

# Pandemic Influenza A (H1N1) 2009 Outbreak Investigation in Nepal

Mahato RK,<sup>1</sup> Bhandari GP,<sup>2</sup> Shrestha JM,<sup>1</sup> Basnet P<sup>2</sup>

<sup>1</sup>Avian Influenza Control Project, <sup>2</sup>Nepal Health Research Council, Kathmandu, Nepal.

## ABSTRACT

**Background:** The World Health Organization, on 24 April 2009, announced a Public Health emergency of international concern caused by a new influenza virus Pandemic Influenza A 2009. The objective of this study was to analyze the basic epidemiology and distribution of Pandemic Influenza A 2009 in order to understand the course of Pandemic Influenza A 2009 in Nepal.

**Methods:** The analyses were based upon all confirmed and probable cases that consulted Avian Influenza Control Project and National Public Health Laboratory during 29 April 2009 to 21 September 2010.

**Results:** Out of total 739 suspected samples collected, Pandemic Influenza A 2009 was detected in 210 cases in different districts of Nepal. The majority of cases were from the urban settlement of Kathmandu valley, Chitwan and Kaski and among age group 11-30 years. The clinical attack rate for Influenza like illness (ILI) was 28.48%. There was no significant difference between the clinical presentation of ILI and confirmed cases of Pandemic Influenza A 2009.

**Conclusions:** This study presented the investigation of outbreak that helped to inform the course of epidemic in affected population and therefore urge for public health interventions.

**Key words:** influenza, outbreak, pandemic

## INTRODUCTION

Influenza pandemic occurs when a new influenza virus sub-type evolve and establish sustained human to human transmission across the continents. The World Health Organization (WHO) announced on 24 April 2009 a Public Health emergency of international concern caused by a new influenza virus Pandemic Influenza A (H1N1) 2009. The initial focus of the infection was Mexico. However, international travel facilitated the geographical spread of influenza A (H1N1) virus throughout the world.<sup>1,2</sup>

In Nepal, the first case of Pandemic Influenza A (H1N1) 2009 was confirmed in June 29, 2009. However, Community transmission within the local population started in different parts of Nepal after October 5, 2009.<sup>3</sup>

Based on the cases that consulted Avian Influenza Control Project (AICP) and National Public Health Laboratory (NPHL), we analyzed the basic epidemiology and distribution of Pandemic Influenza A (H1N1) 2009 in

**Correspondence:** Mr. Raj Kumar Mahato, Epidemiologist- Avian Influenza Control Project Department of Health Services, Teku, Kathmandu, Nepal. Email: mahatork@gmail.com, Phone:9849195850.



The clinical attack rate of ILI was 28.48 %. Throat swabs were collected from 739 suspected cases, among which Pandemic Influenza A (H1N1) 2009 virus detected in 210 (28.41%) cases, Influenza swine A in 8 (3.68%), Influenza H1 in 15 (7%) and both swine A and H1 in 187 (89.04%) suspected cases.

Symptoms were similar in confirmed and negative cases of Pandemic Influenza A (H1N1) 2009. All cases were tested by PCR. Spectrums of disease ranging from non-febrile mild upper respiratory tract illness to severe of fatal pneumonia were described. The most commonly reported symptoms were fever (95.24%), Cough (90.47%), Sore throat (85.71%), Headache (88.09%), Rhinorrhoea (85.23%), Abdominal pain (25.24%), Vomiting (5%). There was no significant difference between the clinical presentation of ILI and confirmed cases of Pandemic Influenza A (H1N1) 2009.

The mean duration of illness (i.e., symptomatic period) was 4 days. Some cases required hospitalization due to high-grade fever and received supportive treatment in terms of antibiotics and antipyretics, balanced diet and adequate rest. Hospitalization ranged between 1 and 6 days (median -3 days). There were three cases of respiratory complications observed in cases at discharge and even at follow-up till first week of September.

## DISCUSSIONS

The article describes an outbreak of the Pandemic Influenza A (H1N1) 2009 in confirmed 210 cases of the suspected 739 cases consulted to AICP and NPHL. This study shows that majority of the confirmed cases of pandemic influenza A (H1N1) 2009 in Nepal are from the urban settlement districts like Kathmandu, Chitwan and Kaski. This finding is similar to other study findings that suggest the infection seeding urban centres.<sup>2</sup>

The majority of cases of Pandemic Influenza A (H1N1) 2009 in Nepal have occurred among adolescents and young adults. Similar to this study, another study findings also suggest that most of the cases occurred among adolescents and young adults.<sup>2</sup>

In this study most of cases of Pandemic Influenza A (H1N1) 2009 were detected during winter months. The occurrence of higher number of cases of Pandemic Influenza A (H1N1) during winter months could be attributed to the fact that winter season is favorable influenza virus transmission.

Following the investigations, since the detection of cases of Pandemic Influenza A (H1N1) 2009 in Nepal, authorities proactively began to administer Oseltamivir to cases and contacts. People with high-grade fever

were temporarily shifted to the hospital and taken care of following better personal hygiene and refrained from group activities (clustering) and close contacts with symptomatic cases. This led to curbing of transmission. Oseltamivir administered to confirmed cases and their close contacts prevented serious complications. A study in India has also suggested similar prevention measures for Pandemic Influenza H1N1 2009.<sup>5</sup>

## CONCLUSIONS

This study showed that out of the total 739 suspected samples collected, Pandemic Influenza A (H1N1) 2009 was detected in 210 cases in different districts of Nepal. The majority of cases were from the urban settlement of Kathmandu valley, Chitwan and Kaski and among adolescents and young adults. The study showed that winter months were favorable for influenza virus transmission. This study presented the investigation of outbreak that helped to inform the course of epidemic in affected population and therefore urge for public health interventions.

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# Serum Gamma glutamyl transferase and Alkaline phosphatase in Acute Cholecystitis

Thapa PB,<sup>1</sup> Maharjan DK,<sup>1</sup> Suwal B,<sup>1</sup> Byanjankar B,<sup>1</sup> Singh DR<sup>1</sup>

<sup>1</sup>Department of General Surgery, Kathmandu Medical College Teaching Hospital, Kathmandu, Nepal.

## ABSTRACT

**Background:** The serum level of gamma glutaryl transferase and alkaline phosphatase is raised in acute calculus cholecystitis and common bile duct stone. However, the rise in serum level of these enzymes in acute cholecystitis implies stone in the common bile duct is not well studied. Thus, it may lead to retained CBD stone on one side and unnecessary CBD exploration on the other during emergency laparoscopic cholecystectomy. The objective of the study is to predict presence of CBD stone by assessing serum level of gamma-glutamyltransferase (gamma-GT) and alkaline phosphatase.

**Methods:** A prospective study was designed which included 40 patients with clinically diagnosed and radiologically confirmed acute cholecystitis and 40 patients who had choledocholithiasis with or without cholangitis. Their serum gamma glutaryl transferase and alkaline phosphatase were analyzed.

**Results:** Both acute cholecystitis and CBD pathology had significant increase in alkaline phosphatase (p-value: 0.05). However, in acute cholecystitis there was  $1.69 \pm 0.118$  fold increase and in CBD pathology there was  $2.5 \pm 0.57$  fold increase in alkaline phosphatase than normal (130 IU /L). There was no statistically significant difference in gamma-GT in both acute cholecystitis and CBD pathology (p-value: 0.390). However it increases by  $2.8 \pm 0.47$  fold in acute cholecystitis and by  $2.2 \pm 0.16$  in CBD pathology (p value: 0.627).

**Conclusions:** Although there is rise in serum gamma-GT and alkaline phosphatase level in acute cholecystitis and CBD stone, only more than 2.5 fold rise in serum alkaline phosphatase level predicts CBD stone.

**Key:** words: acute cholecystitis, alkaline phosphatase, common bile duct stone, gamma glutaryl transferase

## INTRODUCTION

Laparoscopic cholecystectomy is an established treatment modality for acute cholecystitis.<sup>1</sup> However, 10-15% of patients with symptomatic gall stones undergoing cholecystectomy might have associated common bile duct stone.<sup>2-5</sup> Hence, preoperative evaluation are done and choledocholithiasis may be suspected if a patient with gall stone have jaundice, cholestatic liver function test and with abnormal ultrasonography. However, ultrasonography of abdomen to detect CBD

stones have sensitivity of 25-58 % and specificities of 68% to 91%<sup>6-10</sup> despite dilated common bile duct which may be due to obscuration of the distal duct by overlying bowel gas, small stones in a nondilated bile duct and misdiagnosis of soft pigment or an impacted stone as a tumor. Proper selection of patients for further biliary imaging like MRCP, ERCP, and IOC to exclude CBD stones is crucial to minimize patient morbidity and institutional cost. Clinical correlation with liver enzymes, as well as

**Correspondence:** Dr. Prabin Bikram Thapa, Department of General Surgery, Kathmandu Medical College Teaching Hospital, Baburam Sadak, Sinamangal, Kathmandu, Nepal. Email: prabin\_bt@rediff.mail, Phone: 9851002303

USG findings, helps in establishing the pretest probability of CBD stones. Studies have shown that there is raised serum bilirubin level including alkaline phosphatase, transaminases enzyme and gamma-glutamyltransferase (gamma-GT) level in acute cholecystitis, which might suggest further clinical implications of investigations like MRCP, ERCP or intraoperative cholangiogram to rule out CBD stone or perform unnecessary CBD exploration for suspected stone.<sup>11-14</sup> However, in acute calculus cholecystitis without radiological CBD stones, prediction of CBD stones with relation to liver function test has not been well studied.

Thus to overcome expensive and intervening investigations or getting chance of under treatment this study is designed to predict presence of CBD stone by assessing serum level of gamma-glutamyltransferase (gamma-GT) and alkaline phosphatase.

**METHODS**

A prospective case control study was conducted in Department of Surgery, Kathmandu Medical College Teaching Hospital from 1<sup>st</sup> Jan 2008 to 30<sup>th</sup> August 2008. The ethica approval from ethical committee was taken. Total 80 patients were enrolled in this study. Forty patients were clinically diagnosed and radiologically confirmed acute calculus cholecystitis without choledocholithiasis. Another group consisted of 40 patients with radiologically diagnosed choledocholithiasis with or without cholangitis and biliary pancreatitis.

Exclusion criteria were acalculus cholecystitis, acute cholecystitis with incomplete radiological evaluation of CBD. In all patient beside other pre-operative investigations, complete liver functions test were sent and only serum gamma-glutamyltransferase (normal value: 90IU/L) and alkaline phosphatase levels (normal value: 130 IU/L) were evaluated and compared. The statistical packages for social sciences (SPSS) version 11.5 version was used and statistical analysis done using paired t-test

**RESULTS**

In this study, both in acute cholecystitis and CBD pathology, there was significant increase in alkaline phosphatase than normal (130 IU/L) (p-value: 0.05) (Table1). However, there was rise in serum alkaline phosphatase by 2.5±0.57 fold than normal value (130 IU/L) in CBD stone disease while it raised by 1.69±0.118 fold in acute cholecystitis (Figure 1, 2).

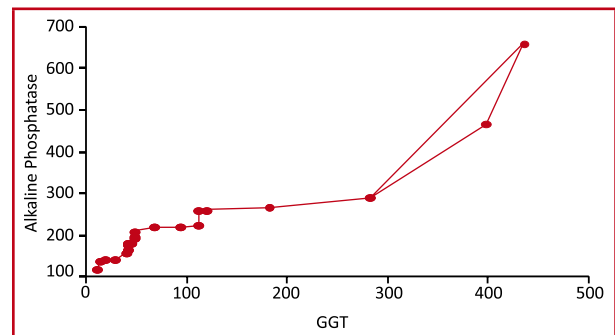
Beside there is no statistically significant difference in GGT in both acute cholecystitis and CBD pathology (p-value: 0.390). However it increases by 2.8±0.47 fold in

acute cholecystitis and by 2.2±0.16 in CBD pathology (p value: 0.627).

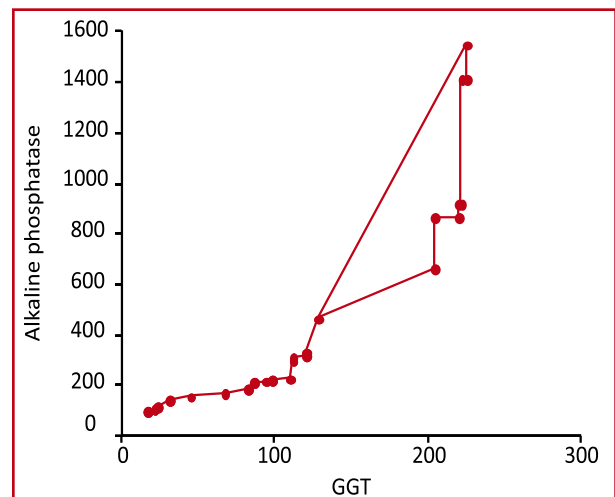
**Table 1. Serum alkaline phosphatase and gamma-glutamyltransferase in acute cholecystitis and CBD pathology.**

	Acute cholecystitis N=40	CBD pathology N=40	P value*
Mean Serum Alkaline phosphatase ± SE	215.70±15.12	394.15±60.21	0.05
Mean Serum Gamma-Glutamyl transferase (gamma-GT) ± S.E.	90.60±15.69	106.90±10.44	0.390

\*paired t-test



**Figure 1. Alkaline phosphatase and gamma-Glutamyl transferase (gamma-GT) in acute cholecystitis**



**Figure 2. Alkaline phosphatase and gamma-glutamyltransferase (gamma-GT) in CBD pathology.**

## DISCUSSIONS

Liver function test has been used as a routine pre-operative evaluation for gallbladder surgery as a tool to check for functional status of the liver. Moreover, it has been used to predict CBD stones along with clinical history of jaundice, raised level of bilirubin, alkaline phosphatase and gamma-glutamyl transferase with ultrasonography of abdomen with dilated CBD stones indicating obstructive biliary outflow after stratification with positive predictable value ranging from 18% (without predictors) to 94% (with positive predictors).<sup>15-17</sup> Though elevated serum alkaline phosphatase only exhibit positive likelihood ratio of less than three,<sup>18</sup> it is cost effective tool for predicting CBD stone along with other parameters. In our study there was rise in serum alkaline phosphatase level by  $2.5 \pm 0.57$  fold than normal value (130 IU/L) in CBD stone disease while it raised by  $1.69 \pm 0.118$  fold in acute cholecystitis with significant statistical difference. So if serum alkaline phosphatase is more than 2.5 folds higher than normal value, we could predict CBD stones.

However, alkaline phosphatase is non-specific indicator of cholestatic liver disease because of multiple sources like bone and placenta beside its production from biliary canalicular membrane<sup>19</sup> hence together with determination of more specific hepatic enzymes such as gamma-glutamyl transferase, it helps to predict cholestasis. Hence in our study both alkaline phosphatase and gamma-glutamyl transferase had to be raised for inclusion criteria to minimize this error.

Similarly, gamma-GT level more than 90 IU/L is considered being high risk to have stone in CBD though not statistically significant in our study which is supported by many series.<sup>20-24</sup>

It is better to predict CBD stones preoperatively with simple cost effective means in order to avoid retained stone in one hand and avoid expensive investigation and unwanted intervention either choledochotomy or ERCP on other hand.

Though MRCP has excellent overall sensitivity 95% and specificity 97% for demonstrating the level and the presence of biliary obstruction,<sup>25</sup> it is expensive as it cost \$135 which exceeds the total cost of laparoscopic surgery in our institute. Thus, it is not economically viable. ERCP had a sensitivity of 90%, a specificity of 98%, and an accuracy of 96% in the evaluation of CBD stones when IOC was used as the reference.<sup>26</sup> However, large prospective case series have found overall complication rates of 5% to 10% and mortality rates of 0.02% to 0.5% after diagnostic and therapeutic ERCP.<sup>27-30</sup> Intraoperative

cholangiogram though recommended by some surgeons, it is time consuming and has a sensitivity of 87% and a specificity of 98% in the detection of CBD stones,<sup>31,32</sup> moreover patients are exposed to radiation hazards and are difficult to interpret.<sup>33</sup> So the authors have made a practice to investigate further to rule out CBD stone if and only serum alkaline phosphatase is more than 2.5 times the normal value.

Although the study was conducted with a small sample size and at a local institute, further studies are recommended in a multicentric approach to validate the finding of the study and provide further evidence.

## CONCLUSIONS

Serum alkaline phosphatase level is raised in acute calculus cholecystitis and CBD stone disease. But stone in CBD is predicted only if its level is raised by 2.5 times the normal value. GGT level is also raised in both clinical conditions. However it doesn't predict stone in CBD.

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