

# Risk factors for acute kidney injury among patients with chikungunya: a multi-center experience from the 2017 chikungunya outbreak in Dhaka, Bangladesh

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## Abstract

**Background:** Chikungunya is an emerging viral infection in Bangladesh. This self-limiting febrile illness may have acute life-threatening features including cardiomyopathy and encephalitis. Acute kidney injury (AKI) is less well described complication of chikungunya. This study was designed to evaluate risk factors for AKI among patients with chikungunya virus infection.

**Methods:** This case-control study was done in 3 different centers in Dhaka, Bangladesh from July to October 2017. Adult patients (>18 years) with confirmed diagnosis of chikungunya were included in this study. AKI was diagnosed as per Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Acute Kidney Injury. Patients suffering from chikungunya complicated by AKI were cases and those without AKI were controls.

**Results:** Total patients were 107 (male 61) with a mean age of 35.6 (range 19-84) years. Common comorbidities were diabetes mellitus (DM) (20.6%), hypertension (17.8%) and chronic kidney disease (CKD) (12.1%). Common presentations included fever (86.9%) or recent history of fever (13.1%), joint pain (88.8%), rash (23.4%), pruritus (15.9%), gastro-intestinal (GI) features like diarrhea and/or vomiting (28%), lymphadenopathy (12.1%), gum swelling/oral ulcer (4.1%) and oedema (8.4%). Fourteen (13.1%) patients required hospitalization. Eleven (10.3%) cases were complicated by AKI. Among the risk factors for AKI, comorbidities like DM (OR 28.73, 95% CI 5.57-148.10,  $p < 0.0001$ ) and CKD (OR 31.0, 95% CI 2.94-326.7,  $p < 0.0001$ ), GI features (OR 16.07, 95% CI 3.22-80.14,  $p < 0.0007$ ), requirement of hospitalization (OR 23.10, 95% CI 2.37-226.31,  $p < 0.0001$ ) and use of angiotensin converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs) (OR 6.65, 95% CI 1.77-24.98,  $p < 0.005$ ) were significant.

**Conclusions:** One-tenth of adult patients suffering from chikungunya were complicated by AKI in this study. DM, CKD, diarrhea and/or vomiting, hospitalization and use of ACEIs/ARBs appeared as significant risk factors for AKI.

**Key words:** acute kidney injury, Bangladesh, chikungunya, Dhaka outbreak, risk factors.

(*BIRDEM Med J* 2019; 9(3): 193-196)

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**Received:** August 31, 2018

**Accepted:** July 31, 2019

## Introduction

Chikungunya is one of the most rapidly spreading mosquito-borne viral infections of global concern.<sup>1</sup> In Bangladesh, it is an emerging infection.<sup>2</sup> Generally, chikungunya is a self-limiting disease with fever and arthritis/arthralgia being the two most common features.<sup>1,2</sup> Chikungunya may have prolonged rheumatological complications and acute life-threatening features including cardiomyopathy and encephalitis.<sup>1</sup> Acute kidney injury (AKI)<sup>3</sup> and nephritis<sup>4</sup> are less well described complications of chikungunya. As patients with chikungunya may require non-steroidal anti-inflammatory drugs (NSAIDs)<sup>2</sup> for pain management, they may develop drug induced AKI as well. This study was designed to evaluate the frequency of AKI among patients with chikungunya and to evaluate associated risk factors in a chikungunya cohort of the 2017 chikungunya outbreak in Dhaka, Bangladesh.

## Methods

This case-control study included patients from 3 different hospitals in Dhaka, the capital city of Bangladesh namely Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital (14), Gulshan Maa O Shishu Clinic Pvt. Ltd. (64) and LabAid Gulshan (29) from July 1, 2017 to October 31, 2017. Adult patients (>18 years) with confirmed diagnosis of chikungunya<sup>5</sup> were included in this study. AKI was diagnosed as per Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Acute Kidney Injury.<sup>6</sup> Patients suffering from chikungunya complicated by AKI were cases and

those without AKI were controls. Increasing age, presence of diabetes mellitus (DM), chronic kidney disease (CKD), gastrointestinal (GI) symptoms including diarrhea and/or vomiting, requirement of hospitalization in severe cases, concomitant use of angiotensin converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs) and NSAIDs were evaluated as possible risk factors for AKI.

## Results

Total patients were 107 (male 61, female 46) with a mean age of 35.6 (range 19-84) years. Over two-thirds (74, 69.2%) of the patients were from Dhaka North City Corporation and rest (33, 30.8%) were from Dhaka South City Corporation.

Common comorbidities were DM (22, 20.6%), hypertension (19, 17.8%), CKD (13, 12.1%), dyslipidaemia (11, 10.3%), fatty liver disease (9, 8.4%) and ischaemic heart disease (7, 6.5%). Common presentations included fever (93, 86.9%) or recent history of fever (14, 13.1%), joint pain (95, 88.8%), rash (25, 23.4%), pruritus (17, 15.9%), diarrhea and/or vomiting (30, 28%), lymphadenopathy (13, 12.1%), gum swelling and/or oral ulcer (5, 4.1%) and oedema (9, 8.4%). Two patients had chikungunya-dengue co-infections.<sup>7,8</sup> Most (93, 86.9%) patients were managed as out-patient basis while 14 (13.1%) patients required hospitalization.

Eleven (10.3%) cases were complicated by AKI. Risk factors for AKI included increasing age, comorbidities like DM ( $p < 0.0001$ ), CKD ( $p < 0.0001$ ), diarrhea and/or vomiting ( $p < 0.0007$ ), requirement of hospitalization ( $p < 0.0001$ ), use of ACEIs/ARBs ( $p < 0.005$ ) and NSAIDs (Table I).

**Table I** Risk factors for AKI among patients with chikungunya (N=107)

Risk factors		AKI (11)	No AKI (96)	Odds ratio, 95% CI, p value
Age (>55 years)	Yes (46)	7	39	2.55, 0.70-9.33, 0.1550
	No (61)	4	57	
DM	Yes (22)	9	13	28.73, 5.57-148.10, 0.0001
	No (85)	2	83	
CKD	Yes (13)	10	3	31.00, 2.94-326.71, <0.0001
	No (94)	1	93	
Presence of GI symptoms	Yes (30)	9	21	16.07, 3.22-80.14, 0.0007
	No (77)	2	75	
Required hospitalization	Yes (14)	10	4	23.10, 2.37-226.31, <0.0001
	No (93)	1	92	
Use of ACEI/ARB	Yes (27)	7	20	6.65, 1.77-24.98, 0.0050
	No (80)	4	76	
Use of NSAIDs	Yes (9)	2	7	2.88, 0.51-15.69, 0.2351
	No (98)	9	89	

## Discussion

AKI is common in community and in hospital settings and may have diverse aetiology.<sup>9-12</sup> Chikungunya viral infections have few but life threatening acute complications like encephalitis<sup>13</sup> and cardiomyopathy<sup>14</sup>, but nephritis<sup>4</sup> is rarely reported. Infection associated glomerulonephritis and AKI is common in tropics<sup>15-17</sup>, but as an aetiology, chikungunya<sup>3,18</sup> is occasionally mentioned. We assume, as a cause of AKI, chikungunya is a potential candidate because patients may have GI symptoms causing volume depletion and pre-renal AKI, they are prone to develop NSAIDs induced AKI as many patients are likely to require pain killers<sup>2</sup> in acute chikungunya arthritis.

In the present chikungunya cohort, one-tenth of patients developed AKI, but this ratio rises to over two-thirds (10/14, 71.4% ) when calculated among patients who required hospitalization, which is much higher than overall incidence of AKI in hospital settings, even if we compare with AKI incidence in intensive care units.<sup>10,11</sup>

Patients with DM are at increased risk for AKI than non-diabetic counterparts<sup>19</sup> which was also evident in the present study. CKD is also a risk factor for AKI.<sup>20</sup> Thirteen of our patients had pre-existing CKD and 10 (10/13, 76.9% ) of them were complicated by AKI.

Diarrhea and vomiting causes intravascular volume depletion and if not properly replaced by oral or intravenous route (if required), they may be complicated by AKI.<sup>21</sup> This is more common in cholera and other causes of acute gastro-enteritis, but also appeared to be true in our chikungunya cohort. In the setting of surgery and volume depletion, concomitant medications like ACEIs/ARBs need to be revised, at least for a temporary basis, as haemodynamic alteration predisposes these patients to AKI.<sup>22</sup> One-third of our patients, who were receiving ACEIs or ARBs had AKI while this ratio was only one-nineteenth among those not receiving such drugs.

NSAIDs are well recognized cause for AKI. Chikungunya characteristically cause arthritis/arthralgia along with fever.<sup>2</sup> Nearly ninety percent of patients had joint pain in this chikungunya cohort. Initially they were managed with paracetamol, but nine patients required NSAIDs for pain management. Two (2/9, 22.2%) had AKI while 9 (9/98, 9.2%) patients who did not require NSAIDs developed AKI. So, use of NSAIDs in

chikungunya arthritis was not proved to be a significant risk factor for AKI in this study, which may be due to small sample size in our cohort.

In conclusion, one-tenth of patients suffering from chikungunya were complicated by AKI in this study and comorbidities like DM and CKD, presence of GI symptoms like diarrhea and/or vomiting, requirement of hospitalization and concomitant use of ACEIs/ARBs appeared as significant risk factors for AKI. So, patients with DM, CKD and those receiving ACEIs/ARBs should be warned for possible development of AKI, if they acquire chikungunya viral infection and suggested for adequate fluid replacement in case of diarrhea and vomiting.

**Conflict of interest:** Nothing to declare.

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