0.8±2.1 units vs 0.7±1.5 units (P=0.733)

Table 2: dynamic predictive scoring system results:

		Total (n=103)	Patients undergoing cardiac surgery		Statistical test		
			With AKI (n=27)	Without AKI (n=76)	t	c^2	P-value
Preoperative dynamic predictive score	**Dynamic predictive score system ± SD (Min-Max)**	2.7±0.9 (1-5)	2.6±0.8 (1-4)	2.7±0.9 (1-5)	0.708		0.481
	The dynamic predictive score system						
	Low	4 (3.9)	1 (3.7)	3 (3.9)		0.372	0.337
	Medium	78 (75.7)	23 (85.2)	55 (72.4)			
	High	21 (20.4)	3 (11.1)	18 (23.7)			
Dynamic predictive score on ICU admission	**Dynamic predictive score system ±SD (Min-Max)**	3.5±1.7 (1-12)	3.4±2 (2-12)	3.5±1.7 (1-12)	0.296		0.768
	The dynamic predictive score system						
	Low	84 (81.6)	24 (88.9)	60 (78.9)		0.233	0.264
	Medium	17 (16.5)	2 (7.4)	15 (19.7)			
	High	2 (1.9)	1 (3.7)	1 (1.3)			
Dynamic predictive score at post operation on 24 hrs	**Dynamic predictive score system± SD (Min - Max)**	4.1±1.7 (2-13)	3.9±2.1 (2-13)	4.2±1.6 (2-13)	-0.0803		0.424
	Dynamic predictive score system n (%)						
	Low	75 (72.8)	22 (81.5)	53 (69.7)		0.267	0.281
	Medium	26 (25.2)	4 (14.8)	22 (28.9)			
	High	2 (2.0)	1 (3.7)	1 (1.4)			

We also found no significant difference between the patients with and without AKI in association to dynamic predictive scoring system over the three phases as shown in table 2.

Discussions

Occurrence of AKI post cardiac surgery:

In this study, the occurrence of acute kidney injury (AKI) among patients undergoing cardiac surgery was 27 cases (26.2%) and 76 (73.8%) normal cases according to diagnostic criteria,19.4% stage 1, 4.9% in stage and 1.9% stage 3 defined by KDIGO criteria . Shi et al., in their meta-analysis study, found that AKI occurrence was in 5%to 33% of pediatric cardiac surgery and 1% to 30% of adult cardiac surgery (6), Ng et al. 2016 reported the incidence of AKI post-cardiac surgery was 29.7% (7). This study result was higher than the 16.4% and 15.7% reported by Anderson et al. in 1993 (8) , And Kumada et al. in 2017 (9) in row, Machado et al., in 2014 among 918 patients found that 43 % developed AKI post-cardiac surgery, 35% classified as stage 1, 27% stage 2 and 5% stage 3 using KDIGO criteria(10). The difference in the occurrence of AKI related to different AKI definitions used by researchers and maybe for a different setting and treatment regimen.

Participants age:

In this study, the mean age of patients identified with AKI post-cardiac surgery was smaller than that of the non-AKI group (p-value 0.102). This study found that preoperative risk factors, including age, are not associated with AKI post-cardiac surgery, which agrees with earlier studies conducted by Gangadharan et al.in 2018, Zakkar et al. in 2016, and Lagney et al. ln 2015 (11–14). While other studies by Ng et al. in 2016, Kim et al. in 2015, and Jiang et al. in 2016 found that age is associated with AKI post-cardiac surgery (7,15,16).

Gender:

the gender in study male group larger than female group with high difference, moreover gender is not associated with AKI post cardiac surgery in this study (p value 0.919). this may be related to small sample of female gender (n=12). The impact of gender on risk assessment of AKI is still not clear. Che et al. in 2010, Khan et al. in 2017 and Xie et al. in 2017 in their retrospective studies showed that males are at more risk of developing AKI post cardiac surgery (Che et al., 2010; Khan et al., 2017; Xie et al., 2017). other retrospective studies have conducted by Machado et al. 2014 and Heise et al. in 2009 found that females at more risk of developing AKI post cardiac surgery (10,20). Ferreiro et al. in 2017 and Fang et al. in 2010 in their studies have proven that gender is not a risk of AKI post-cardiac surgery (21,22). Therefore, gender needs further investigations for the impact on the development of AKI post cardiac surgery.

Diabetes mellitus:

DM has no relationship to the occurrence of AKI post cardiac surgery as shown by results (p value 0.578), many previous studies showed that there was no relationship between DM and AKI post cardiac surgery (7,10,12,14,23), while Lagney et al.2015 found that there is an association between them (13). Most of earlier studies have found that DM is not a risk factor of AKI post Cardiac surgery.

Hypertension:

Hypothesis is: There is a significant relationship between patients with hypertension and occurrence of AKI post cardiac surgery at a level of P value 0.05. this hypothesis

rejected since results showed that HTN Has no association with AKI post cardiac surgery with P value 0.798, HTN had no relationship to AKI post cardiac surgery as reported in previous studies(7,14,15,23). But Jiang et al. 2016 and Lagney et al. 2015 reported no association between HTN and AKI post cardiac surgery (13,16).

Preoperative hemoglobin level:

In results p value is 0.207 which reflect that there is no association between preoperative Hgb level and AKI post cardiac surgery.

Preoperative Hgb value has association to AKI post cardiac surgery according to Ng et al. study in 2016 (7). But Chen et al. 2016 and Lagney et al. 2015 found no association between them (13,23). most of reviewed studies not included preoperative Hgb level in their studies.

Non-steroidal anti-inflammatory drugs (NSAIDs):

The results showed that there is no relationship between the usage of NSAIDs except Aspirin and AKI post cardiac surgery with p value of 0.067, hypothesis rejected, because of the small sample who subjected that they use NSAIDs, only 2 participants used NSAIDs and both developed AKI post operation. Tang et al. in 2020 has a different finding that parecoxib has a significant relation to occurrence of AKI postcardiac surgery(24). In addition, Guan et al. in 2019 confirmed that there is a relationship between NSAIDs usage and occurrence of AKI post cardiac surgery. (25) While Xie et al. in 2017 agreed my results (Xie et al., 2017).

Red blood cells transfusion:

In This study red blood cells transfusion is not associated with occurrence of AKI; P value is 0.771, Kim et al. 2015 and Neyra et al. 2019 found no association between AKI post Cardiac surgery and RBCs transfusion (14,15), while Jiang et al. and Ng et al in 2016 found the odd (7,16).

Baseline serum creatinine:

This study found that no relation between preoperative serum creatinine and occurrence ok AKI post-cardiac surgery with P value of 0.625. previous studies reported in there results that baseline SCr has no association to the occurrence of AKI post cardiac surgery (Kim et al., 2015; Machado et al., 2014), while another five studies found that baseline SCr is significant in occurrence of AKI post cardiac surgery (12,13,16,23,27).

Cardiopulmonary bypass time:

This study found no relation between the CPB and AKI post-cardiac surgery, with a P value of 0.733 and a mean of 88.2 min. Chen et al., in 2016, found the mean of CPB time to be 117.3 min, and Lagny et al., in 2015, found the mean of CPB time to be 85 min; the previously mentioned studies found that CPB time is not associated with AKI post cardiac surgery(13,23). However, Machado et al., in 2014, found CPB time mean of 90 min in the non-AKI group vs (100-110 min) in the AKI group and found. Kim et al., in 2015, found that CPB time of more than 180 min is associated with AKI post-cardiac surgery; these two studies found that CPB time is associated with AKI post-cardiac surgery (10,15).

Usage of vasopressors:

P-value (0.238) in this study usage of vasopressors up to 24 hrs post cardiac surgery showed no significant relationship between usage of vasopressors/inotropes and the occurrence of AKI in study sample. Chen et al., in 2016 in their study showed that 10.8% of study sample received inotropes, and found no relation between the usage of inotropes and AKI post cardiac surgery,

Mechanical ventilation time:

The AKI group's MV time was longer than the non-AKI group's 16.4±30.6 hrs vs. 12.6±26.1 hrs. Gao Xuxia et al. in 2020 found that MV of more than 96 hrs is a risk factor for AKI post-cardiac surgery (28). Moreover, Heringlake et al. 2014 found that an increase in postoperative mechanical ventilation time from 4 hrs to more than 16 hrs increases the incidence of AKI post-cardiac surgery from 17 % to 62.3 % (Heringlake et al., 2014). While Chen et al., in 2016, found that mv time (38.3±7.5hrs) is not associated with the occurrence of AKI post-cardiac surgery however, the aki group time was much higher than the non-AKI group(58.4±11.8 vs. 22.8±2.6 hrs), but in the same study found that 8.2%of study population received MV and has relation between usage of MV and occurrence of AKI post cardiac surgery(Chen et al., 2016; Jiang et al., 2016) .

The dynamic predicative scoring system score:

The dynamic predictive scoring system in this study has no relation to the occurrence of AKI post-cardiac surgery as it measured three times: preoperative, ICU admission, and on 24 hr post-cardiac surgery with a p-value of 0.481 in the preoperative period, 0.768 on ICU admission and 0.424 on 24 hr post cardiac surgery .this scoring system developed in 2016 by Jiang et al., as they found that dynamic predictive scoring system for AKI is suitable for prediction of AKI occurrence post-cardiac surgery with AUROC value of 0.74 preoperatively, 0.75 on ICU admission and 0.82 on 24 hrs post cardiac surgery(16).

Conclusions

The incidence of acute kidney injury (AKI) among patients undergoing cardiac surgery is elevated (26.2%) and the highest percentage in stage 1 (19.4%), followed by 4.9% in stage 2, and the lowest group was stage 3. The results showed no relation between the occurrence of AKI among patients undergoing cardiac surgery and sociodemographic data such as address, gender, age, and BMI (P>0.05). The results showed no association between the occurrence of AKI among patients undergoing cardiac surgery and clinical data were studied (Diagnosis, Years of having diabetes mellitus, Type of surgery, DM, HTN, Years of having HTN, COPD, and NSAIDs)

The results showed no association between patients with and without AKI regarding hemoglobin, creatinine, GFR, left ventricular ejection fraction, and dynamic predictive score (P>0.05). The oliguria time higher statistically significant among patients with AKI compared to those without AKI. There is no relation between AKI regarding CPB time, mechanical ventilation time, Cross clamp time, Packed RBCs, serum creatinine, dynamic predictive score system, intra-Aortic balloon pump usage, valve and CABG, kidney disease (without RRT), CPB application previous, cardiac surgery, hypotension, and vasopressors use.

Patients have AKI not associated with erythrocyte transfusion, dynamic predictive score system, oliguria time, serum creatinine, LCOS, hypotension, and urine output Serum

creatinine on day 3 was higher statistically significant among patients with AKI compared to those without AKI.No relation between the incidence of AKI and days, urine output, and oliguria time.

CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

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Availability of Data

The material is available upon reasonable request by corresponding authors

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