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How much the Nipah threat reduced in Bangladesh?

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The community awareness for Nipah virus infection (Nipah) is supposed to be increased in Bangladesh, especially citizens' high risk behaviours like consumption of raw date palm sap or partially eaten fruits by bats have been observed reduced significantly. But the recent report of Nipah in neighbouring India again increased the concern of the infection. As of May 2018, thirteen deaths due to Nipah were reported from Malappuram and Kozhikode Districts of Kerala State, India.^{1,2} Three among the deaths occurred in a family cluster and a fourth death was subsequently reported in a health care worker who was involved in treatment of the family in the local hospital, indicating person-to-person transmission of the virus.¹ The field investigation team found bats living in an abandoned water well on the premises of a new house and initially, it was suspected that the Nipah infection in Kerala was due to fruit bats. Although specimens collected from the droppings, saliva and blood of bats were tested negative for Nipah virus (NiV) initially in May 2018, subsequently it was found that the specimens were from insectivorous wrong bats.^{3,4} On July 4, 2018 issue of the Times of India mentioning that wrong bats were trapped and tested in May and confirmed, giving reference with Indian Council of Medical Research (ICMR) that fruit bats were the primary source of the Kerala outbreak.⁴ There were few more outbreaks of Nipah or Nipah-like viral encephalitis in India during January-February of 2001 in Siliguri (with 68% mortality) and during April, 2007 in Nadia (with 100% mortality) showing the same person-to-person transmissions,² which are geographically more close to Bangladesh.

In Bangladesh, the first identification of NiV as a cause of an outbreak of encephalitis was reported in 2001 in Meherpur district. Since then, outbreaks of NiV encephalitis have been reported almost every year in some districts of Bangladesh. Since 2001, the Nipah outbreaks in Bangladesh have been reported from 23 districts mostly from the north-western and central part of the country constituting the so-called "Nipah belt". Among the districts, some were frequently hit by repeated attacks of outbreaks include: Rajbari (2004, 2008, 2009, 2010, 2011, 2014, 2015), Faridpur (2004, 2010, 2011, 2014, 2015), Naogaon (2003, 2007, 2012, 2014, 2015), Nilphamari (2009, 2011, 2014, 2015), Mankganj (2008, 2013, 2014), Natore (2007, 2013) and Pabna (2007, 2013).^{2,5-9} Up to February, 2015, a total of 261 human cases of Nipah has been identified in Bangladesh of which 198 (75.8%) died, although the case-fatality was reported to range from 0-100%.⁶⁻⁹

All of the index cases of the outbreaks in Bangladesh have been reported to be transmitted by consumption of raw date palm sap and few others were reportedly transmitted through direct contact with the primary cases during nursing indicating again the person-to-person transmission.^{7,10,11} In the affected areas, it has been observed that consumption of raw date palm sap during the winter evening and early morning hours was very popular. The unparalleled sweet taste of palm sap has an irresistible attraction. There are some village fairs and even in cities where drinking raw date palm juice is a celebration. Perhaps they could not understand

the fact that the juice-extracting head-ends of the date trees were found contaminated by fruits bats several times of their movements during the nights. The bats were caught by Infrared cameras during the nights and found to taste secreting juices from the extracting areas and the collecting tubes. They were also found to leave excreta over the juice extracting areas of the trees.¹⁰ Therefore, it is very obvious that the viruses, they were carrying in their saliva or urine, could easily contaminate the date juices which were drunk raw during the morning by some people. An intervention study to prevent the transmission of NiV from bat to date palm sap revealed that physical barrier may prevent the contact of sap from bat if properly covered the sap area.¹² Drinking Tari, a traditional liquor made from date palm sap, is also found as one of the potential pathways of transmission.¹³ Though alcohol act as the sterilizer of the virus but the alcohol concentration in Tari that is only 5-8 percent might not be high enough to sterilize NiV and the ambient temperature which is 15° to 28°C in Winter is also a factor for the survival of virus.¹⁰ There was no involvement of pigs in NiV transmission in Bangladesh, as was observed in the village Kampung Sungai Nipah of Malaysia or in Singapore during outbreaks in 1998-99.¹⁴ Nipah is a rapidly progressive disease affecting the central Nervous system and Respiratory system. The median incubation period ranges from 6-11 days after exposure to an infected person.¹⁵ Fever, altered mental status, headache, cough or cold, respiratory difficulty, vomiting and convulsion are the most common clinical features.¹⁵ But the epidemiological linkage is very important for the primary suspicion of patient with Nipah.¹⁶

The clinical data from different outbreaks of Nipah in Bangladesh and outbreaks in Malaysia revealed significant differences; with shorter and more narrow range of incubation period in patients from Bangladesh outbreaks.¹⁷ The respiratory symptoms are more common in Bangladeshi patients. There were two distinct strains of virus affecting Bangladeshi and Malaysian population. There is difference in

pathogenicity and transmission pattern and mortality rate, which suggests the virus isolated from Bangladesh are more pathogenic than Malaysian strains.¹⁷ According to the Times of India on 30th May, 2018, scientist of National Institute of Virology, Pune confirmed that the virus responsible for the outbreak in Kerala has the genetic makeup similar to Bangladeshi strain. They reached the conclusion by decoding the full genome sequence of the virus identified from throat swab specimens of the patients.¹⁸

Now, considering the currently available information, it can be concluded that the existence of NiV in the Nipah belt of Bangladesh as well as in other Southeast Asian countries could not be contained adequately. The Malaysian outbreak was contained immediately after the 1998 outbreak by mass culling of the suspected pig population and no other reports have been found, although the identified source of infection of pig industry is still in its full blown growth. Whereas in Bangladesh, the infection is occurring repeatedly in almost every year claiming some lives in spite of all the efforts. Identification of reservoirs of the infection and modes of transmission of NiV requires much more efforts to adopt the effective measures for containment of Nipah in Bangladesh.

In the meantime, the Institute of Epidemiology Disease Control and Research (IEDCR) with the support of Health Education Bureau under Ministry of Health and family welfare in Bangladesh have developed health messages regarding the date palm sap consumption, where instructed to avoid drinking raw date palm juice.¹⁹ Now it appears that we have to work more intensively with the Nipah cases- more careful contact-tracing can explore the exact natures of transmissions in Bangladesh and explore any other possible modes. If consumption of raw date palm sap be the only significant mode of transmission, more aggressive programs involving inter country endeavours to include all possible measures like (i) compulsory addition of barriers on juice extracting areas of date tree to impede contamination by bats²⁰, (ii) banning of

consumption of sale or consumption of raw date palm sap, (iii) extensive health education program in the Nipah belt, etc should be adopted as soon as possible to exclude repeated attacks of Nipah outbreaks in Bangladesh or in the other South East Asian countries.

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Bacterial Isolates and Antibiotic Susceptibility Pattern in Patients with symptomatic Urinary Tract Infection at out Patient settings in Sirajganj, Bangladesh

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ABSTRACT

Introduction: Urinary Tract Infection (UTI) is one of the commonest infections requiring antibacterial treatment. Antibiotic resistance is rising worldwide and a global concern. Knowledge on local spectrum of uropathogens and antibiotic susceptibility may guide selecting appropriate antibiotics and overcoming bacterial resistance.

Methods: We have conducted a cross-sectional study on UTI among symptomatic patients at Nephrology OPD in 250 bed General Hospital, Sirajganj. All symptomatic patients having significant pyuria (pus cells 10/HPF) and not on antibacterial drugs were advised for urine culture and sensitivity test done at North Bengal Medical College Hospital, Sirajganj. **Results:** Among 75 UTI cases 30 (40%) were male and 45 (60%) female. Age ranging was from 4.5 years to 85. Mean age 39.33 ± 19.23 . Among 75 positive culture Escherichia coli 73 (97.34%), one Klebsiella (1.33%) and one Staphylococcus aureus (1.33%) were isolated. Amikacin 64 (87.67%), imipenem 61 (83.56%), chloramphenicol 55 (77.46%) and nitrofurantoin 54 (73.97%) showed sensitivity to E. coli. In contrast erythromycin 69 (95.24%), cephhradine 61 (89.55%) and ceftazidime 60 (88.73%) were resistant to E. coli. **Conclusion:** Periodic surveillance of uropathogens and antibiotic susceptibility is needed for effective empirical treatment of UTI and overcoming antibiotic resistance.

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INTRODUCTION

Urinary tract infection (UTI) is one of the most common bacterial illnesses in adults, and is one of the most common indications for antibiotics.^{1, 2} Women have a one-in-three lifetime chance of developing a UTI³ about 50 times more than for men.⁴ UTI may be symptomatic or asymptomatic, complicated or uncomplicated, upper (pyelonephritis) or lower (cystitis, prostatitis, urethritis) and recurrent (relapse and reinfection). Antibacterial treatment is not indicated always in asymptomatic UTI. Antibiotics should only be started in patients with symptomatic UTI or asymptomatic patients at high risk of developing complications. Antibiotic is recommend in asymptomatic bacteriuria (asymptomatic UTI) in pregnancy as 20-30 fold increased risk of developing pyelonephritis during pregnancy.⁵ The World Health Organization (WHO) and the CDC have implicated antibiotic use in food animals as a contributor to the emerging threat of antibiotic resistant infections⁶ Preliminary research indicates that poultry may be contaminated with resistant bacteria that cause urinary tract infections.⁷ Updated Infectious Disease Society of American (IDSA) Guidelines 2010 emphasize the importance of “collateral damage”- a term describing ecological adverse effects of antimicrobial therapy, such as the selection of drug-resistant organisms and colonization or infection with multi drug resistant organisms, has been associated with use of broad spectrum cephalosporins and fluoroquinolones.^{8,9} Antibiotic for a UTI in primary care acquire resistant bacteria, and these may persist for up to 12 months.¹⁰ The microbial spectrum of uncomplicated cystitis and pyelonephritis consists mainly of *Escherichia coli* (75%–95%), with occasional other species of *Enterobacteriaceae*, such as *Proteus mirabilis* and *Klebsiella pneumoniae*, and *Staphylococcus saprophyticus*.^{11,12} Therefore, local antimicrobial susceptibility patterns of *E. coli* in particular should be considered in empirical antimicrobial selection for uncomplicated UTIs. Since the resistance patterns of *E. coli* strains causing uncomplicated UTI varies considerably between regions and countries, a specific treatment

recommendation may not be universally suitable for all regions or countries. Knowledge on local uropathogens drug susceptibility pattern is helpful to choose appropriate antibiotics and overcoming drug resistance. Many first line antibiotics for UTI are already resistant. Amoxicillin or ampicillin should not be used for empirical treatment given the relatively poor efficacy, as discussed in the 1999 guidelines¹³ and the very high prevalence of antimicrobial resistance to these agents worldwide.¹¹⁻¹³

METHODS

Patients attended at Nephrology OPD of General Hospital, Sirajganj from June 2015 to May 2016 with symptoms of Urinary Tract Infection (UTI) (fever and loin pain in upper UTI/Pyelonephritis and LUTS (Lower Urinary Tract Symptoms) i.e. dysuria, frequency, urgency, strangury for Lower UTI) were sent for urine Routine Microscopic Examination (RME). Those having urinary pus cells 10/HPF were considered having significant pyuria and asked for culture and sensitivity test of clean catch MSU (Mid-Stream Urine) done at North Bengal Medical College Hospital (NBMCH), Sirajganj. Antibiotic sensitivity was tested by disk diffusion method. Patients on antibiotics, or antibiotics taken within 72 hours were excluded. Reports outside NBMCH were not included. 4 reports showing no growth (sterile pyuria) were not included. Sensitivity of 23 drugs Azythromycin, ceftriaxone, ceftazidime, chloramphenicol, nitrofurantoin, cefixime, amoxi-cillin+ clavulanic acid, cephalixin, cefuroxime, ciprofloxacin, imipenem, levofloxacin, tetracycline, doxycycline, clindamycin, linezolid, erythromycin, gentamicin, amikacin, cephradine, cotrimoxazole, pivmecillinam, moxifloxacin were tested. Less used amoxycillin, aztreonam, colistin, netilmicin, vancomycin, fusidic acid, gatifloxacin infrequently tested and were not analyzed in this study. Data was compiled and analyzed in SPSS 20. Means were compared by one way ANOVA.

RESULTS

Total 75 cases were analyzed. Age range was 4.5 - 85 years. Males were 30 (40%) and females 45 (60%) in number. Mean age of participants was 39.33 ± 19.23 . Mean age of male was 44.13 years, and female 36.13. (Table I) Most of the participants belonged to 21-40 years (25, 33.3%) and 41-60 years (25, 33.3%). Some (14, 18.7%) participants were below 20, 10 (13.33%) were within 61-80, and 1(1.33%) above 80 (Table II). *Escherichia coli* was isolated from 73 cases (97.34%). Only 2 cases belonged to other species 1 *Klebsiella* (1.33%) and 1 *Staphylococcus aureus* (1.33%) were isolated.

Susceptibility patterns of different drugs to *E. coli* are shown in Figure 1 and Table III. Highest rate of sensitivity of *E. coli* was to amikacin 64 (87.67%) followed by imipenem 61 (83.56%), chloramphenicol 55 (77.46%) and nitrofurantoin 54 (73.97%). Maximum resistance against erythromycin was 69 (95.24%) followed by cephradine 61 (89.55%) and ceftazidim 60 (88.73%) in *E. coli*. Azithromycin was 23.3% sensitive and 71.2% resistant to *E. coli*. Cephalosporin antibiotics ceftriaxone is 47.22% sensitive, ceftazidime is 8.45%, cefuroxim 19.18%, cefixime is 14.50%, cefalexin 12.67%, and cephradine 10.45% sensitive to *E. coli*. Amoxyclav was 19.12% sensitive (out of 68) and 76.47% resistant to *E. coli*. Among fluroquinolones, ciprofloxacin was 38.89%, levofloxacin 44.44% and moxifloxacin 52.38% sensitive to *E. coli*.

Staphylococcus aureus was sensitive to ceftriaxone, chloramphenicol, nitrofurantoin, netilmicin, cephalaxine, imipenem, tetracycline, clindamycin, linezolid, gentamicin, amikacin and resistant to azithromycin, ceftazidime, cefixime, amoxyclav, cefuroxime, cloxacillin, ciprofloxacin, levofloxacin, moxifloxacin, gatifloxacin, doxycyclin,

erythromycin, cephradine, cotrimoxazole, and mecillinam.

Klebsiella was sensitive to imipenem, nitrofurantoin, doxycycline, tetracycline, gentamicin, amikacin, and was resistant to azithromycin, ceftriaxone, ceftazidime, cefixime, amoxyclav, cefuroxime, ciprofloxacin, levofloxacin, clindamycin, linezolid, erythromycin, cephradine, cotrimoxazole, and mecillinam.

Table I: Sex and age frequency

	Number	Age (mean)
Male	30 (40%)	44.13
Female	45 (60%)	36.13
Total	75 (100%)	39.33

Table II: Number of populations in different age groups

Age group	Number	Percentage %
0-20	14	18.68
21-40	25	33.33
41-60	25	33.33
61-80	10	13.33
≥81	1	1.33
Total	75	100%

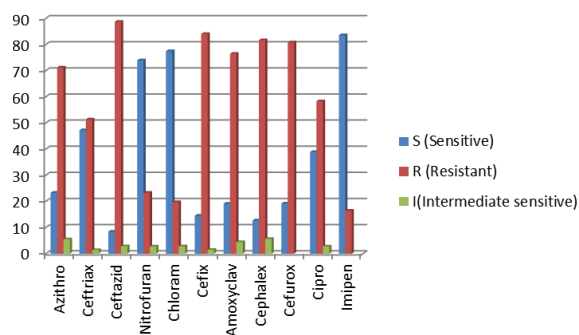


Figure 1 (a): Susceptibility pattern (%) of different antibiotics to *E. coli*.

S- Sensitive, R- Resistant, I- Intermediate sensitive

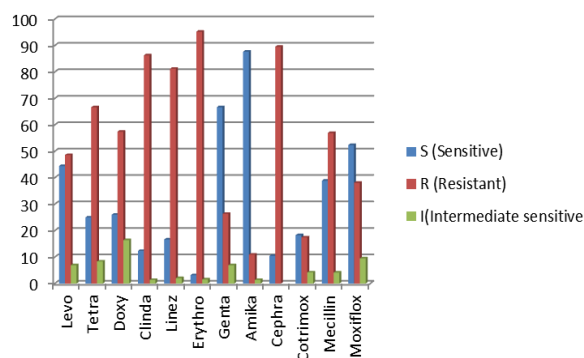


Figure 1 (b): Susceptibility pattern (%) of different antibiotics to *E. coli*.

S- Sensitive, R- Resistant, I-Intermediate sensitive

Table III: Susceptibility pattern (%) of different drugs to *E. coli*

Drugs	S (Sensitive)	R (Resistant)	I (Intermediate)
Azithro	23.3	71.2	5.5
Ceftriax	47.22	51.39	1.39
Ceftazid	8.45	88.73	2.82
Nitrofur	73.97	23.29	2.74
Chloram	77.46	19.72	2.82
Cefix	14.5	84.05	1.45
Amoxycl	19.12	76.47	4.41
Cephalex	12.67	81.7	5.63
Cefurox	19.18	80.82	2.78
Cipro	38.89	58.33	2.78
Imipen	83.56	16.44	6.94
Levo	44.44	48.62	6.94
Tetra	25.0	66.67	8.33
Doxy	26.03	57.43	16.44
Clinda	12.33	86.3	1.37
Linez	16.67	81.25	2.08
Erythro	3.17	95.24	1.59
Genta	66.67	26.39	6.94
Amika	87.67	10.96	1.37
Cephra	10.45	89.55	4.23
Cotrim	18.31	17.46	4.17
Mecillin	38.89	56.94	4.17
Moxiflox	52.38	38.1	9.52

S- Sensitive, R- Resistant, I- Intermediate sensitive

DISCUSSION

Urinary Tract Infection (UTI) is more common in females. Among culture proven 75 UTI cases 45 (60%) were female, 30 (40%) male in our study. *Escherichia coli* are the dominant causative organism worldwide leading to UTI. In our study single colony bacterial isolation were 97.34% for

E. coli, one *Klebsiella* (1.33%) and one *Staphylococcus aureus* (1.33%). *E. coli* isolation in this study is very high (97.34%). Uncomplicated upper and lower UTI are more often caused by *E. coli*, present in 70-95% and *Staphylococcus saprophyticus*, 5% to 20%. *Proteus mirabilis* 1-2% and *Klebsiella spp* 1-2%. In complicated UTI *E. coli* contribute 21-54%.¹⁴ It is notable that we are dealing with symptomatic UTI, while other studies were prevalence study includes consecutive cases of symptomatic and asymptomatic UTI. Nevertheless, our results may not be representative of prevalence in community since consecutive sample was not taken as many patients could not afford urine culture sensitivity study.

In a recent study at Cox's Bazar Medical College *E. coli* was sensitive to imipenem (100%), followed by ceftriaxone (65%), azithromycin (65%) and ciprofloxacin shows 60%.¹⁵ In another study at Indira Gandhi Medical College & Research Institute, Paducherry, India on antibiotic resistance against *E. coli* amoxicillin-clavulanic acid (74.4%), ceftriaxone (71.4%), cefuroxime (72.2%) and cotrimoxazole (64.2%) resistance was documented. While isolates were sensitive to amikacin (82%), nitrofurantoin (82.1%) and imipenem (98.9%).¹⁶ In our study, we observed high rate of sensitivity to amikacin (87.67%) followed by imipenem (83.56%), chloramphenicol (77.46%) and nitrofurantoin (73.97%). While erythromycin (95.24%), cephadrine (89.55%) and ceftazidime (88.73%) showed higher resistance against *E.coli*. Aminoglycoside antibiotic amikacin 87.67% and gentamicin 66.67% sensitive.

Most of the studies do not categorize sensitive and intermediate sensitive entity in antibiogram. Sensitivity would be higher in this study if we combine sensitive and intermediate sensitive as one.

CONCLUSION

Epidemiology of uropathogens and drug susceptibility is changing worldwide. Regular drug susceptibility test could aid in selecting appropriate empirical antibiotic while decreasing drug resistance. Large scale multicentre study involving more patients should be done often to know uropathogens and drug susceptibility pattern in Sirajganj.

Conflicts of Interest: None

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Relationship of Serum Homocysteine concentration with other Risk Factors in Acute Coronary Syndrome Patients

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ABSTRACT

Introduction: Acute Coronary Syndrome (ACS) has become a major health problem in the entire world. The aim of the study was to find out the relationship between serum homocysteine level and other risk factors of acute coronary syndrome. **Methods:** This was a cross-sectional study, conducted in the department of Cardiology, Dhaka Medical College Hospital, Dhaka, during the period of July 2011 to December 2011. In this period, newly diagnosed patients with ACS were taken as cases, and age, sex matched healthy subjects with normal ECG were taken as controls. **Results:** Smoking, dyslipidaemia, family history (F/H) of premature Coronary arterial disease (CAD) and serum Homocysteine level were found to be significantly ($p < 0.05$) associated with ACS-risk, other risk factors (hypertension, diabetes mellitus and obesity) were not significantly associated. **Conclusion:** Serum total homocysteine concentration (tHcy) is recognized as an independent and important risk factor for ACS patients. Smoking and family history of premature CAD were found significantly associated with elevated tHcy.

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INTRODUCTION

Acute Coronary Syndrome (ACS) has become a major health problem and is the most common cause of mortality and morbidity in the entire world.¹ In India, 4% (3.15 crore cases in 78.82 crore rural population) rural and 11% (3.71 crore cases in 33.78 crore urban

population) urban population suffers from Coronary Artery Disease (CAD). CAD are becoming significant burden on healthcare services in Bangladesh too. The average prevalence of CAD from 3 small scale population based studies in Bangladesh was 6.56/1000.^{2,3} The progressively increasing trend of the disease in our country shows that the prevalence was

3.3/1000 in 1976 and 17.2/1000 in 1986 indicating a 5-fold increase in 10 years. Hospital admissions for CAD are increasing rapidly. Socio-economic improvement and changes in life style in respect of increase in tobacco consumption and saturated fat intake, decrease in physical activity, increasing body weight and consequently increasing rate of diabetes mellitus (DM), hypertension (HTN) and dyslipidaemia might have contributed to this increase in our population.

ACS is a multifactorial disease involving well-known risk-factors such as age, male sex, smoking, HTN, DM, obesity, hypercholesterolemia, family history of premature CAD and sedentary lifestyle.⁴ ACS develops when a vulnerable or high risk atheromatous-plaque undergoes disruption of its fibrous cap. Following plaque-rupture, a sufficient quantity of thrombogenic substances are exposed, and the coronary artery lumen may become partially or completely obscured by a combination of platelet aggregates, fibrin and red blood cells. Beletic et al.⁵ have shown the importance of the novel risk factors like Apolipoprotein B/Apolipoprotein A1 ratio, Lipoprotein (a), fibrinogen, C-Reactive Protein and homocysteine (Hcy) in the pathogenesis of ACS.

Relation of high serum Hcy concentration with other risk factors for acute coronary syndrome has been studied by several authors outside Bangladesh, but this association has not been studied in our population. This study was intended to evaluate whether there is any relation of hyperhomocysteinemia with other risk factors in newly diagnosed Bangladeshi ACS patients.

METHODS

This was a cross-sectional study which was conducted in the department of Cardiology,

Dhaka Medical College and Hospital (DMCH), Dhaka, during the period of July 2011 to December 2011. Newly diagnosed patients with Acute Coronary Syndrome (ACS) admitted in the Coronary Care Unit (CCU) of DMCH were taken as cases, age and sex matched healthy subjects (doctors, medical students, nurses and other hospital staffs and patients' attendants from DMCH, Dhaka) with no history of ischaemic heart disease (IHD) and normal ECG were taken as controls. The cases have been diagnosed on the basis of characteristic ischaemic type chest pain, ECG findings of ACS and cardiac bio-marker (Troponin I) findings of ACS, presenting for the first time in the CCU of DMCH, Dhaka. Data were collected by using a pre-tested data sheet. Informed consent was taken from all cases and controls or from their legal guardians. Fasting blood samples were collected for serum homocysteine assay on the morning following the admission day from the cases and the controls and measured from Biochemistry Department of Bangabandhu Sheikh Mujib Medical University (BSMMU).

RESULTS

Smoking, dyslipidaemia and hypertension (HTN) were more common risk factors in both cases and controls. However, smoking and dyslipidaemia were significantly ($p < 0.05$) higher in case group. Other risk factors like-Hypertension (HTN), Diabetes Mellitus (DM)/Impaired Glucose Tolerance (IGT), Family History (F/H) of premature Coronary Artery Disease (CAD) and obese/over-weight were higher in number in cases than in controls (Table I).

Table I: Distribution of the study subjects according to different risk factors for Acute Coronary Syndrome (ACS)

Risk factors	Case (n-60)		Control (n-60)		p value
	n	%	n	%	
Smoking	26	43.3	14	23.3	0.001
Dyslipidaemia	33	55.0	13	21.7	0.001
HTN	21	35.0	12	20.0	0.065
DM/IGT	14	23.3	7	11.7	0.093
F/H of premature CAD	14	23.3	8	13.3	0.609
Obesity/Over-weight	11	18.3	9	15.0	0.624

HTN-Hypertention, DM- Diabetes Mellitus, IGT-Impaired Glucose Tolerance

According to serum Homocysteine level the total study subjects were divided into two sub groups. Smoking and Family History of premature CAD were found significantly ($p<0.05$) higher in >15 mol/L Homocysteine level group in the total

study subjects. Others risk factors like HTN, DM/IGT, smoking and obese/over wt. had no statistically significant difference between the two groups (Table II).

Table II: Distribution of the study subjects according to Serum Homocysteine level and risk factors for Acute Coronary Syndrome (ACS)

Risk factors for ACS	Homocysteine<15 (mol/L) (n-80)		Homocysteine>15 (mol/L) (n-40)		Total (n-120)		p value
	n	%	n	%	n	%	
HTN	21	26.3	12	30.0	33	27.5	0.664
DM/IGT	15	18.8	6	15.0	21	17.5	0.610
Smoking	20	25.0	20	50.0	40	33.3	0.006
Obese/Over-wt.	14	17.5	6	15.0	20	16.7	0.729
Dyslipidaemia	26	32.5	20	50.0	46	38.3	0.063
F/H of premature CAD	10	12.5	12	30.0	22	18.3	0.019

HTN-Hypertention, DM-Diabetes Mellitus, IGT-Impaired Glucose Tolerance

According to serum Homocysteine level, cases were divided into two sub groups. Cases with smoking and F/H of premature CAD show significantly ($p<0.05$) higher in >15 mol/L Homocysteine level in cases by Chi square test.

Others risk factors like HTN, DM/IGT, smoking and obese/over wt. had no statistically significant difference between the two groups (Table III).

Table III: Distribution of the cases according to Serum Homocysteine level (mol/L) and risk factors for Acute Coronary Syndrome

Risk factors for ACS	Homocysteine<15 (mol/L) (n-28)		Homocysteine>15 (mol/L) (n-32)		p value
	n	%	n	%	
HTN	11	39.3	10	31.3	0.515
No HTN	17	60.7	22	68.8	
DM/IGT	9	32.1	5	15.6	0.131
No DM/IGT	19	67.9	27	84.4	
Smoking	8	28.6	18	56.3	0.030
No Smoking	20	71.4	14	43.7	
Obese/Over-wt.	6	21.4	5	15.6	0.562
No Obese/Over-wt.	22	78.6	27	84.4	
Dyslipidaemia	13	46.4	20	62.5	0.211
No Dyslipidaemia	15	53.6	12	37.5	
F/H of premature CAD	3	10.7	11	34.4	0.031
No F/H of premature CAD	25	89.3	21	65.6	

HTN-Hypertention, DM-Diabetes Mellitus, IGT-Impaired Glucose Tolerance, CAD-Coronary Artery Disease

Among the smokers the mean serum Homocysteine level was 18.5±7.4 mol/L and 12.5±2.2 mol/L in cases and controls respectively. Similarly, in those with F/H of premature CAD the

mean serum Homocysteine level was 15.1±2.9 mol/L in case and 12.5±1.9 in control group. The mean serum Homocysteine differences were statistically significant ($p<0.05$) in smokers and in those with F/H of premature CAD between the two groups by unpaired 't'test (Table IV).

Table IV: Distribution of the study subjects according to mean serum Homocysteine level and risk factors for Acute Coronary Syndrome

Risk factors for ACS	Case (n-60)				Control (n-60)				p value
	n	Mean	± SD	(min-max)	n	Mean	± SD	(min-max)	
Smoking	26	18.5	7.4	(8.5-38.7)	14	12.5	2.2	(9.1-16.2)	0.005
F/H of premature CAD	14	15.1	2.9	(11.5-20)	8	12.5	1.9	(8.7-15.2)	0.039
HTN	21	21.8	25.4	(7.4-129.1)	12	13.3	7.6	(7.4-31.4)	0.367
DM/IGT	14	15.6	5.1	(10.3-26.1)	7	12.0	2.5	(8-15.1)	0.097
Obese/Over-wt.	11	17.8	11.5	(7.4-50)	9	11.2	2.1	(9.1-15.2)	0.107
Dyslipidaemia	33	20.7	20.4	(7.4-129.1)	13	13.6	2.0	(9.9-14.5)	0.281

HTN-Hypertention, DM-Diabetes Mellitus, IGT-Impaired Glucose Tolerance, CAD-Coronary Artery Disease

A smoker compared to a non-smoker was 4.19 (95% CI 1.61 to 10.85) times more likely to have ACS. For dyslipidaemic subject, the reference group is non-dyslipidaemic subject. A

dyslipidemic subject compared to a non-dyslipidemic subject was 5 times more likely to have ACS. For F/H of premature CAD, the reference group is those with no F/H of

premature CAD. A subject with F/H of premature CAD was 3.95 (95% CI 1.11 to 14.02) times more likely to have ACS than those with no F/H of premature CAD. Smoking, dyslipidaemia, F/H of premature CAD and serum Homocysteine level

were found to be significantly ($p < 0.05$) associated with ACS-risk; other risk factors (HTN, DM/IGT and obese/over-wt.) were not found to be significantly associated with ACS-risk (Table V).

Table V: Risk factors analysis for Acute Coronary Syndrome, (multiple logistic regression models) (n-120)

Risk factors for ACS	OR	95.0% CI for Odd ratio (OR)		R ²	p value
		Lower	Upper		
HTN	2.71	0.98	7.47	0.17	0.054
DM/IGT	1.68	0.54	5.22	0.11	0.371
Smoking	4.19	1.61	10.85	0.41	0.003
Obese/Over-wt.	1.29	0.44	3.79	0.09	0.646
Dyslipidaemia	5.94	2.16	16.35	0.35	0.001
F/H of premature CAD	3.95	1.11	14.02	0.29	0.033
S. Homocysteine level	6.70	2.48	18.06	0.44	0.001
Constant	0.129				0.000

HTN-Hypertention, DM-Diabetes Mellitus, IGT-Impaired Glucose Tolerance, CAD-Coronary Artery Disease

DISCUSSION

In this study it was observed that smoking (43.3% versus 23.3%) and dyslipidaemia (55.0% versus 21.7%) were significantly ($p < 0.05$) higher in both cases and control group. However, other risk factors like- Hypertension (HTN) (35% versus 20%), Diabetes Mellitus (DM) /Impaired Glucose Tolerance (IGT)(23.3% versus 11.7%). Family History (F/H) of premature Coronary Artery Disease (ACD) (23.3% versus 13.3%) and obese/over-weight (18.3% versus 15%) were higher in number in cases but not significantly ($p > 0.05$) higher than controls. Tungsubutra et al.⁶ observed that risk factors such as tobacco use and a positive family history were more frequent in the ACS patients, whereas diabetes and hypertension were less frequent. Badran et al.⁷ showed that cigarette smoking, positive family history and dyslipidaemia were the most common risk factors in patients with ACS, while hypertension and diabetes mellitus were less frequent. These findings were in agreement with

the observation from Avezum et al.⁸ All these findings suggest that neither diabetes nor hypertension are major risk factors for ACS. In our country, Khan et al.⁹ concluded that dyslipidaemia and family history were more prevalent. Almost similar findings were also observed by Majumder et al.¹⁰ and Haque et al.¹¹ In the present study, it was found that smoking and family history of premature Coronary Artery Disease (CAD) were significantly ($p < 0.05$) higher in >15 mol/L homocysteine level in the total study subjects. Other risk factors like HTN, DM/IGT, dyslipidaemia and obese/overweight were not significantly associated with high serum homocysteine level. Similar results were also observed among the case subjects. In this study, mean serum homocysteine level was significantly ($p < 0.05$) higher in smokers and in those with F/H of premature CAD among the cases compared to controls; but regarding the other risk factors the mean serum homocysteine differences were not significant ($p > 0.05$). In

short, this study showed a significant association of serum homocysteine level with risk factors for ACS like smoking and F/H of premature CAD; but no significant association was found with HTN, DM/IGT, dyslipidaemia and obese/overweight. These findings were consistent with reports from other studies.^{12,13} Dey found that serum homocysteine level was significantly higher among the smokers, dyslipidaemics and those with family history of ischaemic heart disease, but no statistically significant association of serum homocysteine level was found with DM and HTN. The findings of the current study were almost consistent with the findings of Puri et al.¹ too. In the multiple logistic regression analysis with ACS as dependent variable and risk factors for ACS as independent variables, it was revealed that, serum total homocysteine level had odds ratio (OR) 6.70 for the development of ACS patients. Among the traditional risk factors-smoking had OR 4.19, dyslipidaemia 5.94, F/H of premature CAD 3.95, HTN 2.71, DM/IGT 1.68 and obese / overweight 1.29. Serum homocysteine level, F/H of premature CAD, dyslipidaemia and smoking were significantly ($p<0.05$) associated with ACS-risk where HTN, DM/IGT and obese/over-weight were not ($p>0.05$). In the current study, very high levels of homocysteine were found in cases (maximum up to 129.05 $\mu\text{mol/L}$) than in controls (maximum up to 31.4 $\mu\text{mol/L}$), which can probably explain the high OR associated with homocysteine. Puri et al.¹ showed that patients with elevated serum homocysteine level had a 6.05 times increased risk of CAD. In that study, HTN, smoking, DM and F/H of premature CAD had OR 3.60, 1.30, 7.37 and 1.80 respectively for CAD-risk. Dey observed significant association of smoking, hypertension, dyslipidaemia and serum homocysteine level with acute myocardial infarction (AMI)-risk. Souissi et al.¹⁴ (OR=2.99; 95% CI=1.18-7.59; $p=0.02$) also found independent association between high serum homocysteine and increased CAD-risk. The

results of the present study regarding the independent association of serum homocysteine level and other risk factors with ACS-risk were also sustained by similar observations made by Taylor et al.¹⁵ and Boushy et al.¹⁶ etc.

CONCLUSION

Acute coronary syndrome (ACS), a multifactorial disease, has become a major health problem and an important cause of mortality and morbidity in the entire world. Serum total homocysteine (tHcy) is increasingly being recognized as an independent and important risk factor for ACS patients. In the present study, an attempt was made to find out the relation between serum homocysteine concentration and other risk factors of ACS patients in Bangladeshi population. Smoking, dyslipidaemia and HTN were more common risk factors in both cases and controls. However, smoking (43.3% versus. 23.3%) and dyslipidaemia (55.0% versus. 21.7%) were significantly ($p<0.05$) higher in the case group. Other risk factors like- HTN, DM/IGT, F/H of premature CAD and obese/over-weight were higher in number in cases but not significantly ($p>0.05$) higher than controls.

In the current study fasting serum homocysteine was significantly ($p<0.05$) higher in cases than controls both in terms of mean concentration (19.5 ± 16.3 versus. 12.6 ± 3.3 mol/L) and hyper-homocysteinemia (>15 mol/L) incidence (53.3% versus 13.3%). High serum homocysteine was strongly associated with ACS-risk in patients having OR=7.43 (95% CI=2.80 to 20.34). Smoking and F/H of premature CAD were found significantly ($p<0.05$) associated with elevated tHcy in this study while other traditional risk factors of ACS like- HTN, DM/IGT, dyslipidaemia and obese/overweight had no such association.

Conflict of Interest There is no conflict of interest

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Pattern of Ear, Nose and Throat Diseases among Subjects below 18 years attending at ENT OPD in a Tertiary Hospital

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ABSTRACT

Introduction: Children having Ear, Nose and Throat (ENT) problem are often unrecognized and neglected by parents and the society. Early detection and proper management can help to minimize serious complication and adverse effects on both patients and their parents. **Methods:** This cross-sectional study was conducted among patients less than 18 years who attended the ENT out patient's department (OPD) of North Bengal Medical College Hospital (NBMCCH) for a period of 6 months (01.07.2016 to 31.12.2016). A total 1045 cases were enrolled irrespective of sex. Data were collected on a check list which comprised of age, sex, duration of diseases, examination findings and diagnosis. **Results:** A total 3225 patients with ENT diseases attending the ENT OPD of NBMCCH during 6 months period, out of which 1045 were less than 18 years. Among them males were 498 (47.65%) and females were 547 (52.34%). Most of the patients came to the hospital with Chronic Suppurative Otitis Media (CSOM) 290 (27.75%), followed by tonsillitis 180 (17.22%), otitis media with effusion 107 (10.27%), impacted wax 98 (9.37%), adenoids 70 (6.69%), foreign body 57 (5.45%), parotitis 52 (4.97%), furunculosis 47 (4.49%), preauricular sinus 44 (4.21%), otitis externa 41 (3.92%), traumatic rupture of tympanic membrane 38 (3.6%) and others 21 (2.01%). **Conclusion:** This study suggests that the subjects under 18 years mostly suffer from chronic suppurative otitis media, tonsillitis, otitis media with effusion and impacted wax. So, primary ENT health care services should be promoted among children and adolescent.

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INTRODUCTION

Ear, nose and throat problems are more common in children than adult, especially diseases such as acute suppurative otitis media, acute tonsillitis, acute epiglottitis, laryngotracheobronchitis and rhinitis etc. This trend could be due to various factors such as wide and horizontal Eustachian tube, under developed immunity, malnourishment, poor hygiene and sanitary conditions, overcrowding, lower socioeconomic status etc.¹ Prevalence of ENT diseases among children is not well documented in Bangladesh. A very few studies have been conducted regarding the ENT problems in paediatric group. The most common type of ENT problem of children is not known.

A healthy population is likely to be a productive population that will lead to a growing economy. The purpose of this study was to investigate the pattern of common ENT diseases in children in the northern part of our country and its relation to economy, life style and culture.

METHODS

This was a cross-sectional study carried out in the out patient's department of ENT in North Bengal medical college hospital (NBMCH), during the period of 01.07.2016 to 31.12.2016. All subjects 18 years and below were included and those above 18 years were excluded from the study.

Sociodemographic data from the study subjects were recorded in a semi-structured questionnaire. The otolaryngological examinations including otoscopy, anterior rhinoscopy, posterior rhinoscopy, oropharyngoscopy, indirect laryngoscopy and tuning fork tests were done for diagnosis of diseases.

RESULTS

Majority of the cases (441, 42.2%) were between 11-18 years of age group, mostly girls (233, 52.83%), unmarried, completed primary level (27.75%), Muslims (79.52%) and rural areas (63.92%).

Table I (a): Sociodemographic profile of children attended into ENT OPD of North Bengal Medical College Hospital

Profile of children	Number (%) of children		
	Girls	Boys	Total
0-5	166 (54.1%)	141 (45.9%)	307 (29.4%)
6-10	154 (51.85%)	143 (48.14%)	297 (28.42%)
11-18	233 (52.83%)	208 (47.2%)	441 (42.2%)
Total	553 (52.9%)	492 (47.1%)	1045 (100%)
Gender			
Male	492 (47.1%)	-	-
Female	553 (52.9%)	-	-
Total	1045 (100%)	-	-
Marital status			
Married	103 (9.9%)	-	-
Unmarried	942 (90.1%)	-	-
Total	1045 (100%)	-	-

Table I (b): Sociodemographic profile of children attended into ENT OPD of North Bengal Medical College Hospital

Profile of children	Number (%) of children		
	Girls	Boys	Total
Religion			
Muslim	831 (79.52%)	-	-
Hindu	207 (19.8%)	-	-
Others	07 (0.66%)	-	-
Total	1045 (100%)	-	-
Educational level			
Illiterate	143 (64.7%)	78 (35.29%)	221 (21.14%)
Not started school yet	100 (47.62%)	110 (52.38%)	210 (20.09%)
Primary	170 (58.62%)	120 (41.37%)	290 (27.75%)
Secondary	66 (45.2%)	80 (54.79%)	146 (13.97%)
SSC	44 (44%)	56 (56%)	100 (9.56%)
HSC	30 (38.46%)	48 (61.54%)	78 (7.46%)
Total	553 (52.92%)	492 (47.1%)	1045 (100%)
Habitation			
Rural	304 (45.51%)	364 (54.5%)	668 (63.92%)
Urban	179 (47.48%)	198 (52.52%)	377 (36.07%)
Total	483 (46.22%)	562 (53.78%)	1045 (100%)

Among 1045 patients, majority were diagnosed as CSOM (27.75%) followed by tonsillitis (17.22%), otitis media with effusion (10.23%), impacted wax (9.37%), enlarged adenoid (6.69%), foreign body (5.45%) and parotitis (4.97%),

furunculosis (4.49%), preauricular sinus (4.21%), otitis externa (3.92%), traumatic rupture of tympanic membrane(3.6%) and others (2.01%) which are shown in Table II.

Table II: Diagnosis of disease among children attended in ENT out patients department

Diseases	Number (%) of children		
	Girls	Boys	Total
CSOM	154 (53.1%)	136 (46.89%)	290 (27.75%)
Tonsillitis	97 (53.88%)	83 (46.11%)	180 (17.22%)
Otitis media with effusion	55 (51.4%)	52 (48.59%)	107 (10.27%)
Impacted wax	52 (53.1%)	46 (46.94%)	98 (9.37%)
Enlarged adenoid	31 (44.28%)	39 (55.71%)	70 (6.69%)
Foreign body	30 (52.63%)	27 (47.36%)	57 (5.45%)
Parotitis	27 (51.92%)	25 (48.1%)	52 (4.97%)
Furunculosis	25 (53.19%)	22 (46.81%)	47 (4.49%)
Preauricular sinus	23 (52.27%)	21 (47.73%)	44 (4.21%)
Otitis externa	22 (53.66%)	19 (46.34%)	41 (3.92%)
Traumatic rupture of tympanic membrane	17 (44.74%)	21 (55.26%)	38 (3.6%)
Others	10 (47.61%)	11 (52.38%)	21 (2.01%)

DISCUSSION

In this study, we evaluated at first time in the northern part of our country to observe the intensity of Ear Nose and Throat diseases with its relation to the relevant factors for diseases process in our community. Among the study subjects most common type of ENT problem was CSOM. It is typically a persistent or intermittent disease, insidious onset, often capable of causing severe tissue destruction and irreversible sequel and clinically manifests with deafness and discharge.² This is one of the most common community health disorders of childhood in many developing countries including Bangladesh.³ The World Health Organization (WHO) suggests that children should be screened at school entry in all developing countries.⁴ It was also found that complications of CSOM were commonest in the first two decades of life.³ In our study the prevalence of CSOM is 27.43%, which is consistent with other study done in several hospitals and rural areas in which the prevalence of CSOM varies between 7.39 to 39.50 %.⁵⁻⁹ In present study, majority were adolescent (between 11 to 18 years) and regarding sex, girls were slightly higher than boys. This could be the result of more girls' school situated nearby to study place.

Regarding attendance of the higher incidence of children were reported from rural area. This occurrence was reported in the previous study.¹⁰ We may hypothesize that our hospital was located in the city area, which may provoke people to attend for seeking ear care facilities. However, this present study does not reflect the overview of ENT health problems of our country due to limitations, scarcity of data with single study center. We will have future plan to study in the multicentre, randomly selected large scale long duration of cases to evaluate epidemiology which is necessary to find out the diseases and risk factors.

CONCLUSION

The children need ear care services for developing their healthy future. Special ear care facilities are indispensable for prevention of otitis

media at home, school and society to ensure their better quality of life.

Conflict of interest: None

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Incidence of Animal Bites and Stings in Sherpur, Bogura, Bangladesh

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ABSTRACT

Introduction: World Health Organization had estimated that 10 million animal bites around the world each year and about 50,000 people die annually from animal bite. This retrospective study was carried out from January 2016 to December 2016 at emergency department of Sherpur Upazila Health Complex (UHC) to determine the incidence and characteristics of the injuries caused by animals among the population of Sherpur, Bogura, Bangladesh. **Methods:** The medical records of 77 patients admitted to hospital with animal bites were studied. Data including epidemiological aspects, clinical findings and outcomes of treatment were analyzed using descriptive statistics and the χ^2 test. **Results:** Of 77 patients 54 (70.13%) were male, and the median age of males and females was 24.4 years and 26.2 years, respectively. Dogs, Cats, Fox, and Mice/muskrat were the most commonly involved animal species, causing injuries with a frequency of 38 (49.35%), 12 (15.58%), 15 (19.48%) and 7 (9.09%), respectively. Feet 39 (50.64%) and hands 27 (37.66%) were the most commonly affected body parts, followed by the face and other parts. No case of rabies was observed in these patients nor any case of death was reported. **Conclusion:** Animal bite is a major public health problem in Sherpur, Bogura, with a high rate of hospitalization but low rate of mortality.

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INTRODUCTION

World Health Organization states that 10 million people are bitten by animals around the world each year and are considered for prophylaxis and treatment for rabies, from which almost 50000 people die annually. The highest rates of mortality and morbidity in Asia were observed among developing countries.¹⁻³ It was found that most patients are bitten by dogs, and that a considerable proportion of these were young children, who were at greater risk of developing rabies in the absence of treatment due to the location of the bites they receive.⁴ In countries where animals, especially dogs, are kept in poor hygienic conditions, dog bites are the most common animal bites and can result in complicated bacterial infection, predominantly related to the dog's oral flora.^{5,6} Bites and scratches represent the most important public health issue related to dogs and cats because of the associated physical and psychological trauma, wound infection by different microorganisms, and the risk of rabies transmission.^{5,7,8-11} Cellulitis was the most common clinical feature, and rarely, sepsis, osteomyelitis and rabies may develop after bite injury.⁵ Vaccination against rabies before and after animal bite was the most effective measure to prevent rabies.^{4,5} Annually, 140 cases of animal bite per 100000 population were estimated to occur in Iran; more than 85% of them were dog bites.^{3,4} Khuzestan province is ranked ninth in the country in this respect. The high frequency of animal bites/stings (3000–6000 cases per year), due to large number of stray dogs, the high prevalence of scorpions and snakes in some areas of Khuzestan.¹⁴ This current study was performed to determine the incidence and characteristics of the injuries caused by animals among the population in the northern area of Bangladesh.

METHODS

This was a retrospective descriptive study performed using register books of the emergency department in Sherpur Upazila Health Complex(UHC), Sherpur, Bogura, Bangladesh. This health complex covers a population of 3,32,825. The medical records were of those persons who were bitten by animals between January 2016 to December 2016 and attended in the emergency departments of Sherpur UHC. Data were collected on age, gender, residence (rural or urban), type of animal, site of bite or sting, number of bites, symptoms, treatment and preventive measures carried out at the primary health center. Data were analyzed in SPSS 20 (SPSS- IBM Inc., Chicago, IL, USA) by using descriptive statistics and the χ^2 test.

RESULTS

During the period of study, 77 cases of animal bite were reported to Sherpur Upazila Health Complex. Of the 77 studied patients, 54 (70.13%) were male, and 23 (29.87%) were female. The age and gender distributions of patients with animal bites and stings are shown in Table I.

Table I: Age and gender distribution of patients with animal bites

Age (in years)	Number (%) of the patients		Total
	Male	Female	
1 to 10	21 (38.9%)	8 (34.8%)	29 (37.7%)
11 to 20	5 (9.3%)	2(8.7%)	7 (9.0%)
21 to 30	11 (20.4%)	4 (17.4%)	15 (19.5%)
31 to 40	8 (14.8%)	4 (17.4%)	12 (15.6%)
41 to 50	6(11.1%)	3 (13.0%)	9 (11.7%)
51 to 60	2 (3.7%)	0%	2 (2.6%)
>60	1 (1.8%)	2 (8.7%)	3 (3.9%)
Total	54	23	77

Dog, cat, fox, mouse and monkey bites were the most common, with frequencies of 38(49.35%), 12 (15.58%), 15 (19.48%), 7 (9.09%) and 3 (3.89%) respectively (Table II). Statistically significant differences in the number of animal bites between the rural and urban populations were

observed: Dogs (23, 60.53% versus 15, 39.47%), Mice (4, 57.15% versus 3, 42.85% respectively) and Foxes (11, 73.33% versus 4, 26.67% respectively) and cats (8, 66.67% versus 4, 3.33% respectively). Snakes had similar frequencies in rural and urban population (Table II).

Table II: Animal bites and stings according to animal species and patient's residence

Animal	Total	Total	
		Urban	Rural
Dogs	38 (49.3%)	15 (39.4%)	23 (60.5%)
Cats	12 (15.5%)	4 (33.3%)	8 (66.6%)
Foxes	15 (19.4%)	4 (26.6%)	11 (73.3%)
Monkeys	3 (3.8%)	1(33.3%)	2 (66.6%)
Mice/Muskrats	7 (9.0%)	3 (42.8%)	4 (57.1%)
Snake	2 (3.8%)	1 (50%)	1 (50%)

Animal bites and stings according to different animal species in relation to patient`s gender distributions are shown in Table III.

Table III: Animal bites and stings according to animal species and patient's gender

Animal	Number (%) of patient's gender		Total
	Male	Female	
Dogs	29 (76.3%)	9 (23.6%)	38 (49.3%)
Cats	5 (41.6%)	7 (58.3%)	12 (15.5%)
Foxes	13 (86.6%)	2 (13.3%)	15 (19.4%)
Monkeys	2 (66.6%)	1 (33.3%)	3 (3.8%)
Mice/Muskrats	4 (57.1%)	3 (42.8%)	7 (9.0%)
Snake	1 (50%)	1 (50%)	2 (3.8%)

Dogs, and snakes frequently affected the feet (23 in number), where as cats and mice affected the hand (10 in number)(Table IV). Multiple bites and injuries were observed to be caused by cats and dogs. Hospital medical records showed that 11 patients had infectious complications such as soft tissue infection (11,14.2%), sepsis (2, 2.5%). All patients with mammal bites were vaccinated

against rabies and treated with anti-rabies immunoglobulin and there were no cases of rabies among these patients.

Table IV: Body part affected according to animal species

Animal	Face (n%)	Hands (n%)	Foot (n%)	Other parts (n%)	Total
Dogs	2 (5.2%)	11 (28.9%)	22 (57.8%)	3 (7.8%)	38
Cats	1 (8.3%)	8 (66.6%)	2 (16.6%)	1 (8.3%)	12
Foxes	1 (6.6%)	4 (26.6%)	9 (60.0%)	1 (6.6%)	15
Monkeys	2 (66.6%)	1 (33.3%)	0 (0%)	0 (0%)	3
Mice/Muskrats	0 (0%)	2 (28.5%)	5 (71.43%)	0 (57.1%)	7
Snake	0 (0%)	1 (50%)	1 (50%)	0 (0%)	2

DISCUSSION

In this study health centers and hospital in the study region showed that, 4.2% of animal bites and stings were treated. This finding is consistent with previous reports that the majority of animal bites result in mild injuries that patients do not seek medical help for.^{6,16} Findings of this study that children and young adults were affected more than other age groups and men were affected more than women, with a male to female ratio of 2.3:1 (Table I). This findings are in agreement with Nogalski et al.,⁷ Weis et al.,¹² Hon et al.,¹³ Matteucci et al.¹⁷ and Shetty et al.¹⁸ O'Neil et al.¹⁶ Mac Bean et al.⁸ explained that female adults were more likely than male adults to be attacked by cats. The present study showed that dog bites constitute about 50% of all animal bites that affected people, while the remaining 50% were caused by other animals such as cats, foxes, monkeys, rats and snakes. Many investigators reported that dogs, cats and horses were the most common animals injuring humans.^{6, 7,11,12,15,18,19} These differences might be due to variation in the behaviors, occupations and belief of people living in different socioeconomic and epidemiological situations. The present study revealed that most dog bites occurred in rural areas, whereas those bitten by mice, monkey were predominantly in urban areas. Snake bites

were similar in both areas. Nogalski et al.⁷ reported that the threat of animal attack is similar in urban and rural areas.⁷ MacBean et al.⁸ explained that in Australia, most injuries by animals occurred in the home and were caused by pet dogs and cats. These differences may be related to many factors, such as the high number of stray dogs in rural areas of the region of our study, the high number of mice in sewage canals and entering homes in urban areas of our region, the high number of pet dogs and cats in industrial countries, and differences in occupation, behaviour and socioeconomic background around the world. In our study, the majority of infectious complications were seen in dog bites and snake bites. This finding was confirmed by the data from another researcher.⁵ Two main factors are responsible for this observation. The first is the bacterial flora of dog and snake saliva, which infects human tissue, and the second factor is the trauma caused by powerful dog's jaws, which results in tissue ischemia in the region of the bite. In addition, the cytotoxic effects of snake toxin predispose the affected tissue to infection.^{5,6} In our study, the mortality rate in hospitalized patients was 0%. Nogalski et al.⁷ found that the mortality rate in hospitalized patients was 5.88%, mostly due to serious injuries caused by large animals such as horses, cows and pigs. Weis et al.¹² reported a mortality rate

among hospitalized animal bite patients of 1.6 per 1000. These differences may be due to: (1) the presence of potentially lethal scorpion species such as *Hemiscorpius lepturus* in the area, (2) severe and serious injuries to the head, face and abdomen caused by horses and cows, (3) the medical facilities and best management of injured patients in the emergency departments of industrialized countries. In the present study, it was observed no case of rabies or tetanus. The threat posed by rabies is increasing in Iran due to the high number of stray dogs and cases of dog bite in humans.³ Dao et al.¹⁹ reported 10 cases of human rabies in their retrospective study covering a four-year period (2000–2003). Dog bites caused maximum morbidity (92%). Second most common biting animal was monkey (3.2%), followed by cat (1.8%), fox (0.4%) etc. Most bites (64.3%) were unprovoked bites by stray (64.7%) animals. In this study, 72.4% animal bite victims were males and 47.5% were children in age group of 2-18 years and 63% had category III exposure as per the WHO classification.²⁰

CONCLUSION

From the present study it was concluded that dog, foxes, cats were mostly responsible for animal bites, snake for strings in this study area with no incidence of rabies. The study suggests Government concern as well as public awareness regarding animal bite, strings to reduce their incidences.

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Conflict of Interest There is no conflict of interest.

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Wound Infections following Emergency Gastrointestinal Surgery

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ABSTRACT

Introduction: Postoperative wound infection still causes considerable morbidity and high cost of healthcare system. The main determinants of infection are agent, host and environment. The objective of this study is to identify the underlying factors responsible for postoperative wound infection following emergency GI surgery and also to explore the causative organism including their antibiotic sensitivity. **Methods:** This study was carried out in the department of surgery, Rajshahi Medical College Hospital, Rajshahi during the period of July 2012 to December 2012 where 142 patients were selected randomly. These patients were admitted for emergency surgery. **Results:** In this study, 142 patients with emergency GI surgery were included among which acute appendicitis was 62 (infection rate 8.0%), burst appendix 12 (infection rate 33.3%), DU perforation 15 (infection rate 13.3%), small intestinal obstruction 30 (infection rate 13.3%), ileal perforation 19 (infection rate 42.1%), sigmoid volvulus 2 (infection 50%) and obstructed inguinal hernia 2 with no infection, The infection rate is high (18.3%) where operation was done by assistant registrar/IMO and nil where operation done by Professor. The infection rate is high 47.36% in dirty operation and low 5% in clean operation. Wound infection rises with COPD (28.5%), DM (33.3%) and anaemia (45.8%). Organisms isolated from infected wound swab were *Escherichia coli* 45.5%, *Staphylococcus aureus* 37.5%, *Klebsiella pneumoniae* 8.5%, *Pseudomonas aeruginosa* 8.5% out of total 24 culture positive cases. Regarding antibiotic sensitivity all the above mentioned organisms were 100% sensitive to Imepenem, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* were 100% sensitive to ceftriaxone, but other antibiotics like ciprofloxacin, cephradine were sensitive to 50% only. **Conclusion:** The incidence of postoperative wound infection in emergency GI surgery is bound to come down with only minimal use of antibiotics when there are provisions of well-equipped surgical ward with sterile environment, a planned operation theatre and isolation facilities for infected patients.

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INTRODUCTION

Surgical wound infection still causes considerable morbidity and high cost to the health care system and is becoming increasingly important in medicolegal aspects.¹ Infections increase the discomfort and disability experienced by patients following surgical procedure and in their most severe form may endanger life.² The main determinants of infection are the microorganism, the environment and the host defense mechanism and there is continuous interaction between these three factors. The purpose of this study was i) to identify the different underlying factors/agents responsible for postoperative wound infection following emergency GI surgery, ii) prevention of that factors/agents and also to identify the causative organisms and iii) determination of antibiotic according to the culture sensitivity report of wound swab. In abdominal surgery, the source of bacteria may be endogenous (from the patients viscera 98% and skin), contamination from the air in the operation theatre, direct contamination from surgeon's hands wearing punctured gloves.³

On the basis of contamination surgical wound is classified into four categories: clean wound where infection rate is 1.5-2%, clean contaminated wound (Infection rate 5 to 7%) contaminated wound (Infection rate 15.2 to 20%) and dirty wound where infection rate is up to 40%.

Usually postoperative wound infection appears between 3rd to 5th postoperative days but it may appear as early as in the 1st day of surgery and even after the patient has left the hospital. Classically, the presence of postoperative wound infection has been confirmed by documenting the typical clinical signs of inflammation along with drainage of purulent or culture positive materials from the wound.

Early diagnosis by clinical features and isolation of organism from the wound by culture and sensitivity of the isolates using most appropriate antibiotic, the morbidity and mortality due to postoperative wound infection specially following emergency GI surgery can be reduced.

METHODS

This study was a prospective one where 142 patients were selected randomly from surgery department of Rajshahi Medical College Hospital, Rajshahi, during the period of six months (July 2012 to December 2012). All the patients studied were admitted for emergency surgery for acute appendicitis, perforated peptic ulcer, ileal perforation, acute intestinal obstruction, burst appendix, volvulus of sigmoid colon, obstructed inguinal hernia.

For bacteriological study, wound swabs were collected from infected postoperative wound, aseptically. The specimens were sent to the department of microbiology laboratory after proper labeling.

RESULTS

Out of 142 patients with emergency Gastro-intestinal surgery in this series, 62(43.7%) cases were acute appendicitis, 12(8.5%) cases were burst appendix, 15 (10.6%) cases were duodenal ulcer Perforation, 3 cases were small intestinal obstruction 19 cases were ileal perforation, 2 cases each were sigmoid volvulus and obstructed inguinal hernia. Wound infection rate of specific type of operation shown respectively in the Table I and Figure 1. The overall wound infection rate was 16.9%.

Table I: Wound infections according to diseases (n-142)

Name of disease	Name of operation	No.(%) of operation	No.(%) of infection among cases	Total No. (%) of infections
Acute appendicitis	appendectomy	62 (43.7%)	5 (8.1%)	20.8 %
Burst appendix	appendectomy with peritoneal toileting	12 (8.4%)	4 (33.3%)	16.6%
Duodenal ulcer perforation	Repair of perforation with thorough peritoneal toileting	15 (10.6%)	2 (13.3%)	8.3%
Small intestinal obstruction due to band and adhesion	Laparotomy with division of band and adhesion	18 (12.7%)		
Small intestinal obstruction needs resection and anastomosis	Resection and anastomosis	12 (8.4%)	4 (33.3%)	16.6%
Ileal perforation	Repair and peritoneal toileting	19 (13.9%)	8 (33.3%)	42.1%
Volvulus of sigmoid colon	Resection and Anastomosis	2 (1.4%)	1 (4.1%)	50.0%
Obstructed inguinal hernia	Herniotomy and herniorraphy	2 (1.4%)	0 (0%)	0%
Total		142		



Figure 1: Bar diagram of rate of wound infection.

Table II and Figure 2 shows that infection rate is higher (18.33%) where the operation were done by assistant registrar/indoor medical officer and relatively lower (12.50%) where it was done by registrar and nil (00%) where operations were done by Professor.

Table II: Surgeon and infection

Types of surgeon	No of operation	No. (%) of infection
Professor	6	0 (0%)
Registrar	10	2 (12.50%)
Assistant Registrar/IMO	120	22 (18.33%)

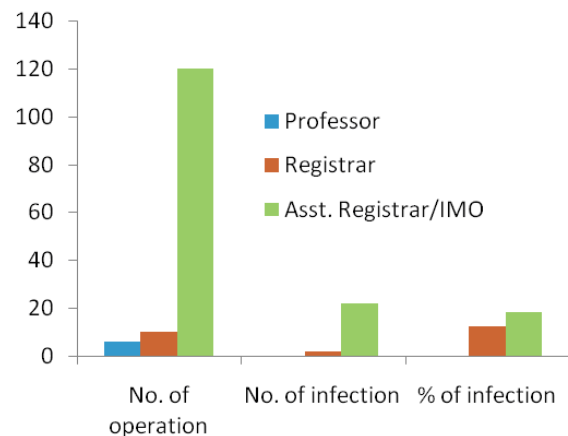


Figure 2: Bar Diagram of surgeon and infection rate

Infection rate varies with duration of operation. Up to 1 hours, it was 7.3% whereas operations taking more than 1 hour, infection rate is higher and it is 30% (Table III).

Table III: Duration of operation and wound infection rate.

Duration of operation (In hours)	No of cases	No. (%) of wound infection
upto 1 hour	82	6 (7.3%)
More than 1hour	60	18 (30%)

In this series, the rate of infection of clean wound was 5%, clean contaminated wound was 19.37%, contaminated wound was 26.90% and dirty wound was 47.36% (Table IV & Figure 3)

Table IV: Analysis of infection rates related to wound types.

Types of wound	No of cases	No. (%) of wound infection
Clean	20	1 (5%)
Clean contaminated	64	7 (19.3%)
Contaminated	29	7 (26.9%)
Dirty	19	9 (47.3%)

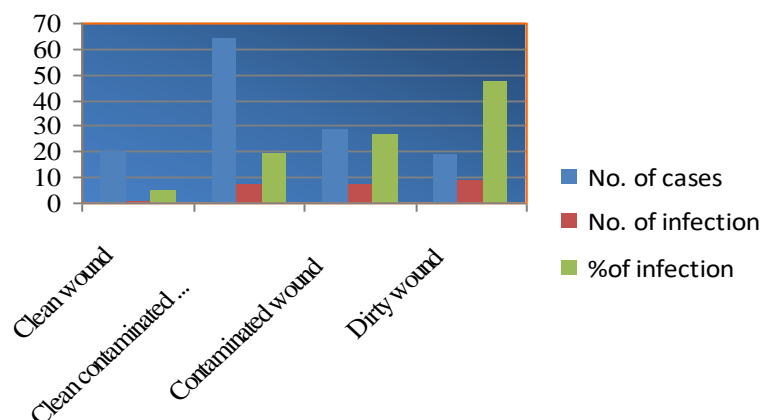


Figure 3: Bar Diagram of wound infection in various wound type

Table V shows that wound infection rate rises with chronic obstructive pulmonary disease (28.5%), diabetes mellitus (33.3%), medical jaundice (50%), anaemia (45.8%) (Hb%<60%).

Table V: Host conditions and wound infection rate

Host conditions	No of cases	No. (%) of infection
Anaemia	24	11 (45.8%)
Chronic obstructive pulmonary disease	7	2 (28.5%)
Medical jaundice	2	1 (50.0%)
Diabetes mellitus	6	2 (33.3%)

Total number of causative pathogens detected were 24, of which 11 (45.8%) were *Escherichia coli*, 9 (37.5%) were *staphylococcus aureus*, 2 (8.3%) were each of *Klebsiella* and *Pseudomonas aeruginosa*. No growth found in 2 cases (Table VI & Figure 4)

Table VI: Character of discharge or pus and organisms cultured

Character of discharge	No of cases	Organisms cultured
Serosanguinous	1	No growth
Thick creamy pus	9	<i>Staphylococcus aureus</i>
Muddy, thin & odourless	11	<i>Escherichiacoli</i>
Blue green pus	2	<i>Pseudomonas aeruginosa</i>
Yellow fishy odour	2	<i>Klebsiella</i>

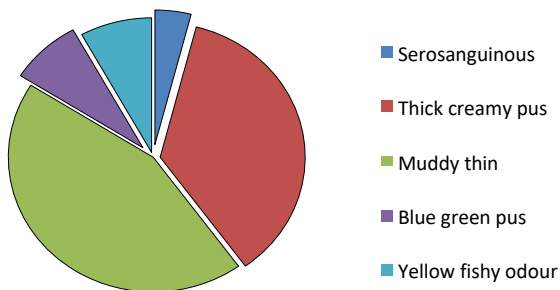


Figure 4: Pie chart of Character of discharge

Total number of infected wound shows *Escherichia coli* (45.5%), *Staphylococcus aureus* (37.5%), *Klebsiella* and *Pseudomonas* (8.5%) each (Table VII).

Table VII: Frequency of organism cultured from the postoperative infected wounds.

Total no. of infected wound	Isolated organism	Total no. of single isolated bacteria
24	<i>E. Coli</i>	11 (45.5%)
	<i>Staph. aureus</i>	9 (37.5%)
	<i>Kl. Pneumonia</i>	2 (8.5%)
	<i>P. aeruginosa</i>	2 (8.5%)
Total		24

E. coli, *S. aureus*, *Kl. pneumoniae* and *P. aeruginosa* all were sensitive to Imepenem but 72.7%, 88.9%, 100% and 100% sensitive to ceftriaxone. *E. coli* were 45.5%, 54.5%, 45.5% and 9.09% sensitive to ciprofloxacin, cephradine, cotrimoxazole and nitrofurantoin respectively. *S. aureus* were 44.4%, 44.4%, 55.5% sensitive to ciprofloxacin, cephradine and flucloxacillin respectively. *K. pneumoniae* were 50% sensitive to cephradine and cotrimoxazole each. *P. aeruginosa* is also 50% sensitive to ciprofloxacin and nitrofurantoin each (Table VIII).

Table VIII: Antibiotic sensitivity of the cultured organisms from infected wound.

Name of Organisms	Name of sensitive antibiotics & percentage (%)					
	Ciprofloxacin	Cephadrin	Cotrimoxazole	Flucloxacillin	Nitrofurantoin	Ceftriaxone
<i>E. coli</i>	45.5	54.5	45.5		9.1	72.7
<i>S. aureus</i>	44.4	44.4		55.5		88.9
<i>Kl. pneumoniae</i>		50	50			100
<i>P. aeruginosa</i>	50				50	100

DISCUSSION

Surgical infection as was studied by Louis Pasteur and Joseph Lister, hundreds of years ago, is still a subject of controversy and problem all over the world.⁴ In this study 142 cases were included and operative treatment was carried out for different acute abdominal conditions.

The findings of this study were compared with the results of the studies made by Rasul G, Ashraf SA et al,⁵ Cruse PJE, Frood R⁶, Saha SC, Zaman MA and Khan MR et al.⁷

Surgeons and infection

In this series wound infection is higher where the operation is done by assistant registrar/medical officer (22/120 i.e. 18.3%) in comparison to the registrar (2/16 i.e. 12.5%) and Professor (0/6 i.e. 0%) through the registrar and assistant registrar dealt with most of the contaminated case.

There is a relation between the length of operating time and infection rate. In this series the rate of wound infection is four times more when the duration is two times more. Other studies also show a rise in infection rate associated with prolongation of the operation time.⁸

Wound infection rate varies according to the types of operation. Infection rate is known to be higher in emergency surgery as compared to elective procedure.⁹⁻¹¹ In this series, wound infection was detected in 24 patients (16.9%). The wound infection rate in clean cases was 5%

(1 in 20), clean contaminated cases was 19. 3% (7 in 64), contaminated cases 26.90% (7 in 29) and in dirty cases 47.3% (9 in 19 cases). The rate of infection is higher as compared with the studies done by Cruse PJE and Frood R, who reported among 62939 wounds infection rate was 1.5% in clean wounds, 7.7% in clean contaminated wounds, 15.2% in contaminated wounds and 40% in dirty wounds.¹²

Another study on 696 operations by Renvall et al showed that the overall wound infection rate was 9.8%, where infection among clean wound was 4.2%, clean contaminated wound 9.1%, contaminated wound 14.4% and dirty wound 28.8%.¹³

In the present study, wound infection rate increased with clinically anaemic to 45.8%, chronic obstructive pulmonary disease 28.5%, diabetes 33.3%.¹⁴ Another study showed clean wound infection rate rises with diabetes to 10.7%, anaemia to 16.6%.¹⁵

This study revealed that out of 142 cases wound infection were found in 24 (16.9%). Causative pathogens detected were *E. coli* in 11 cases (45.5%), *S. aureus* in 9 cases (37.5%), *Klebsiella* in 2 cases (85%), *Pseudomonas* in 2 cases (85%). This findings showed similarities with the work of Ashraf and Matin.¹⁶⁻¹⁷

In all cases, antibiotics were used in both preoperative and in the postoperative period as therapeutic or prophylactic measures. Antibiotics mostly used were ciprofloxacin, ceftriaxone, cephalosporin, gentamycin and metronidazole. Rasul and Ashraf did not used any antibiotic in 65

selected cases. There was not a single incidence of infection. The results of recent clinical trials of perioperative antibiotic therapy after emergency abdominal surgery support such policies.¹⁸

CONCLUSION

This study indicates that this high 9 (47.36%) in dirty operations and low (5%) in clean operations. The study also showed that infections are more common in patients with COPD, DM and anaemia. If we had a well-equipped surgical ward with clean environment and adequate resuscitative facilities, a planned operation theatre, isolation facilities for septic patients and overall health consciousness of the patient, the incidence of postoperative wound infection in emergency GI surgery is bound to come down with only minimal use of antibiotics.

Conflict of Interest: None

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Treatment of Chronic Hepatitis B virus Infection: An update 2018

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ABSTRACT

Hepatitis B virus-related morbidity and mortality remain a major global health threat. The first effective nucleoside analogue against the hepatitis B virus was registered almost two decades ago. Since then major progress has been made in the management of chronic hepatitis B infection. The costs and the need for prolonged therapy are the obstacles. New biomarkers such as quantitative hepatitis B surface antigen might help to determine if HBeAg antigen negative patients can be taken off nucleos(t)ide analogues. On the other hand, novel compounds that target the viral life cycle or modulate host immune response are in the pipeline. In the next few years, one should expect breakthrough advancement to be made leading to a "cure" for patients with chronic hepatitis B infection by inducing hepatitis surface antigen loss with or without the development of the hepatitis B surface antibody.

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INTRODUCTION

In Bangladesh, different studies showed that seroprevalence of hepatitis B is 2.3-9.7% among apparently healthy populations.¹⁻³ Trend of prevalence of HBsAg in both adult and children in Bangladeshi population is negative. In last two decades, sero prevalence among child has been reduced about more than three times. In 1984 Islam et al. reported that prevalence of HBsAg among children was 15.4%;⁴ in 2003 Zakir et al.⁵ reported 8.5%. In 2011, Alam et al. showed in his study that, it was 4.2% and was declining from previous studies.⁶

In case of adult, last two decades' seroprevalence of HBsAg reduced about four times. In 1984 Islam et al.⁴ reported 27.2%; in 1991 Ahmad et al.⁷ reported 8.6%; 1997 Rahman et al.⁸ reported 6.4%; in 2008, Mahtab et al.⁹ reported 5.5% and in 2011 Rudro et al.¹⁰ 6.5%. Overall prevalence of HBV infection in Bangladeshi general population has been decreasing for last several years. In 2007, Rahman et al.¹¹ reported 8.1%; in 2015 Rukunuzzaman et al.¹² reported 3%.

Chronic hepatitis B infection affects around 250 million people world wide(3.61% of the global

population) and if left untreated, around one-quarter of them will die of cirrhosis, liver failure or hepatocellular carcinoma.¹³⁻¹⁸ Variations in hepatitis B surface antigen (HBsAg) seroprevalence are wide it is the lowest in Norway and the UK (0.01%) and the highest (more than 20%) in countries such as South Sudan and Kiribati.¹⁷ The number of affected individuals is highest in the Western Pacific region, defined by the World Health Organization as 37 countries including China, Japan, South Korea, the Philippines and Vietnam, with 95.3 million (prevalence estimates of 5.26%) and Africa, with 75.¹⁸ million (prevalence estimates of 8.83%) accounting for nearly 70% of all chronic hepatitis B infection globally.^{17,19} Despite recommendations for universal hepatitis B vaccination in 1992, it has not been fully implemented in endemic countries due to economic and logistic constraints. This is further compounded by the use of unsafe blood products and medical procedures in resource-poor countries and has contributed to the increase in mortality and disability adjusted life years (DALYs) due to hepatitis B infection between 1990 and 2013.²⁰ Thus, chronic hepatitis B (CHB) infection remains one of the most important causes of morbidity and mortality in humans.

This article represents view on the treatment of CHB infection based on the treatment guidelines published by the three continental Hepatology societies.^{13,16,18}

Who needs treatment and with what?

The goal of therapy for CHB infection is to improve quality of life and survival in infected persons by preventing disease progression to cirrhosis, decompensated cirrhosis, end stage liver disease, hepatocellular carcinoma (HCC) and death.^{13,16,18} This goal can be achieved with

significant suppression of HBV replication which has been shown to correlate with a significant reduction in hepatic necro inflammation, reversal of liver fibrosis and reduction in the development of cirrhosis and HCC. The ideal endpoint in both hepatitis B antigen (HBeAg)-positive and HBeAg-negative patients is sustained off therapy HBsAg loss, with or without seroconversion to anti-HBs. This is associated with complete and permanent remission of CHB activity and improved long-term outcome.²¹ However, such a “cure”, with loss of HBsAg with or without the development of HBsAb can rarely be achieved with current registered therapies against CHB because eradication of covalently closed circular DNA (cccDNA) in the nucleus of infected hepatocytes and integrated hepatitis B virus (HBV) is very difficult.²² This is at least partly due to the inability of current therapeutic agents to effectively repair virus specific and global T-cell dysfunction mediated by multiple regulatory mechanism, such as virus-specific IL-10 response, FOXP3+ regulatory T-cell frequency and T-cell expression of PD-1 and CTLA-4.²³ Thus, a more realistic endpoint is the induction of sustained or maintained virological remission. Induction of sustained off therapy virological response in both HBeAg-positive (with sustained anti-HBe seroconversion) and HBeAg-negative patients is a satisfactory endpoint, because it has been shown to be associated with an improved prognosis. If a sustained off therapy response cannot be achieved then maintained, virological remission (undetectable HBVDNA by a sensitive PCR assay) with long term antiviral therapy in HBeAg-positive patients who do not achieve anti-HBe sero-conversion and in HBeAg-negative patients is the next best endpoint.^{13,15,16,18} Based on clinical evidence and experts’ opinion, the American, Asian Pacific and European Liver Associations (AASLD, APASL and EASL) have formulated management guidelines to help physicians make

treatment decisions. All these guidelines are based on clinical status, serum HBV DNA and alanine aminotransferase (ALT) levels, HBeAg status, and the degree of liver fibrosis.^{13,15,16,18} All guidelines recommend starting treatment as soon as possible in patients with life-threatening liver disease: acute liver failure, decompensated cirrhosis or severe acute exacerbation of chronic hepatitis B, regardless of HBVDNA and ALT levels. These guidelines also recommend antiviral treatment for patients with compensated cirrhosis whatever the ALT levels but there are minor differences in threshold HBV DNA levels for initiating treatment. All guidelines agree that treatment should be initiated in patients without cirrhosis with serum HBV DNA levels >20,000 IU/mL and persistently elevated ALT levels and/or histological evidence of moderate or severe inflammation or fibrosis. However, cut-off values of ALT and the need for liver biopsy or the noninvasive assessment of liver fibrosis to determine treatment indications differs among guidelines.

In the past two decades, seven drugs have been approved for the treatment of CHB infection, namely conventional and pegylated interferon (PEG-IFN), and five nucleos(t)ide analogues: lamivudine, telbivudine, adefovir, entecavir and tenofovir.²⁴⁻³² The effectiveness of these antiviral therapies in reducing the risk of cirrhosis, decompensated liver diseases and hepatocellular carcinoma in CHB patients with treatment indications, was supported by a recent systemic review and meta-analysis.^{33,34} In addition, based on recent encouraging phase 3 data, tenofovirafenamide (TAF), a new form of tenofovir, is the next registered agent for the treatment of CHB. TAF has been shown to be as effective as the tenofovir disoproxil fumarate (TDF) formulation in both HBeAg-positive and negative patients, but with fewer detrimental

effects on bone and kidney biomarkers. In both studies, patients receiving TAF experienced a significantly smaller mean percentage decrease from baseline in hip and spine bone mineral density at week 48 compared to patients receiving TDF. Smaller increases in serum creatinine were observed in HBeAg-positive patients receiving TAF. Moreover, the median change in estimated glomerular filtration rate (eGFR) from baseline to week 48 favoured TAF in both studies.³⁵⁻³⁶ All guidelines recommend initial treatment with PEG-IFN, entecavir or tenofovir as monotherapy.^{13,15,16,18} Although IFN is not recommended in patients with acute liver failure, decompensated cirrhosis or severe exacerbations of chronic hepatitis B, it may be used with caution in patients with compensated cirrhosis. While guidelines consider PEG-IFN, entecavir and tenofovir to be equivalent first-line anti-HBV drugs, in our clinical practice as do many others, entecavir and tenofovir are used much more often than PEG-IFN even in patients with no contraindications to the use of IFN. This is related to patients' preference for route of administration (injection versus oral) and the presence of medical/psychiatric comorbidities that contraindicate use of or decrease tolerance to IFN, as well as the cost of the treatment. However, in some circumstances, other factors such as the desire to raise a family in the near future in female patients or the desire to use a more finite rather than long-term therapy (PEG-IFN for 1 year versus >3 years of nucleos(t)ide analogues) can make PEG-IFN more preferable. Recently, the cost has become a less important concern because entecavir and tenofovir has or will soon go off-patent, and both drugs have markedly lower rates of drug resistance (0-1% after 5-6 years of continuous therapy) compared to lamivudine, adefovir or telbivudine. Tenofovir and entecavir have similar potencies and barriers to antiviral resistance, and either drug may be

used as first-line treatment in nucleoside-naïve patients. Because of a low risk of nephrotoxicity, entecavir is preferred in older patients, patients with baseline impaired renal function and those with other medical conditions such as hypertension or diabetes that increase the risk of renal insufficiency. Although telbivudine has been reported to improve renal function, the high risk of antiviral drug resistance and the potential for other adverse reactions such as myopathy and polyneuropathy make this a poor choice as a first-line treatment.²⁵ Tenofovir effectively suppresses not only wild type HBV but also lamivudine, telbivudine or entecavir resistant HBV and to a lesser extent adefovir resistant HBV. It is therefore a better choice in patients who have been previously treated with other nucleos(t)ide analogues. Tenofovir is also a preferred choice for women of reproductive age because of its safety record in pregnancy.³²

Recently, the use of PEG-IFN was further fine-tuned with the use of a 12-weeks stopping rule, based on no decline or a $<0.5 \log_{10}$ decline of qHBsAg or qHBsAg $>20\,000$ as the stopping rule. However, these rules are based on retrospective analyses of data from large clinical trials and have never been tested prospectively.^{14,15,19-23} An ideal stopping rule should have a negative predictive value (NPV) of 95% for both intermediate-term and long term response and should be applied to all patients. The NPV from these studies varies between 72% and 97%, with the lowest NPV in Asian patients. Furthermore, different stopping rules have been identified to predict a long term response and it has been shown that some patients who meet criteria for stopping treatment based on a low probability of intermediate response might have a late response with HBsAg clearance. These data show that one universal stopping rule probably cannot provide sufficiently accurate predictions for a

response to PEG-IFN for it to be applied in clinical practice.

Can we stop treatment with nucleos(t)ide analogues?

With the wide availability of nucleos(t)ide analogues for nearly two decades, many patients with chronic hepatitis B infection have been maintained on treatment. One of the frequent concerns is the long term safety and cost of this “infinite” treatment. Most of these patients have been treated with entecavir or tenofovir because these drugs have a very low rate of drug resistance. Recommendations on when to stop nucleos(t)ide analogues vary. All guidelines recommend that nucleos(t)ide analogues be stopped in HBeAg-positive patients when the patient has completed 6-12 months of consolidation therapy after HBeAg seroconversion. EASL guidelines recommend continuing treatment until HBsAg loss in patients with advanced fibrosis or cirrhosis to avoid flares associated with viral relapse. AASLD and EASL guidelines recommend that nucleos(t)ide analogues be continued in HBeAg-negative patients until HBsAg loss while APASL guidelines state that treatment may be withdrawn after completing at least 2 years of treatment with undetectable HBV DNA documented on three occasions 6 months apart. All three guidelines recommend life long nucleos(t)ide analogue treatment in patients with cirrhosis before treatment unless they had compensated cirrhosis and had cleared HBsAg. In a recent meta-analysis including 25 studies with more than 1700 patients in whom nucleos(t)ide analogues were discontinued, the duration of an on-therapy virological response was shown to be the most important predictor of a durable off therapy virological relapse (VR) with a significantly increased pooled probability (12 months:

36% versus 75%) in patients who remained in VR under nucleos(t)ide analogues for more than 24 months. These findings contradict APASL guidelines, which recommend discontinuation of nucleos(t)ide analogues in HBeAg CHB who remain in VR for only 18 months. However, the optimal duration of on therapy VR before stopping nucleos(t)ide analogues remains unknown.³⁷ On the other hand, recent data suggest the usefulness of end-of-therapy and post-treatment quantitative hepatitis B surface antigen (qHBsAg) to predict VR and biological relapse (BR). The usefulness of end-of-treatment qHBsAg in predicting a sustained viral response after stopping nucleos(t)ide analogue treatment has been explored. It has been suggested that end-of-treatment serum qHBsAg levels can predict off-therapy sustained virological response³⁸ and patients with a low qHBsAg level <10 IU/mL did not relapse.³⁹ However, larger prospective studies are certainly needed for validation. Nevertheless, patients with CHB and without cirrhosis who are receiving nucleos(t)ide analogues with virological response >2 year scan stop treatment as long as they can be closely monitored.³⁷

New therapeutic agents for chronic hepatitis B to meet the unmet need: “a cure”

None of the existing anti-HBV agents is effective in achieving the ideal goal of therapy-HBsAg loss (functional cure) or HBsAg seroconversion (complete cure). This is mainly because current therapy is ineffective in clearing cccDNA or preventing transcriptional cccDNA activity. Even following 48 weeks of PEG-IFN, HBsAg loss will only occur in less than ten per cent of the patients. This means that most patients must be maintained on “lifelong” nucleos(t)ide analogue therapy, resulting in escalating costs and an increased risk of side effects. In an attempt to

increase the rate of HBsAg loss, registered agents have been combined in various fashions (sequential or concomitant) with little success. Thus, new therapeutic agents are clearly needed. To date, various anti-HBV drugs or biological agents that are directed at specific steps in the viral life cycle and spread, that increase and restore host immune response and target cccDNA, are in the development pipeline, either in the preclinical or early clinical phases.⁴⁰ Among them, siRNA, HBsAg inhibitors and capsid inhibitors have reached clinical trials. However, none of these agents are expected to become available before the next few years and these agents will probably need to be combined with existing ones.

CONCLUSION

In 2018, PEG-IFN and nucleos(t)ide analogues with high resistant barriers (tenofovir and entecavir) are expected to remain the mainstay of treatment for CHB, based on guidelines from the different continental hepatology societies. Recently, TAF is available to provide safer long-term use of nucleotide analogues in CHB patients. With the development of new therapeutic agents targeting various key steps in the viral life cycle and/or improving the host immune response to the virus, a cure for CHB can be expected in the next decade. This, together with full implementation of the HBV vaccine programme, should pave the way to a “Hepatitis B free generation” by 2030.

Conflict of Interest: None

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Does Autoimmune Disease act as a Hidden Trigger for Aggressive form of Gastroesophageal Malignancy in young Adult?

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ABSTRACT

Autoimmune disease and cancer both arise from dysfunctions of the immune system. Autoimmunity occurs when the body mistakenly attacks itself, launching an immune response against self-antigens that are not actually harmful. Cancer occurs when the body's mechanisms for controlling cell growth and death malfunction, preventing old cells from dying and allowing them to proliferate out of control. Despite the dramatic differences in their underlying mechanisms, for many years, researchers have observed that certain autoimmune diseases are positively or negatively associated with certain cancers. A young woman with Hashimoto's thyroiditis, behavioral disorder of repeated suicidal tendency, pancreatic carcinoma, angiolipoma over left great toe, right sided oropharyngeal lymphoma and poorly differentiated gastro-oesophageal adenocarcinoma is discussed in present case study.

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INTRODUCTION

An autoimmune disease occurs when the body tissues are attacked by its own immune system. Patients with autoimmune diseases frequently have unusual antibodies circulating in their blood that target their own body tissues.^{1,2} Examples of autoimmune diseases include systemic lupus erythematosus, Sjogren's syndrome, Hashimoto thyroiditis, rheumatoid arthritis, juvenile (type1) diabetes, polymyositis, scleroderma, Addison's disease, vitiligo, pernicious anaemia, glomerulo-

nephritis, and pulmonary fibrosis. Recent studies suggest that the pathogenesis that plays a vital role for developing autoimmune disease can also cause different types of malignancies of different sites.³⁻⁵ As these are uncommon, case reports are the main source of information.

The Case

A young lady, 22 years of age, was presented to Department of Oncology, Khwaja Yunus Ali Medical College Hospital, Enayetpur, Sirajganj, Bangladesh as a diagnosed case of loco-regionally advanced pancreatic adenocarcinoma. Abdo-

minal severe pain, repeated vomiting, pronounce weakness and behavioral disorder was observed following 1st cycle Gemcitabine based chemotherapy. She was treated accordingly and went through detailed history taking where family history of consanguineous marriage in

between her parents was found followed by history of excision of right sided oropharyngeal mass (probable neurogenic tumour/lymphoma in CT scan finding) in 2006, histopathology of which revealed hyperplastic lymphoid follicle with prominent germinal center (Figure 1, 2).

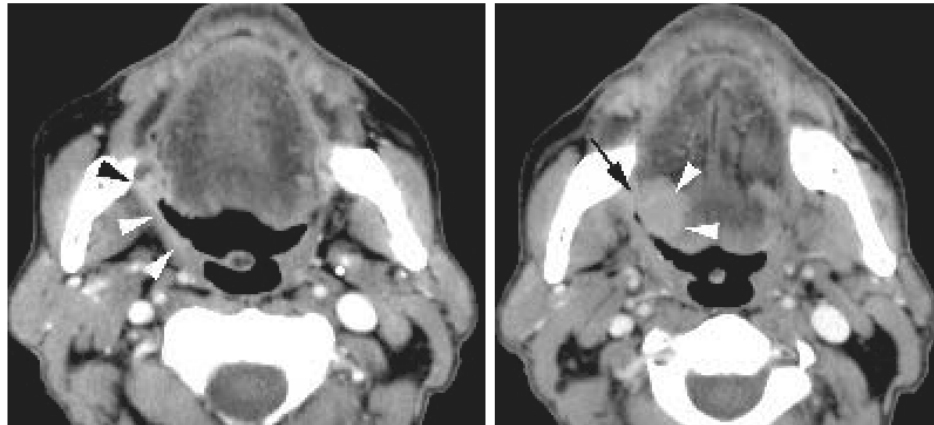


Figure 1: CT Scan of neck showing right sided oro-pharyngeal mass (Arrow).

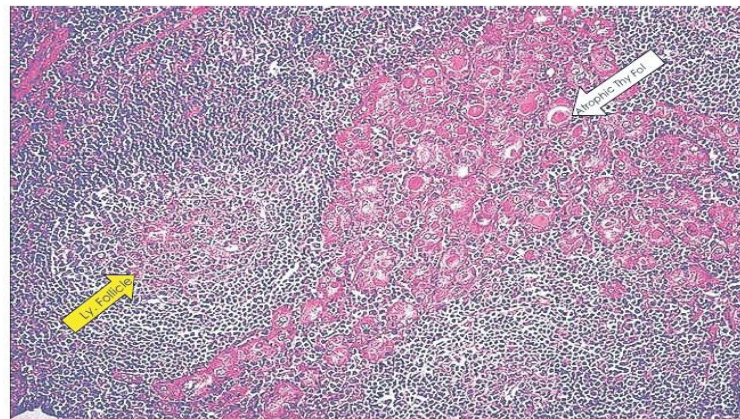


Figure 2: Photomicrograph showing hyperplastic lymphoid follicle with prominent germinal center (Arrow).

History of 3rd excision of a swelling over left great toe in march, 2015 (slowly and gradually increasing since 2010 but suddenly became larger within one month) histopathology revealing angiolipoma, 4th history of hemithyroidectomy in December, 2015, histopathology of which revealed Hashimoto's thyroiditis and 5th history of suffering from behavioral disorder, repeated suicidal tendency which started one month after thyroid surgery. Thorough investigations including upper GI endoscopy, colonoscopy, CT

scan whole abdomen was performed. Reports revealed gastro-oesophageal malignancy with invasion of surrounding structures including pancreas (Figure 3, 4) and clinically gross hypothyroidism. Endoscopic biopsy from lower oesophageal growth revealed poorly differentiated adenocarcinoma. Her hypothyroid state was gradually corrected and after that she was on chemotherapy with EOX regimen with good subjective and objective response.

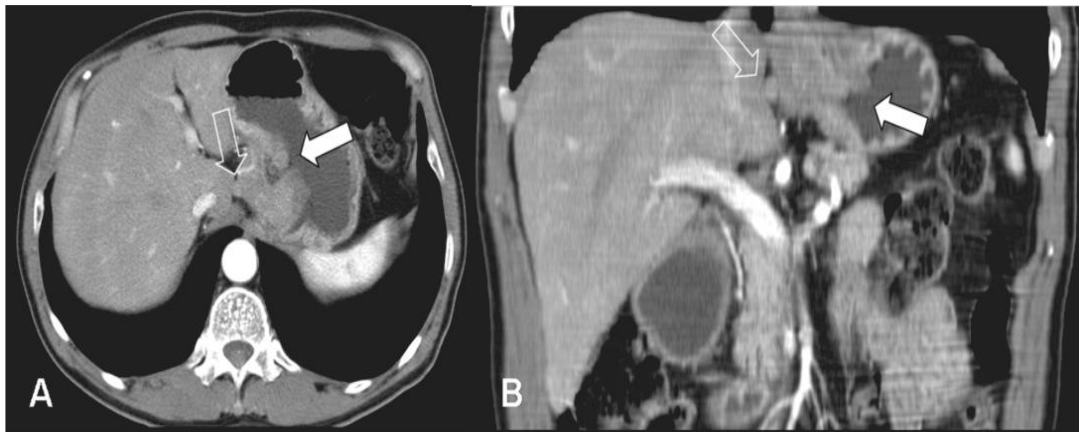


Figure 3: CT scan of whole abdomen showing esophageal growth (Arrow).

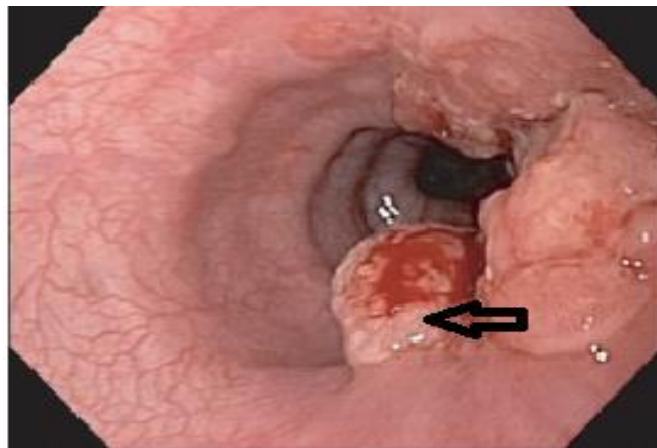


Figure 4: Endoscopy of upper GIT showing huge gastric antral growth (Arrow).

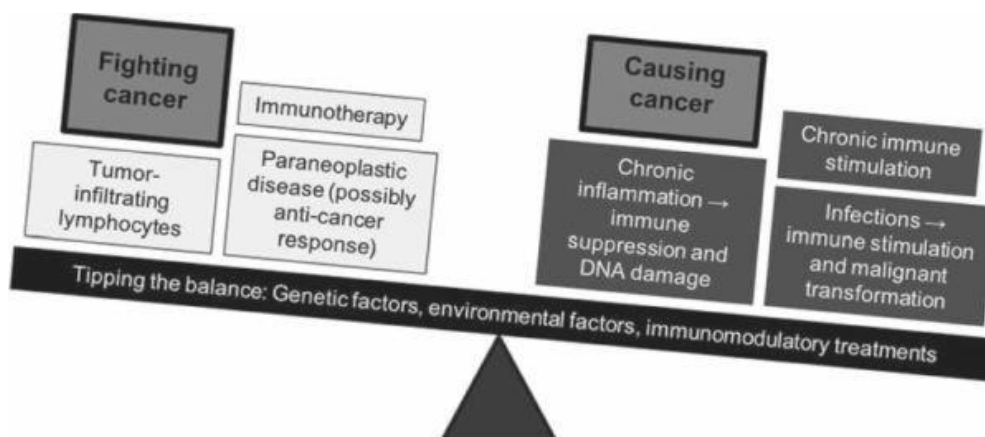


Figure 5: Relation in between autoimmunity and carcinogenesis (adopted from Anticancer Res. 2012; 32(4): 1120) (Arrow).

DISCUSSION

There are more than 80 disorders that occur due to autoimmune action causes of which still not known clearly. Recent studies suggest that these autoimmune conditions can also play significant role in the pathogenesis of different malignancies. Similarities in the pathologies of autoimmune diseases with cancer lead to chronically overactive immune response, production of inflammatory cytokines and growth factors mediating overt cell proliferation and carcinogenesis.¹ Autoimmune metaplastic atrophic gastritis (AMAG) is an example of inherited autoimmune disease that attacks parietal cells, resulting in hypochlorhydria and decreased production of intrinsic factor. Consequences include atrophic gastritis, B12 malabsorption, and, frequently, pernicious anemia.^{2,3} Risk of gastric adenocarcinoma increases 3-fold in this disease. Diagnosis is done by endoscopy.² This AMAG has a close association with autoimmune thyroiditis sometimes where chronic thyroiditis can activate autoimmunity against gastro oesophageal epithelium thus leading to aggressive form of gastro oesophageal malignancy.^{4,5}

CONCLUSION

Evidence demonstrates that autoimmune diseases are associated with the development of different forms of malignancies where gastrointestinal tract malignancies are uncommon. This relationship implies the importance of surveillance of patients who are treated as autoimmune disease, especially autoimmune thyroiditis for prevention of auto immunity related second malignancies like aggressive form of gastroesophageal malignancy.

Conflict of interest: The authors have no conflict of interest.

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Anorectal Anomaly in two Cases

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ABSTRACT

Anorectal malformations (ARMs) are the most common surgically treated congenital anomalies in newborns. Early diagnosis and timely surgical intervention affords the best opportunity for correction without complications. We report two cases of ano-rectal malformation. First baby was six days old male while second baby was three days old male child admitted in the department of paediatrics, North Bengal Medical College Hospital, Sirajganj with the complaints of not passing meconium since birth with gradual distention of abdomen and absence of anal opening in the perineum. Mothers also complained of vomiting for several times for last two days. For confirmation of the diagnosis, we performed invertogram for both babies. We observed that first baby has anorectal anomaly (imperforate anus -low variety) while the second baby has high variety anorectal anomaly. First baby was surgically corrected by cutaneous anoplasty, while the second baby was initially corrected by colostomy.

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INTRODUCTION

Imperforate anus' has been a well-known condition since antiquity.¹ Now-a-days, broadly termed as anorectal malformations (ARMs). No specific cause has been described. The average incidence worldwide is 1 in 5000 live births.² When compared to older children, neonates have a wide divergence in physiology, anatomy, immunity and response to stress and

when they have surgical illness they are further compromised by the condition itself which predisposes anaesthesia and surgery.³⁻⁵ Anorectal malformations are the major surgical emergencies in neonatal intestinal obstruction (NIO). Defects range from the very minor easily treated with an excellent functional prognosis, to those that are complex, difficult to manage, are often associated with other anomalies, and have a poor functional prognosis. Many neonates with

imperforate anus have an abnormal sacral progression, as well as a fistula between the rectum and the genitourinary tract, demonstrated by finding meconium in the urine. NIO presented with a triad of bile stained vomiting, abdominal distension and failure to pass meconium.⁶ Failure to pass meconium (48% of normal neonates pass meconium in the first 24 hours of life) is symptomatic of lower intestinal obstruction. Normally it takes between 3 and 6 hours for the gastric contents to reach the small bowel. The intestinal contents reach the Caecum in a liquid state. It then takes about 20 to 24 hours for that faecal material to reach the rectum and become formed stool with the absorption of water that occurs in the colon. The rectum and sigmoid colon acts as a reservoir and holds the faecal material for a variable period of time. First the clinician must perform a thorough perineal inspection, which usually provides the most important clues about the type of malformation that the patient has. It is important to not make a decision about a colostomy or a primary operation before 20 to 24 hours of age. Radiologic evaluations do not show the real anatomy before 24 hours because the rectum is collapsed by the muscle tone of the sphincters that surround its lower part. Therefore radiologic evaluations done too early (before 24 hours) will likely reveal a "very high rectum" and thereby yielding a false diagnosis. After 24 hours, if there is no meconium on the perineum, we recommend obtaining a crosstable lateral radiograph with the patient in the prone position. Historically, an invertogram was used to identify whether the anomaly is high or low. When a low anomaly (perineal fistula) is diagnosed, the fistulous track to the perineum is always located anterior to the sphincter mechanism. A limited posterior sagittal anorectoplasty can be performed in the newborn period. If air in the rectum is seen distal to the coccyx and the

patient is in good condition with no significant associated defects, one may consider performing a posterior sagittal operation without a protective colostomy. A more conservative alternative would be to perform the posterior sagittal repair and a protective colostomy at the same stage. Conversely, if the rectal gas does not extend beyond the coccyx, or the patient has meconium in the urine, an abnormal sacrum, or a flat bottom, we recommend a colostomy. With emerging advancements in perinatology and prenatal ultrasound techniques, anorectal malformations are more commonly being suspected.⁷ Sonographic findings such as a dilated rectum or hydrocolpos or demonstration of an associated anomaly such as an absent kidney, a vertebral anomaly such as a hemisacrum, or an orthopaedic problem such as a missing radius can make the perinatologist suspicious that the neonate may in fact have an anorectal malformation. With improving technology, it is likely that this area of diagnosis and even neonate intervention for, perhaps, a massive hydrocolpos will continue to advance.^{8,9} We reported two cases of anorectal malformations.

The Cases

We reported two patients having ano-rectal malformation. First one was six days old male baby (Figure 1) while second patient was 3 days old male term baby, admitted in the department of paediatrics in North Bengal Medical College Hospital, Sirajganj with the complaints of not passing meconium since birth with gradual distension of abdomen. Mothers also complained of vomiting for several times for last two days. On clinical examination, we found the first baby was mildly icteric, activity and tone was normal, respiratory rate was 36 breaths/minute, heart rate was 120 beats/minute, Temperature-99⁰ F,

mildly anaemic, abdomen was hugely distended, hard in consistency, bowel sound was absent, ascites was also absent, there was no organomegaly. Genitourinary system was normal, there was no fistulous communication with urethra but a small opening present in the perineum. Other systems examination revealed normal findings.



Figure 1: Clinical picture of patient 1 showing perineal fistula with well-developed buttock (Arrow).

During clinical examination of second case, we found the baby was mildly pale, anicteric, vital signs were normal, abdomen was hugely distended and hard in consistency, bowel sound was absent, ascites was also absent, there was no organomegaly, other systems examination was normal. For confirmation of the diagnosis we performed invertogram of both babies. By the invertogram, we observed that first baby has imperforate anus (low variety) as shown in Figure 2 and 3, but second baby has high variety anorectal anomaly (Figure 4 & 5). Both children were treated by surgical correction. First baby was surgically corrected by cutaneous anoplasty while second baby was initially corrected by colostomy.

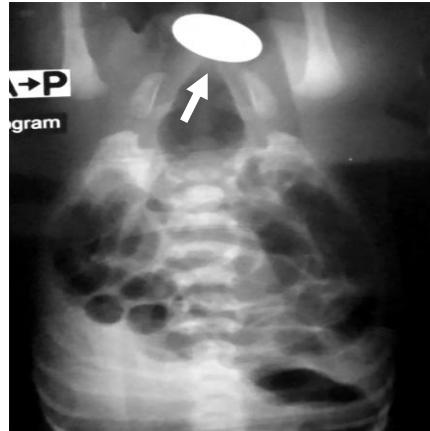


Figure 2: The invertogram of patient 1 showing low variety (AP view) (Arrow).



Figure 3: Invertogram of patient 1 showing low variety (lateral view) (Arrow).



Figure 4: Invertogram of patient 2 showing high variety (AP view) (Arrow).

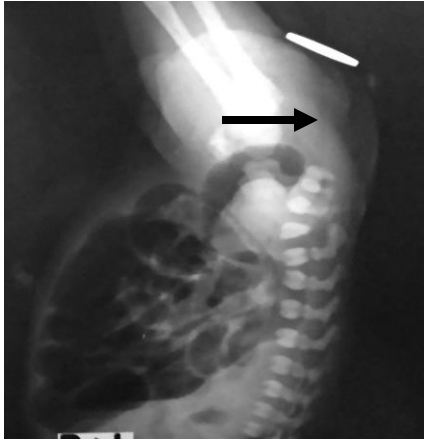


Figure 5: Invertogram of patient 2 showing high variety (lateral view) (Arrow).

DISCUSSION

Anorectal malformations represent a wide spectrum of defects. The terms ‘low,’ ‘intermediate,’ and ‘high’ are arbitrary and not useful in current therapeutic or prognostic terminology. A therapeutic and prognostically oriented classification is depicted.¹⁰ In the case of boys, the perineal body, the median raphe, scrotum, and penis should be carefully inspected.¹¹ Meconium being expressed from the urethral meatus is indicative of a fistulous connection between the Rectum and the urinary tract. The finding of “meconuria” is typically a trigger for a diverting colostomy with staged reconstruction.

In girls, it is vitally important to determine the number and location of perineal orifices. However, the presence of 3 orifices does not exclude an Anorectal Malformation (ARM). The fistulous opening can be located either in the perineal body, as seen in an anterior anus, or more commonly in the vestibule of the vaginal vault outside the hymen (rectovestibular fistula). Hence, determining the location of all orifices is as important as accounting for them. The presence of two orifices is indicative of a

urogenital sinus. In this case, the genitourinary tract and reproductive tract share a common channel, and the gastrointestinal tract has a separate opening in the normal location. Female hypospadias can sometimes be confused with this, and is considered a milder form of urogenital sinus. Note that all boys by definition have a urogenital sinus. A single orifice is consistent with a cloacal anomaly. In this anomaly, the reproductive, urinary, and gastrointestinal tracts share a common orifice. This is the most complex form of female ARM and requires extensive evaluation and staged corrective surgery.

On occasion, fistulous connections may be difficult to identify immediately. A waiting period of approximately 24 hours allows the meconium to descend, and subsequently facilitates visualization. In addition to determining the number and location of the orifices, additional physical findings that should be observed include the “flatness” of the bottom, presence of an anal dimple, midline groove, and whether there is a presacral mass. Patients with relatively flat bottoms are thought to have had poor development of the pelvic musculature, and subsequently have a higher chance of incontinence. A presacral mass with ARM and sacral anomaly are present in infants with the Currarino triad. The presence of an ARM should prompt an evaluation for VACTERL (vertebral anomalies, anal atresia, cardiac defects, tracheoesophageal fistula and/or esophageal atresia, renal and radial anomalies, and limb defects) anomalies. Transthoracic echocardiography, renal ultrasound, and plain film radiography of the chest and abdomen are necessary in the initial evaluation for VACTERL. The presence and extent of associated anomalies may affect the choice of the surgical approach for the ARM, as well as the timing for definitive reconstructive surgery. Once an anorectal anomaly is suspected, a paediatric surgical consultation is recommended.

The vast majority of ARMs do not require emergent surgical intervention. The timing of surgery is typically after the first 24 to 48 hours after birth. During the first 24 hours, gas and meconium descend through the rectum to either the lowest level of the pouch or into the fistula. This time allows for a more accurate assessment of the extent of the anomaly. For further management of baby, it is described that two main questions must be explored during the initial postnatal evaluation which is there a need for a staged approach with colostomy or primary repair, and other is there an associated anomaly that requires more urgent intervention?¹¹⁻¹³

Conflict of Interest: None

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Emphasize new and important results and the conclusions that follow including implications and limitations. Relate observations to other relevant studies.

Conclusion

Include brief findings and authors suggestions on basis of findings of study.

Acknowledgments

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