RESEARCH ARTICLE

Incidence of acute kidney injury and assessment of its associated risk factors in patients undergoing transarterial chemoembolisation for hepatocellular carcinoma

Kamran Muddasar Saeed,[1] Afifa Aftab,[2] Muhammad Abu Bakar,[3] Junaid Iqbal[4]

Abstract

Objectives: To determine the incidence of acute kidney injury in intermediate stage hepatocellular carcinoma patients undergoing trans-arterial chemoembolisation, and to analyse various causative factors.

Method: The retrospective study was conducted at the Shaukat Khanum Cancer Memorial Hospital, Lahore, Pakistan,, and comprised data from January 2012 to December 2015 of adult patients of either gender with intermediate stage hepatocellular carcinoma and undergoing trans-arterial chemoembolisation with Child-Pugh score A. Outcomes were measured in the form of development of acute kidney injury, and its causative factors. Data was analysed using SPSS 20.

Results: Of the 133 patients, 90(67.6%) were male. The overall mean age of the sample was 59±8.4 years (range: 26-86 years). Of these, 19(14%) developed acute kidney injury. Higher alpha-fetoprotein levels and lower albumin levels were found to be the significant causative factors ($p<0.05$).

Conclusion: The incidence of trans-arterial chemoembolisation-related acute kidney injury was 14%. Higher baseline alpha-fetoprotein and lower baseline albumin levels were found to be the significant risk factors.

Keywords: Transarterial chemoembolisation, TACE, Acute Kidney Injury, AKI, Hepatocellular carcinoma, HCC, Risk factors. (JPMA 72: 1057; 2022)

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Introduction

Hepatocellular carcinoma (HCC) ranks 6th in the world among the most common malignancies, and has an annual incidence of about 600,000.[1] HCC treatment is determined according to the stage of the disease. The Barcelona clinic liver cancer (BCLC) classification defines intermediate-stage HCC as multifocal tumour foci without vascular invasion and cancer-related symptoms, along with preserved liver function.[2] These intermediate stage HCCs are not definitely curable and are managed with trans-arterial chemoembolisation (TACE) which is considered an effective first-line therapy for HCC in such settings.[3] TACE is done by injecting a chemotherapeutic drug directly into the tumour-feeding artery employing interventional radiological guidance.[4] Like other radiologically-guided vascular procedures, a contrast agent is used for viewing the vessel(s) of interest. The use of contrast can be complicated by the development of acute kidney injury (AKI).[5] The incidence of contrast-related AKI among cardiovascular radiological procedures has been reported to range from 2% to 30%.[6] Specifically for TACE, the incidence of AKI has been reported in as many as 8.6% to 23.8% patients.[7] Various risk factors have been proposed for the predisposition of contrast-induced AKI, including hypovolaemia, diabetes mellitus (DM), cardiovascular disease (CVD), hypertension (HTN), nephrotoxic drugs, multiple myeloma, hyperuricemia, female gender, advanced age, and the volume and type of the contrast medium used.[8]

The current study was planned to determine the incidence of AKI in intermediate stage HCC patients undergoing TACE, and to analyse various causative factors.

Materials and Methods

The retrospective study was conducted at the Shaukat Khanum Memorial Cancer Hospital & Research Centre, Lahore, Pakistan, and comprised data from January 2012 to December 2015. After approval from the institutional ethics review board, data was retrieved from the hospital's electronic record system for consecutive patients aged >18 years who were diagnosed as having intermediate stage HCC based on the BCLC criteria,[2] and underwent their first TACE procedure. Only Child-Turcotte-Pugh (CTP) class A patients were included. The primary endpoint was the occurrence of AKI based on the acute kidney injury network (AKIN) criteria.[9]

AKI was defined as an increment in creatinine (Cr) of >0.5mg/dl or an increase of >25% from the pre-TACE baseline Cr level within 3 days (72 hours) post-procedure. The patients' files, including inpatient notes,

[1]KRL Hospital, Islamabad, Pakistan, [2]University of Sheffield, Sheffield, England, [3,4]Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan.

Correspondence: Kamran Muddasar Saeed. Email: dockamranms@gmail.com

procedure notes, and radiology reports as well as demographics, baseline clinical characteristics and the presence or absence of AKI, were reviewed. Also, AKI risk factors, like HTN, DM, ischaemic heart disease (IHD) and chronic kidney disease (CKD), were noted on the basis of the initial detailed pre-medical history obtained upon admission to hospital. Additionally, history of use of potentially nephrotoxic drugs, like non-steroidal anti-inflammatory drugs (NSAIDs) and aminoglicosides, in the preceding 3 months was noted. Data was analysed using SPSS 20. Categorical data was expressed as frequencies and percentages, while continuous variables were expressed as mean and standard deviations. Bivariate analysis was done using Chi-square or Fisher exact test, as appropriate, to compare categorical variables. Inferential statistics were computed using Chi-square or Fisher exact test (Rao-Scott adjustment). An independent t-test was employed for continuous explanatory variables. Statistical analysis was done using univariate and multivariate logistic regression models. Odds ratio (OR) with 95% confidence interval (CI) were calculated. $P \leq 0.05$ was considered statistically significant.

Table-1: Demographic data.

Variables	Categories	Akin Criteria	
		No-AKI 114 (85.7%)	AKI 19 (14.3%)
Sex	Male	78 (68.41%)	12 (63.16%)
	Female	36 (31.58%)	7 (36.84%)
CTP	A5	81 (71.1%)	10 (52.6%)
	A6	33 (28.9%)	9 (47.4%)
Total Bilirubin	mean ± SD	0.87 ± 0.47	1.02 ± 0.50
Albumin	mean ± SD	3.77 ± 0.44	3.52 ± 0.37
INR	mean ± SD	1.13 ± 0.13	1.13 ± 0.08
AFP	mean ± SD	58.38 ± 35.09	77.63 ± 35.91
Ascites	No	108 (94.7%)	19 (100.0%)
	Yes	6 (5.3%)	0 (0.0%)
Hepatitis	Both Negative	11 (9.6%)	1 (5.3%)
	HBV	7 (6.1%)	0 (0.0%)
	HCV	96 (84.2%)	17 (89.5%)
	Both Positive	0 (0.0%)	1 (5.3%)
Prior Drug	No	64 (56.1%)	17 (89.5%)
	Yes	50 (43.9%)	2 (10.5%)
NSAIDs	No	110 (96.5%)	19 (100.0%)
	Yes	4 (3.5%)	0 (0.0%)
ARB	No	88 (77.2%)	17 (89.5%)
	Yes	25 (21.9%)	2 (10.5%)
Diuretics	No	94 (82.5%)	19 (100.0%)
	Yes	20 (17.54%)	0 (0.0%)
ACEI	No	107 (93.9%)	19 (100.0%)
	Yes	7 (6.1%)	0 (0.0%)
Smoking History	No	90 (78.9%)	13 (68.4%)
	Yes	9 (7.9%)	2 (10.5%)
	Ex-Smokers	15 (13.2%)	4 (21.1%)
Obesity	Underweight	1 (0.9%)	0 (0.0%)
	Normal	36 (31.6%)	7 (36.8%)
	Overweight	46 (40.4%)	6 (31.6%)
	Obese	30 (26.3%)	6 (31.6%)
Diabetes	No	57 (50.0%)	13 (68.4%)
	Yes	57 (50.0%)	6 (31.6%)
HTN	No	60 (52.6%)	11 (57.9%)
	Yes	54 (47.4%)	8 (42.1%)
IHD	No	96 (84.2%)	15 (78.9%)
	Yes	18 (15.8%)	4 (21.1%)
Co-morbidity	No	37 (32.46%)	8 (42.11%)
	Yes	77 (67.54%)	11 (57.89%)

AKI: Acute kidney injury, CTP: Child-Turcotte-Pugh score, INR: International normalised ratio, AFP: Alpha-fetoprotein, NSAIDs: Non-steroidal anti-inflammatory drugs, ACEI: Angiotensin-converting enzyme inhibitors, HTN: Hypertension, IHD: Ischemic heart disease, SD: Standar deviation, HBV: Hepatitis B virus, HCV: Hepatitis C virus.

Results

Of the 133 patients, 90(67.6%) were male. The overall mean age of the sample was 59±8.4 years (range: 26-86 years). Of these, 19(14%) developed AKI. Complete demographic and clinical profile of the entire sample was done (Table-1).

Univariate and multivariate analysis sowed higher AFP and lower albumin levels to be the significant causative factors ($p<0.05$) (Table-2). The history of NSAID use was also significant ($p<0.05$), but the history was found in only 2(10.5%) AKI patients.

Table-2: Univariate and multivariate analyses.

Factors analysis,	Category	Univariate Analysis, odds ratio (95% CI), p-value	Multivariate odds ratio (95% CI), p-value
Age in years		1.03 (0.97, 1.09), 0.38	1.07 (0.99 1.16), 0.08
Total Bilirubin		1.79 (0.72, 4.60), 0.21	1.48 (0.36 6.09), 0.58
Albumin		0.24 (0.07, 0.85), 0.03	0.21 (0.04 1.06), 0.05
INR		0.69 (0.01, 39.91), 0.86	0.09 (0.01 17.41), 0.37
AFP		1.01 (1.00, 1.03), 0.03	1.02 (1.00 1.04), 0.01
Lipidol Volume		0.99 (0.95, 1.03), 0.71	0.99 (0.94 1.05), 0.76
Comorbidity	No	Ref	Ref
	Yes	0.66 (0.24 1.78), 0.41	0.55 (0.15 1.99), 0.36
Sex	Female	Ref	Ref
	Male	0.79 (0.29, 2.18), 0.65	0.54 (0.14 2.01), 0.36
BMI	Underweight	Ref	Ref
	Normal	1.25 (0.39, 4.01), 0.702	0.35 (0.07 1.71), 0.19
	Overweight	0.61 (0.17, 2.16), 0.40	0.63 (0.14 2.78), 0.55
	Obese	1	1
Prior Drug	No	Ref	Ref
	Yes	0.15 (0.03, 0.68), 0.01	0.09 (0.15 0.50), 0.01

Model good of fit with p-value (0.69).

CI: Confidence interval, INR: International normalised ratio, AFP: Alpha-fetoprotein, BMI: Body mass index.

Discussion

The incidence of AKI in the current study was 14%. The use of iodinated contrast media is a vital visual aid tool, be it a diagnostic imaging modality or an interventional procedure.[10] The contrast media can cause various side-effects, like nausea, vomiting, thyroid dysfunction, and hypersensitivity reactions, ranging from urticaria to anaphylactic shock.[11] Some of the risk factors for contrast-induced AKI include chronic renal insufficiency (estimated glomerular filtration rate [eGFR] <60 ml/min/1.73m^2), older age (>75 years), heart failure, nephrotoxic drugs, including aminoglycosides, NSAIDs, and amphotericin B, dehydration, sepsis, amount of contrast used, and intra-arterial administration.[12] Contrast-related AKI, however, is considered one of the most significant adverse effects, and this type of AKI is estimated to be the third commonest cause of hospital-based AKIs.[10,13] Rates of AKI development in interventional cardiology procedures are estimated to be 2-30%.[6] Data on other interventional radiology procedures are scarce, whereas, for patients undergoing TACE, the reported incidence ranges from 8.6% to 23.8%.[7] A population-based study evaluated the relationship between TACE in HCC patients and the development of AKI. A total of 2,324 HCC patients were evaluated in two equal groups; 1,132 who underwent TACE, and 1,132 who did not. After adjustment for age, gender, co-morbidities and drugs, the development of AKI in the TACE arm was found to be of statistical significance with a hazard ratio (HR) of 1.66, (95% CI: 1.17-2.34, p<0.05).[14] A retrospective study[15] showed an AKI incidence of 9.8% among 442 TACE treatment sessions in 236 patients. Risk factors in the study were found to be lower baseline serum albumin (OR: 0.29, 95% CI: 0.15-0.56, p<0.01), higher Cr levels (OR: 12.02, 95% CI: 3.49-41.39, p<0.01) and HTN (OR: 3.24, 95% CI: 1.21-8.72, p=0.02). All of these were independent risk factors for AKI development.

In a retrospective study,[16] the incidence of AKI was estimated to be 9.05%. The study cohort comprised 380 patients undergoing 453 TACE sessions. The statistically significant predictive risk factors included the CTP score (OR: 3.784, 95% CI: 1.899-7.542, p=0.000), pre-operative serum uric acid (OR: 1.450, 95% CI: 1.202-1.750, p=0.000), and proteinuria (OR: 2.393, 95% CI: 1.139-5.031, p=0.021). Another study[17] showed a similar incidence of post-TACE AKI and reported it to be 9% in a cohort of 101 patients undergoing 221 TACE procedures. The associated risk factor reported after multivariate analysis included CTP score (OR: 1.5; p=0.015). Similarly, a retrospective[18] study analysed a data set of 166 patients having undergone 301 TACE sessions. The AKI incidence was 7.59%, according to AKIN criteria, and 9.84%, according to Barrett and Parfrey criteria.[18] Multivariate logistic regression analysis revealed bilirubin (OR: 1.871) and haemoglobin (Hb) (OR: 1.823) to be independent risk factors for the development of AKI.

In comparison to the above-cited literature, the incidence of AKI in the current study was somewhat higher at 14%. Also, compared to the risk factors identified by the above-cited literature, the only risk factors found significant in the current study were higher levels of AFP and lower levels of albumin.

The possible reason for the disparity may be the relatively smaller sample size of the current study coupled with its retrospective nature, both of which are the study's limitations.

Conclusion

The incidence of TACE-related AKI was 14%. Higher baseline AFP and lower baseline albumin levels were found to be the significant risk factors. Early recognition of rising Cr or a fall in urine output can help reduce the risk of further decline in renal function, and improve patient outcomes.

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