

Vol. 4 No. 1
January 2018

Barind Medical College Journal



Preoperative serum CEA level >5 ng/ml should not be used as a single screening test for colorectal carcinoma . Preoperative high serum CEA concentration (>10 ng/ml) correlating with the signs and symptoms of CRC may be used in multiphasic screening of CRC for further confirmatory diagnostic test.

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Volume 4 Number 1 January 2018

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Golden statue of Acharya Nāgārjuna at
Kagyu Samye Ling Monastery, Scotland.

Acharya Nagarjuna (c. 150- c. 250 CE), Indian Buddhist philosopher who articulated the doctrine of emptiness (shunyata) and is traditionally regarded as the founder of the Madhyamika ("Middle Way") school, an important tradition of Mahayana Buddhist philosophy. He is believed to be an alchemist who worked extensively with mercury, and advocated the use of chemical cures rather than preparations made from herbs and vegetables. He described details of the circulatory system, and referred to blood as rakta dhatu. He made many specially concocted chemicals with therapeutic value called bhasmas. He redacted sushruta samhita. His major works in the field of medicine and alchemy include Vighraha Vyavar Vartika, Rasa Ratnakar.

BMCJ, a peer reviewed biannual medical journal, is the official journal of Barind Medical College, Rajshahi, Bangladesh.

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Published By
Barind Medical College
Rajshahi, Bangladesh

Annual Subscription
Tk. 200/- for local subscribers
US\$ 20 for overseas subscribers



BARIND MEDICAL COLLEGE JOURNAL (BMCJ)

Official Journal of Barind Medical College

Volume 4 Number 1

January 2018

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Management of inflammatory bowel disease (IBD): current and future perspective

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Cite this as:
BMCJ 2018;4(1): 1-2

Received : 11 November 2017
Accepted : 7 December 2017

Inflammatory bowel disease (IBD) encompasses chronic idiopathic inflammatory disorders of gastrointestinal tract with a multifactorial pathophysiology. They include Ulcerative Colitis (UC) and Crohn's Disease (CD) with different clinicopathological entity. Ulcerative colitis is characterised by diffuse inflammation affecting the mucosa of Rectum and distal colon only whereas Crohn's disease involves patchy transmural ulceration that can affect any part of the gastrointestinal tract. Around 5% of patients have features of both subtypes.

Complete understanding of pathology of IBD is still out of sight. However as a multifactorial disorder the components involved in IBD pathogenesis include environmental, genetic, microbial and immunological factors. These components are continuously being investigated to contribute to the development of advanced management tools.

The gastrointestinal (GI) tract maintains immune homeostasis, involving non-pathogenic commensal organisms, self-antigens, and food antigens, and other immune complexes for protecting the host against pathogenic organisms by mounting an inflammatory response. The fine line between tolerance and inflammation of the GI immune system, when disrupted, may result in diseases such as inflammatory bowel disease (IBD).¹ Role of microbial factors may be explained as mucosal immune response against gut microorganisms in genetically susceptible individuals.² At the same time some environmental factors play an very important role in the overall pathogenesis of IBD.³ Role of innate immunity and adaptive immunity in IBD pathogenesis is much more complex than can be postulated with available scientific facts. However, improved understanding of

the immunopathogenesis of IBD has led to development of successful biological therapies.

Therapeutic immunomodulation for IBD can take place at various stages of the inflammatory cascade. Current approved therapies have been successful in targeting TNF, with the use of infliximab, adalimumab, certulizumabpegol and golimumab and T-cell homing to the gut, with the use of vedolizumab blocking $\alpha 4\beta 7$ integrin. Newly approved drugs, JAK inhibitor tofacitinib and IL-12/23 p40 subunit blocker ustekinumab, interfere with effector T-cell differentiation. Management plans in the future for approval include the cytokine-based therapies such as IL-23 p19 subunit inhibitor risankizumab and IL-6R antagonist tocilizumab, the lymphocytes homing modulator ozanimod, the selective JAK1 inhibitor filgotinib, the TLR9 agonist cobitolimod, and Treg cell based therapies. A number of undetermined management options include IFN- γ neutralization with fontolizumab and recombinant human IL-10 therapy.⁴ In the next line novel targeting strategies are being evaluated in animal studies. Emerging human studies include modulation of the natural killer group 2 member D (NKG2D) receptor with an inhibitory antibody (NNC0142-0002) for the prevention of mucosal damage in CD.⁵ A recent study characterized a new subset of IBD patients with high levels of serum and mucosal IgG4 which were more likely to have severe and extensive lesions, and IgG4 may be a biomarker for a new subtype of IBD.⁶ Now the question is how to identify and match the individual patient with the most suitable therapeutic option. Therefore, we are in bad need of biomarkers that can very precisely define the particular therapy response to give the right treatment to the particular patient and minimize unnecessary exposure and adverse events. Continued understanding of the immunopathogenesis of IBD is, therefore, of utmost importance to further expand the therapeutic potential for patients.

In spite of unprecedented advance in the molecular therapy of IBD, surgical intervention plays a very important role in case of complications related to the disease.⁸ Indications for surgery differ with anatomic distribution, pathophysiology and related complications. Advances in surgical approach and technology have led to decrease in associated morbidity and mortality. Although the need for surgical therapy is declining at least 10% of ulcerative colitis patients and 50% of patients with Crohn's Disease will need surgical intervention within first ten years after diagnosis.¹

The combination of immunosuppression and surgical therapies with judicious selection, each with their own complications and risks, will make the decision of a successful optimal treatment plan for an individual patient.

The future of management plan for IBD looks more promising as several novel treatment options have been identified and clinical studies are underway to determine the efficacy and safety of these therapies. These agents may have huge implications over the future of IBD. We have to wait to see their effectiveness and safety studies during the next decade to come.

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Significance of Carcinoembryonic Antigen (CEA) levels in colorectal carcinoma

SM Abu Horaira^a, SM Badruddoza^b

Abstract

Background: Colorectal cancer (CRC) is the third most common cancer and the fourth most common cancer cause of death globally. Though it is relatively less common in Indian sub continent, but now a days it is also identified as an important health problem in Bangladesh.

Objectives : To find out the clinico-demographic Characteristics of colorectal carcinoma.

Methods: This descriptive cross-sectional study was conducted among 72 patients with colorectal carcinoma confirmed by histopathology attending at the department of Surgery, Rajshahi Medical College during the period of January 2009 to December 2010. Data regarding patient's age & gender, information about the tumour like, anatomic subsite, diameter, staging, histological pattern, and preoperative serum Carcinoembryonic Antigen (CEA) level were collected by a pretested questionnaire. Fisher exact probability test and One Way ANOVA test were applied to verify the associations among the variables. **Results:** A total of 72 CRC patients, 32 (44.4%) patients had rectal, 27 (37.5%) had right colon and the rest 13 (18.1%) had left colon carcinoma. Male and female ratio among the study subjects was 2.6:1. Highest incidence (23, 31.9%) of the carcinoma was in the 30-39 years age group. Of the study subjects, 12 (16.7%) cases were Dukes' stage A (stage I), 16 (22.22%) were Dukes' stages B (stage II), 30 (41.66%) were Dukes' stage C (stage III) and 14 (19.44%) cases were Dukes' stage D (stage IV). Out of 72 cases, 63 (87.5%) cases had elevated preoperative CEA serum levels (>5ng/ml). Preoperative elevated CEA levels was significantly associated ($p<0.05$) with Dukes' stage of the carcinoma. The mean preoperative CEA serum level was significantly differed with the degree of tumor differentiation ($p<0.001$). **Conclusion:** Preoperative serum CEA level >5 ng/ml should not be used as a single screening test for colorectal carcinoma. Preoperative serum CEA concentration >5ng/ml correlating with the signs and symptoms of CRC may be used in multiphasic screening of CRC for further confirmation.

Key words: Carcinoembryonic Antigen(CEA), colorectal carcinoma.

Introduction

Colorectal carcinoma (CRC) is not an uncommon disease now a day. Colorectal cancer is predominantly a disease of Westernized countries, with about two-thirds of the world cases occurring in developed nations.¹ In Western countries, cancer of colon & rectum ranks second after cancer of lung in incidence & death rates.² In recent periods, there is an increasing incidence of carcinoma of right colon with an associated decrease in the incidence of carcinoma of sigmoid colon & rectum.³ Rates in immigrants from low-risk areas to these high-risk areas are known to rapidly increase to the level of the host population (e.g., in Japanese immigrants to the United States).⁴ Most colorectal carcinomas occur sporadically in

the absence of well defined familial syndromes. The peak incidence for colorectal carcinoma is between ages 60 and 79 years. Fewer than 20% of cases occur before age of 50 years.⁵ Though CRC incidence rates generally are higher among males, than females, at all anatomic subsites, the male-to-female incidence rate ratio (MF IRR) increases progressively across the colon from the cecum to the rectum.^{6,7}

Some aspects of Western lifestyle, primarily a high caloric intake and little physical activity, resulting in a positive energy balance, weight gain and, ultimately, obesity, are suspected to play a role in the etiology of colorectal disease. Physical activity, both at work and during leisure time, has consistently been

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Cite this as:
BMCJ 2018; 4(1): 3-11

Received : 12 March 2017
Accepted : 24 May 2017

inversely associated with this disease.^{8,9} Several large cohort studies reported that smoking doubles the risk of colorectal polyps, known precursors for colorectal cancer.¹⁰

Carcinoembryonic antigen (CEA) was first described in 1965 by Gold and Freedman, when they identified an antigen that was present in both fetal colon and colon adenocarcinoma but that appeared to be absent from healthy adult colon. Because the protein was detected in only cancer and embryonic tissue, it was given the name carcinoembryonic antigen, or CEA. Subsequent work showed that CEA, or at least a CEA-like molecule, was also present in certain healthy tissues, although concentrations in tumors were on average 60-fold higher than in the nonmalignant tissues. Fifty years after its initial detection in serum, CEA is one of the most widely used tumor markers worldwide and certainly the most frequently used marker in colorectal cancer.¹¹ Carcinoembryonic antigen (CEA) is a glycoprotein related antigen that has been detected in the serum of 42% to 79% of patients with colorectal carcinoma at the different tumor stages. It disappears after resection of the tumors and reappears in the event of recurrence or metastases. Higher values are found in advanced stage of tumors that have spread beyond the bowel wall, in well differentiated neoplasms, and in tumors associated with blood vessel, lymphatic, and perineural invasion.^{5,12}

Survival rates for cancers of large bowel have steadily improved with the improvement in the diagnostic techniques and availability of better method of treatment.¹³ Though the incidence of colorectal carcinomas in our country is no less than the Western world, there is no broad based study regarding this. So definitely it is highly important to carry out a study of these cancers in our country because the knowledge about age, gender, anatomic subsite, tumor stage, tumor grade (histological pattern) and preoperative serum Carcinoembryonic Antigen (CEA) level

distribution in patients with colorectal carcinoma in our country will invariably strengthen our efforts to combat this killer disease.

Methods

This was a cross sectional descriptive study conducted at Surgery department of Rajshahi Medical College Rajshahi, Bangladesh. The patients with colorectal carcinoma admitted in the above mentioned hospitals constituted the study population. Total 72 admitted patients with colorectal carcinoma confirmed histopathologically during the period of January 2009 to December 2010 were included in the study as sample with their consent to participate after explaining the purpose and procedure of the study. Data were collected with the help of a pre-tested questionnaire. The questionnaire was designed to record patient's age & gender, information about the tumour like, anatomic subsite, diameter, staging, histological pattern of the tumour and preoperative serum Carcinoembryonic Antigen (CEA) level. The information were recorded from interview with the patients, the patients' treatment file/card, investigation reports, and consultation with the concerned doctors if necessary. Preoperative CEA level was determined by Enzyme - linked Immunosorbent Assay (ELISA) method. Data were analyzed by computer using SPSS for windows. Descriptive analytical techniques involving frequency distribution and computation of percentage were applied. Fisher exact probability test was applied to verify an association between anatomical subsite and size (diameter) of colon carcinoma, and Dukes' stage of the carcinoma and preoperative serum CEA level. One Way ANOVA test was also applied to check the correlation between histological pattern of colorectal carcinoma and preoperative CEA level.

Results

A total of 72 CRC patients, 32 (44.4%) patients had rectal, 27 (37.5%) had right colon and the rest 13 (18.1%) had left colon

carcinoma. Considering all the anatomical subsite of CRC, males were more than the females except in case of sigmoid colon. Over all Male and female ratio was 3.2:1 (Table 1). The highest number of the study subjects, 23 (31.9%) patients were in the age group of 30 to 39 years. Next common age group (17, 23.6%) was 20 to 29 years (Figure 1).

Weight loss and weakness was the most common (59, 81.9%) clinical presentation of the study subjects. Other common complaints were anorexia (56.9%), abdominal pain (52.7%), abdominal discomfort (48.6%), per rectum bleeding (47.2%), altered bowel habit (43.8%) and abdominal lump (43.8%). Abdominal discomfort was more common among the patients of colon carcinoma than rectal carcinoma. Per rectum bleeding was more common in rectal carcinoma than colon carcinoma (Table 2).

Out of 40 colon carcinoma, majority (28, 70.0%) were 3-5 cm in diameter, 7(17.5%) were < 3 cm and the rest 5 (12.5%) were >5cm in diameter. The percentage of carcinoma having diameter < 3cm in right colon was 42.8%. The percentage of the carcinoma with diameter 3-5 cm in right

colon was increased to 71.4% . It was increased to 80.0% among the carcinoma having diameter >5cm. But there was no significant association between size and anatomic subsite of the carcinoma (Table 3).

Out of 72 CRC cases, 12 (16.7%) cases were Dukes' stage A (stage I), 16 (22.22%) were Dukes' stages B (stage II), 30 (41.66%) were Dukes' stage C (stage III) and 14 (19.44%) cases were Dukes' stage D (stage IV). Among them 63 (87.5%) cases had elevated CEA serum levels (>5ng/ml) before surgery. The proportion of the patients having preoperative elevated CEA levels was gradually increased in advanced stage (higher Dukes' stages) of carcinoma than in early. There was a statistically significant ($P < 0.05$) association between Dukes' stage of the carcinoma and preoperative elevated CEA levels ($p < 0.05$)(Table 4).

The mean CEA serum level (16.2ng/ml) was highest in well differentiated carcinoma. It was 10.7 ng/ml and 6.1 ng/ml in moderately and poorly differentiated carcinoma respectively. The mean preoperative CEA serum level was significantly differed with the degree of tumor cell differentiation ($p < 0.001$)(Table 5).

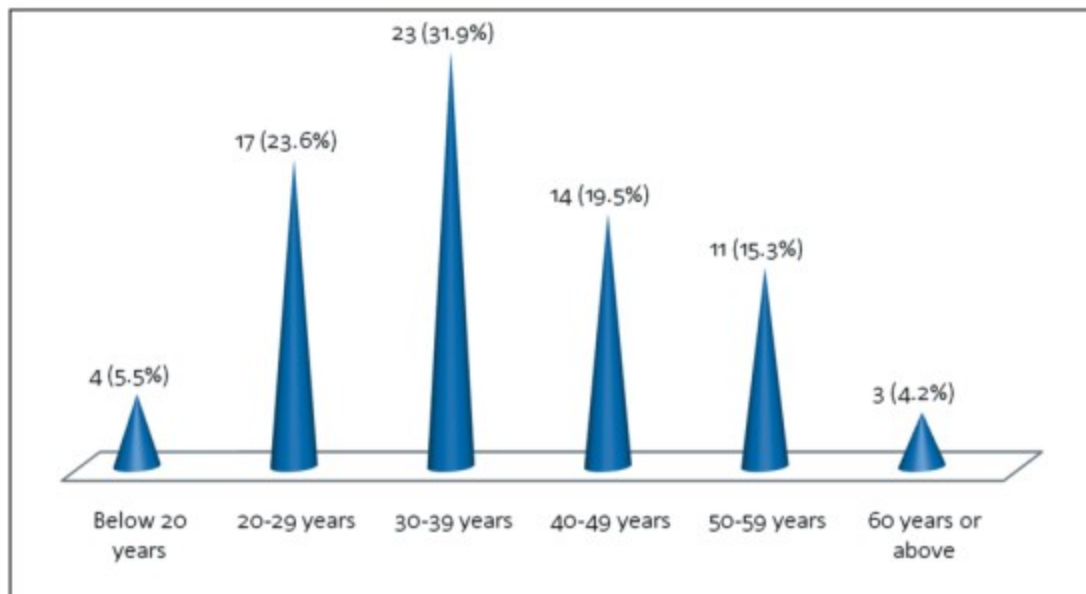


Figure 1: Age distribution of the patients (n=72)

Table 1: Sex and site of lesion (n=72)

Site of lesion		Gender		Total N (%)	Male : Female
		Male	Female		
		N (%)	N (%)		
Rights Colon	Caecum	13	2	15	
	Ascending colon	6	1	7	
	Right colic flexure	4	1	5	
	Total	23 (85.2)	4 (14.8)	27 (37.5)	5.7:1
Left Colon	Transverse colon	1	0	1	
	Left colic flexure	3	0	3	
	Descending colon	1	1	2	
	Sigmoid colon	4	3	7	
	Total	9 (69.2)	4 (30.8)	13 (18.1)	2.3:1
Rectum		23 (71.9)	9 (28.1)	32 (44.4)	2.7:1
Total		55 (76.4)	17 (23.6)	72 (100.0)	3.2:1

Table 2 : Presenting symptoms of colorectal carcinoma in relation to sites.

Symptoms	Rt colon (n=27) N(%)	Lt colon (n=13) N(%)	Rectum (n=32) N(%)	Total (n = 72) N(%)
Weight loss & weakness	20(74.5)	11(84.6)	28(87.5)	59 (81.9)
Anorexia	15(55.5)	9(69.2)	17(53.2)	41(56.9)
Abdominal pain	15(55.5)	6(46.15)	17(53.15)	38 (52.7)
Abdominal discomfort, dyspepsia	20(74.5)	8(61.5)	7(21.8)	35(48.6)
Bleeding P/R	00(0.0)	6(46.2)	28(87.5)	34 (47.2)
Altered bowel habit	6(22.2)	9(69.2)	16(50.0)	31(43.8)
Abdominal lump	18(66.6)	9(69.2)	4(12.3)	31(43.8)
Diarrhoea	6(22.2)	3(23.1)	7(21.9)	16 (22.2)
Constipation	01(5.0)	04(44.0)	11(52.0)	15 (20.8)
Nausea/Vomiting	6(22.2)	6(46.15)	00 (0.0)	12 (16.6)
Intestinal obstruction	06(22.2)	03(23.1)	00 (0.0)	09 (12.4)
intestinal perforation	01(5.0)	04(44.0)	01(4.0)	06 (8.3)
Painful defaecation	00 (0.0)	00 (0.0)	04(19.0)	04 (5.5)

Table 3: Distribution of patients by site and size of the colon carcinoma.

Size	Right side N (%)	Left side N (%)	Total N (%)
<3cm	3 (42.8)	4 (57.2)	7 (17.5)
3-5cm	20 (71.4)	8 (28.6)	28 (70.0)
>5cm	4 (80.0)	1 (20.0)	5 (12.5)
Total	27 (67.5)	13 (32.5)	40 (100.0)

P = 0.381 (Fisher exact probability test)

Table 4: Dukes' stage of colorectal carcinoma and serum CEA Level.

Dukes' Stage	Serum CEA level		Total N (%)
	≤ 5ng/ml N (%)	>5ng/ml N (%)	
A	4 (33.3)	8 (66.7)	12 (16.6)
B	3 (18.7)	13 (81.3)	16 (22.2)
C	2 (6.7)	28 (93.3)	30 (41.7)
D	0 (00.0)	14 (100.0)	14 (19.5)
Total	9 (12.5)	63 (87.5)	72 (100.0)

p = 0.033 (Fisher exact probability test)

Table 5: Tumor grade of colorectal carcinoma and preoperative serum CEA level.

Cell Differentiation	Number n	Mean CEA (ng/ml) serum level	F	significance between groups
Well Differentiation	22	16.2 ^a	11.92	0.001
Moderate Differentiation	36	10.7 ^b		
Poor Differentiation	14	6.1 ^c		

Values in the same column not sharing common superscript letter are significantly (p<0.05) difference

Discussion

The present study findings revealed that majority of colorectal carcinoma occurred in rectal area (44.4%) followed by right colon (37.5%) and then left colon (18.1%). This study corresponds with the previous studies^{14,15} as 36.9% to 40.3% of the total number of the lesions occurred in rectum and recto - sigmoid area.

Colorectal carcinoma (CRC) incidence rates in males is notably higher than females, at all anatomic subsites.^{6,7} In the present study, the same pattern of sex differences was also observed. This pattern is unexplained and may be a result of a combination of better awareness of screening in women, more exposure of males to risk factors like high body mass index/body fatness, alcohol intake, smoking, and protective effects of both endogenous and exogenous hormones in female.¹⁶ There is a space to explore the different aspects of this sex differences in Bangladeshi perspectives.

The peak incidence for colorectal carcinoma is between ages 60 and 79. Fewer than 20% of cases occur before age of 50 years.⁵ But recent reports have demonstrated an alarming increase in incidence of CRC among young adults aged 20-49 years in the US.¹⁷ The present study findings is consistent with the recent US reports. This shift of the incidence towards the younger age group may be due to increasing obesity, the consumption of lots of fast food, alcohol and highly processed meat in young adults. At the same time, eating little fiber and a sedentary lifestyle are also may be linked to a higher risk of colorectal cancer in young adults.

In previous studies^{18,19} abdominal pain, anorexia, weight loss and weakness, per rectum bleeding, altered bowel habit and abdominal lump were identified as the common complaints of the patients having colorectal carcinoma. The present study also agreed with them. In this study, per rectum bleeding was the most common specific

symptoms in case of rectal carcinoma. So per rectum bleeding may be suggestive for rectal carcinoma.

Several studies emphasized that larger tumors are more frequent in the right colon than left.²⁰⁻²² Similar finding also found in this study. Right-sided tumors mostly do not cause any signs or symptoms in the early stages, and they are generally diagnosed when they attain a large size. This may be one of the reasons to have larger tumor in right colon than left. These tumors are diagnosed in the early stages with the technological improvement and common use of colonoscopy, but the present study findings suggest that the problem is still going on.

Many investigators have shown that preoperative serum CEA levels correlate with the extent of colorectal cancer.^{12, 23} In 1994, Wang et al. reported, a total of 318 patients with colorectal cancer, 133 (42%) had preoperative CEA level >5 ng/ml (9). In this study, it is quite double (87.5%). Wang et al also reported that the incidence of preoperative CEA levels of >5 ng/ml in Dukes stages A, B, C and D diseases were 0, 32, 48 and 79%, respectively. Similarly, in a report by Ladenson et al.²³, a total of 203 patients with colorectal cancer, the incidence of preoperative CEA >5 ng/ml in Dukes' A, B, C and D stages were 3, 25, 45 and 65%, respectively. The current study confirmed this trend, but the percentage of preoperative CEA >5ng/ml among the patients of the respective stages comparatively higher than the previous studies. In this study, the incidence of preoperative CEA >5ng/ml in Dukes' A, B, C and D stages were 66.7, 81.3, 93.3 and 100.0%, respectively. Besides malignant diseases like colorectal cancer, elevated serum CEA levels >5 ng/ml are frequently found in other benign disorders, like smoking, peptic ulcer, inflammatory bowel disease and a variety of benign liver diseases, including hepatitis, cirrhosis, cholelithiasis, obstructive jaundice and cholangitis.²⁴ There is a high prevalence of

smokers, peptic ulcer, inflammatory bowel disease, hepatitis B virus infection and cholelithiasis in Bangladesh. So these were the possible enhancing factors for high percentages of serum CEA levels >5 ng/ml among the study subjects in the different Dukes' stages. It suggests that serum CEA levels >5 ng/ml is nonspecific test for the screening of CRC. But in benign diseases/conditions, it is rare to rise serum CEA values >10 ng/L. A well designed study is needed considering all the confounding factors to identify the independent effect of CRC on serum CEA level in Bangladeshi people.

Several studies have shown that well differentiated colorectal cancer produce more CEA per gram of total protein than poorly differentiated specimens.²⁵ Bhatnagar et al.²⁵ 1999 observed that tissue CEA levels were highest for well differentiated adenocarcinomas (5.2-37.0 micrograms/g protein) with progressively lower levels seen in moderately differentiated and poorly differentiated tumors, and in normal. Mean serum CEA levels were 1.5 ng/ml for normal and 4.2, 6.4, 23, and 102 ng/ml for Dukes' A, B, C and D stage tumors, respectively. In their report mean concentration of CEA in well differentiated, moderately differentiated and poorly differentiated colorectal neoplasm were 18.0, 5.5 and 2.2 ng/ml of protein, respectively. Similarly, serum concentration of CEA tends to be higher in patients with well differentiated tumors compared with those with poorly differentiated tumors.²⁶ The present study findings agreed with the this findings.

This study has some limitations that must be taken into consideration. First, sample size was small. Secondly, there was no option of controls (healthy, without CRC) in the study design, that is why the sensitivity and specificity of preoperative serum CEA level >5 ng/ml were not calculated for the screening of CRC. Third, serum CEA enhancing factors other than CRC were not considered as confounding variables in this

study. Finally, it is not clear whether the analysis of this restricted patient group introduced a selection bias, and these findings may or may not reflect the situation in the overall population.

Preoperative serum CEA level >5 ng/ml should not be used as a single screening test for colorectal carcinoma. Preoperative high serum CEA concentration (>10 ng/ml) correlating with the signs and symptoms of CRC may be used in multiphasic screening of CRC for further confirmatory diagnostic test.

Acknowledgements

The authors would like to thank all the patients who participated in the study.

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Calcium status of perinatal asphyxiated newborn babies

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Abstract

Background: Birth asphyxia is one of the major neonatal problems in Bangladesh. It is a common cause of neonatal hospital admission. **Objective:** To evaluate calcium status in birth asphyxiated babies of different grading of Hypoxic Ischemic Encephalopathy admitted into pediatrics department of Rajshahi Medical College Hospital. **Methods:** This cross sectional comparative study was conducted among birth asphyxiated babies admitted in Rajshahi Medical College Hospital. Total 266 neonates, 133 asphyxiated and 133 healthy neonates were selected as cases and controls by inclusion and exclusion criteria. Data were collected by data collection sheet through interview of the mothers, pathological reports and patients' treatment files and attending doctors if needed. Data were analyzed in computer by using SPSS version 18. Chisquare and One Way ANOVA test were applied. **Results:** Out of 133 asphyxiated neonates mean serum calcium values in mild, moderate, severe asphyxia were 8.37 ± 1.51 , 8.47 ± 1.37 and 8.03 ± 1.14 respectively. Among the cases 20(15.0%) neonates had hypocalcaemia. Among these hypocalcaemic babies 6(25.0%) had mild, 9(45.0%) had moderate, and 5(25.0%) had severe perinatal asphyxia respectively. Hypocalcaemic neonates were only 6(4.5%) in controls. There was no association found between the grading of asphyxia and serum calcium level. But the incidence of hypocalcaemia in asphyxiated neonates was significantly ($p < 0.005$) higher than that of controls. **Conclusion:** A provision of serial measurement of serum electrolyte especially calcium for perinatal asphyxiated neonates should be made available.

Key words: hypocalcaemia, perinatal asphyxia, convulsion.

Introduction

Out of 130 million newborn infants born each year globally, about 4 million die in the neonatal period.¹ In the least developed countries perinatal asphyxia remains a major cause of death and disability. According to WHO, perinatal asphyxia and injuries accounts for 23% of neonatal deaths.² So perinatal asphyxia is an important determinant of perinatal mortality.³ Many of them manifested as perinatal asphyxia and may developed life-long neurological deficits.⁴ Fluid, electrolytes and metabolic abnormalities are the commonest derangements encountered in critically ill asphyxiated neonates. There may be hypocalcaemia in perinatal asphyxia, which further cause convulsion or tetany.

A variety of metabolic problems are present in asphyxiated infants including hyponatremia, hypoglycaemia, hypocalcaemia and hypomagnesaemia.⁵ Some of the biochemical disturbances may trigger seizure or potentiate further brain

damage in asphyxiated infants. Therefore, high index of suspicion, prompt recognition and careful understanding of common electrolyte abnormalities are necessary to ensure their correction and improving neonatal outcome. With this vision the present study has been conducted to find out the pattern of calcium abnormalities in asphyxiated neonates.

Methods

This study was carried out in neonatal unit of Paediatrics Department, in collaboration with Department of Gynecology and Obstetrics, Rajshahi Medical College Hospital during January 2013 to December 2013.

All the Asphyxiated babies admitted into Paediatrics, and Gynaecology and Obstetrics wards of RMCH constitute the study population. Total 266 subjects were selected with which 133 were case (asphyxiated babies) and 133 were control (healthy, without asphyxia). Cases were selected by some inclusion and exclusion criteria.

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Cite this as:
BMCJ 2018; 4(1): 12-15

Received : 21 September 2017
Accepted : 6 November 2017

Inclusion criteria of cases: Live born babies with perinatal asphyxia who have delay to establish first breath within sixty seconds, delayed cry over 90 seconds, heart rate <100 beats/minute at birth, bluish colorations of whole body over first 60-90 seconds, if the newborn remains hypotonic or floppy over hours, APGAR score <7 at 5 min, early neonatal seizures.

Inclusion criteria of Controls: In this study 133 healthy (without asphyxia) newborns, who were delivered in the department of Obstetrics and Gynecology, RMCH and admitted in neonatal ward for suspicion of illness other than birth asphyxia, were included as control.

Exclusion criteria of both cases and controls: Babies with a diabetic mother, septicemia, very low birth weight (<1.5 Kg) babies, inborn error of congenital metabolic disorders and lethal congenital deformity were excluded from the study.

3 ml of blood was collected from peripheral vein within 24 hours of birth in a clean sterilized vial with due precautions to avoid haemolysis and contamination. Serum was separated by using a micropipette after centrifuged at 3000-4000 rpm from 5-10 minutes. Samples were analyzed on the same day. Serum calcium is estimated by orthocresolphthalein complexone method.^{6,7}

Data were collected by data collection sheet through interview of the mothers, pathological reports and patients' treatment files and attending doctors if needed. The data collection sheet was designed to record the information about parity of the mother and infant's gender, place of delivery, status of hypoxic-ischaemic encephalopathy (HIE) and serum calcium level. Data were analyzed in computer by using SPSS version 18. Chi-square and One Way ANOVA test were applied.

Results

A total of 133 asphyxiated neonates, 79 (59.4%) were male and 54 (40.6%) were female. Majority (94, 70.7%) of their mothers were primipara and the rest (39, 29.3%) were multipara. 51(38.3%) asphyxiated neonates were delivered at hospital, 47(35.3%) were delivered at clinic and the rest 35(26.3%) were delivered at home.

Out of 133 asphyxiated babies, 47 (35.3%) presented with hypoxic-ischaemic encephalopathy (HIE) stage I. Among them 25 (31.6%) babies were male and 22 (40.7%) were female. While 58 (43.6%) babies presented with HIE stage II. Among them 39(67.2%) were male and 19(32.8%) were female. The rest 28 (21.1%) babies were presented with HIE stage III, where 15(53%) were male and 13(46.4%) were female respectively. Of the 47(35.3%) mildly asphyxiated neonates, all excellently recovered. In moderately asphyxiated neonates, 35(60.3%) survived and 23 (39.7%) died. Of the total 28 severely asphyxiated neonates, only 1 (3.6%) survived and unfortunately 27(96.4%) died.

Of the total 133 asphyxiated neonates, 20 (15.0%) were hypocalcaemic. Among the hypocalcaemic babies 6(30.0%) had mild, 9(45.0%) had moderate and 5(25.0%) had severe perinatal asphyxia. But there was no association ($p>0.05$) found between the grading of asphyxia and serum calcium level (Table 1). The mean serum calcium values among mild, moderate and severe asphyxiated babies were 8.37 ± 1.51 , 8.47 ± 1.37 and 8.03 ± 1.14 respectively. These were not significantly ($p=0.3791$) differed from each other (Table 2).

But the incidence of hypocalcaemia in asphyxiated neonates was significantly ($p<0.005$) higher than that of controls, neonates without asphyxia (Table 3). Among the 50 dead asphyxiated neonate 7(14.0%) were hypocalcaemic and 43(86.0%) were normocalcaemic.

Table 1: Relationship of asphyxiated babies by grading of HIE and serum calcium level (n=133):

Serum calcium level	Grading of asphyxiated baby							
	Mild (n=47)		Moderate (n=58)		Severe (n=28)		Total(133)	
	N	%	N	%	N	%	N	%
Hypocalcaemia (<7 mg/dl)	6	30.0	9	45.0	5	25.0	20	15.0
Normal calcium level	41	36.3	49	43.4	23	20.4	113	85.0
Total	47	35.3	58	43.6	28	21.1	133	100.0

$$\chi^2 = 0.375, \text{ df}=2, \text{ p}>0.05$$

Table 2 Serum calcium level among the infants having different grading of asphyxia

Level of asphyxia	Number N	Mean serum calcium level (mg/dl)	F	Significance between groups
Mild	47	8.37 ^a	0.9772	0.3791
Moderate	58	8.47 ^a		
Severe	28	8.03 ^a		

Values in the same column sharing common superscript letter are not significantly ($p < 0.05$) different

Table 3: Comparison of serum calcium level between case and control (n=266):

S.calcium level	Case (n=133)		Control (n=133)		Total (266)	
	N	%	N	%	N	%
Hypocalcaemia (<7 mg/dl)	20	15.0	6	4.5	26	9.8
Normal calcium level	113	85.0	127	95.5	240	90.2
Total	133	50.0	133	50.0	266	100.0

$$\chi^2 = 8.35, \text{ df}=1, \text{ p}<0.05$$

Discussion

Out of 133 asphyxiated neonates 79 (59.4%) were male and 54 (40.6%) were female. There was predominance of male babies over female babies in this study. Male predominance was observed in birth asphyxia. The present study findings also consistent with the previous studies.⁸⁻¹¹

Parity may be an important factor as the newborn of primipara had higher incidence of

perinatal asphyxia. This fact is reflected in this study which showed that 94(70.7%) asphyxiated neonates were born of primigravida and 39(29.3%) born of multigravida mothers. Similar result was also found by Shireen et al,¹⁰ Choudhury¹¹, Bhuiyan.¹² Less expansibility of birth canal in primipara with the consequence of prolongation of labour might have some causal relationship with the high incidence of birth asphyxia in primipara mothers.

In a study conducted at Rajshahi medical college hospital in 2005 by Haidary et al¹³ showed that 18.32% mildly, 20.94% moderately and 60% babies were severely asphyxiated. Comparing with that the present study findings suggest that the current situation is far better than that time. It may be due to improved perinatal health care facilities, increased awareness of the people and better communication.

Hypoxic ischemic encephalopathy is the most common and important consequence of perinatal asphyxia. Out of 133 asphyxiated babies majority 58(43.6%) babies presented with HIE stage II. This study indicates that HIE stage II is the common presentation of asphyxiated babies where convulsion is common. This study is consistent with Azam et al⁸ in Pakistan.

In different studies birth asphyxia appears to play a role in neonatal calcium homeostasis. Stoliar et al (1971)¹⁴ in their study on serum calcium levels in birth anoxic neonates found 26.76% incidence of hypocalcaemia in full term infants and 58.3% in premature infants. Tsang et al (1973)¹⁵ in their study found that hypocalcemia was significantly higher in the asphyxiated newborns than the healthy babies. Jajoo D (1995)¹⁶ studied on 35 term infants with asphyxia. Asphyxiated infants had significantly lower serum calcium levels than control infant during each of time period studied. The present study findings also agreed with these studies findings.

The results of this study have certain implication in clinical practice. The study findings suggest that monitoring of calcium as well as electrolyte level of asphyxiated newborn is very important to manage them properly. A provision of serial measurement of serum electrolyte specially calcium for perinatal asphyxiated neonates should be made available.

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Endoscopic assessment of gastroesophageal reflux disease patients and risk factors of esophageal lesions.

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Abstract

Background: Gastro-esophageal reflux disease (GERD) is a common esophageal disorder in Bangladesh. GERD is associated with significant impaired quality of life and sometimes complicated with high morbidity and mortality. **Objective:** To investigate upper GI endoscopic findings in patients having typical symptoms of GERD and the risk factors of esophageal lesions in GERD patients. **Methods:** This was a cross-sectional descriptive type of study conducted at a private clinic in Rajshahi city. All the adults attending at the clinic having typical GERD symptoms more than 6 weeks constituted the study population. Total 108 GERD patients were included in this study. Data were collected by a data collection sheet through interview and patient examination including UGI endoscopy. Chi-square test was applied to find out the association between Clinico-demographic characteristics and GERD status of the study subjects. Multiple logistic regression analysis was done to identify the risk factors to develop esophageal lesion in GERD patients. **Results:** A total of 108 GERD patients, 88 (81.5%) were nonerosive reflux disease (NERD) patients and the rest 20 (18.5%) patients had esophageal lesions. Of those 20 GERD patients with esophageal lesion, 9 (8.3%) had erythema, 5 (4.6%) had erosion, 4 (3.6%) had hiatus hernia with esophagitis and only 2 (1.8%) had Barretts. Twenty four (22.2%) patients had endoscopic evidence of gastroduodenal lesions. Older age and diabetes mellitus were identified as risk factors of esophageal lesion. **Conclusion:** Gastroduodenal lesions may be an important underlying cause for GERD in Bangladesh. UGI endoscopy should be performed routinely in GERD patients. Special consideration should be taken during the management of GERD in elderly and diabetic patients.

Key Words: GERD, esophageal lesion, gastroduodenal lesions, risk factors.

Introduction

gastro-esophageal reflux disease (GERD) is a common esophageal disorder in which repeated reflux of gastric content into esophagus creating troublesome symptoms and/or histological inflammatory changes.¹ It is a prevalent disease globally, particularly in developed countries. The prevalence of GERD is estimated to be 10 to 20% in Europe and North America and 5 % in Asia.² Recent studies showed the prevalence of GERD in India ranges between 8-20% which is comparable to Western countries.^{3,4} The increasing prevalence in Asian populations are most likely related to changing dietary and personal habit.

The exact prevalence of GERD in Bangladesh is not known. GERD is associated with significant impaired quality of life and sometimes complicated with high morbidity and mortality. The diagnosis of GERD is initially made by typical clinical symptoms only. The typical symptoms are

heartburn, regurgitation and epigastric pain.⁵ gastro-esophageal reflux is ideally confirmed by 24 hours PH monitoring which considered as gold standard. Practically 24 hours Ph monitoring facilities are not widely available. That is why others alternative investigations like UGI endoscopy and Barium esophagram are frequently warranted. UGI endoscopy is warranted as initial tool of choice for investigation of GERD in clinical practice as well as clinical research. Endoscopic findings of esophagus particularly severity of erosion is the good predictor of response to therapy. 40 to 60 % patients with typical reflux do not have any endoscopic lesion in esophagus and considered as nonerosive reflux disease (NERD).⁶

Empirical therapy without endoscopy is suggested in most of guidelines and this invasive procedure is virtually recommended in patients with GERD symptoms and alarm features or patient not

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Cite this as:
BMCJ 2 018;4(1): 16-22

Received : 21 September 2017
Accepted : 28 November 2017

responding to empirical PPI therapy.⁷ The endoscopic esophageal changes caused by reflux disease are not only helpful diagnostically but also identify patients exposed to a significant risk of disease chronicity.⁸ But It should be borne in mind that many gastro duodenal diseases like peptic ulcer diseases and delayed gastric emptying is observed high particularly in areas where H pylori infection are prevalent. For this reason such treating instead of testing strategy remain controversial.

So The aim of this study is to investigate upper GI endoscopic findings in patients having typical symptoms of GERD with or without alarm features and also to find out gastro-duodenal lesion in such group of patients in our perspective.

Methods

This cross-sectional descriptive type of study was conducted at a private clinic in Rajshahi city. All the adults (>18 years) patients attending at the clinic having typical GERD symptoms i.e. heartburn, regurgitation and epigastric pain more than 6 weeks constituted the study population. Total 108 patients with typical GERD symptoms attending at the clinic during the period from January 2015 - July 2016 were enrolled in this study with their written consent. Before the enrolment, the 108 volunteers were briefly informed

about the study specially UGI endoscopy. Those patients, who were on PPI or other antiulcer therapy, were advised to discontinue the therapy and would be on only life style modifications for at least 4 weeks. Patients with NSAID, steroids and bisphosphonate were not enrolled in the study. Pregnant patient and those who are not fit for UGI endoscopy were also excluded from the study.

Data were collected by a data collection sheet through interview and patient examination including UGI endoscopy. The data collection sheet was designed to record the information on Patient's clinical, demographical, lifestyle profiles and endoscopic findings. UGI endoscopic procedure was done by Olympus machine. Lidocaine spray was used for oropharyngeal anaesthesia prior to procedure. All patients were kept fasting for at least 8 hours.

The statistical analysis was performed using SPSS, version 16. Descriptive analytical techniques involving frequency distribution, computation of percentage etc were done. Chi-square test was applied to find out the association between Clinico-demographic characteristics and GERD status of the study subjects. Multiple logistic regression analysis was done to identify the risk factors to develop esophageal lesion in GERD patients.

Table 1. GERD status on endoscopic findings of GERD patients

GERD status on endoscopic findings	Frequency (percentage) N (%)
NERD	88(81.5)
Normal endoscopic findings	64(59.3)
Gastroduodenal lesions	24 (22.2)
Gastric or duodenal Erosions	6(5.5)
Gastric ulcer	3(2.7)
Duodenal ulcer disease	6(5.5)
Gastritis	9(8.3)
Esophageal lesions	20(18.5%)
Erythema	9(8.3)
Erosions	5((4.6)
Hiatus hernia with Esophagitis	4(3.6)
Barretts	2(1.8)

Results

A total of 108 GERD patients, 88 (81.5%) were Non-erosive Reflux Disease (NERD) patients, had no any endoscopic evidence of esophageal lesion and the rest 20 (18.5%) patients had esophageal lesions. Of the total 88 NERD patients, 64(59.3%) had normal endoscopic findings. Of those 20

GERD patients with esophageal lesion, 9 (8.3%) had erythema, 5 (4.6%) had erosion, 4 (3.6%) had hiatus hernia with esophagitis and only 2 (1.8%) had Barretts. Twenty four (22.2%) patients had endoscopic evidence of gastroduodenal lesions. Of them, gastritis was in highest number (9, 8.3%) (Table 1).

Table 2. Clinico-demographic characteristics and Gastro esophageal reflux disease (GERD) status of the study subjects

Clinico-demographic characteristics	GERD status		p-value
	Non-erosive Reflux Disease (NERD) n (%)	Esophageal Lesion n (%)	
Age (in completed year)			
<40 (n=31)	29 (93.5)	2 (6.5)	0.032
40 and above (n=77)	59 (76.6)	18 (23.4)	
Gender			
Male (n=77)	65 (84.4)	12 (15.6)	0.167
Female (n=31)	23 (74.2)	8 (25.8)	
Alcohol habit			
Alcoholic (n=14)	10 (71.4)	4 (28.6)	0.242
Nonalcoholic (n=94)	78 (83.0)	16 (17.0)	
Smoking/Tobacco habit			
Have (n=52)	43 (82.7)	9 (17.3)	0.694
Have not (n=56)	45 (80.4)	11 (19.6)	
Diabetes Mellitus			
Diabetic(n=33)	22 (66.7)	11 (33.3)	0.009
Non-diabetic (n=75)	66 (88.0)	9 (12.0)	
Rapid urease test (RUT)			
Positive (n=74)	59 (79.7)	15 (20.3)	0.343
Negative (n=34)	29 (85.3)	5 (14.5)	
BMI			
<25 (n=54)	47 (87.0)	7(13.0)	0.328
25 – 29.9 (n=34)	26 (76.5)	8 (23.5)	
30 and above (n=20)	15 (75.0)	5 (25.0)	

Majority of study subjects were ≥ 40 years (77, 71.3%) with a mean age of $48.5(\pm 14.88)$ and male (77, 71.3%). Of the total study subjects, 14 (13.0%) were alcoholic, 52 (48.1%) were smoker/tobacco consumer, 33 (30.6%) were diabetic and 54(50%) were with the BMI < 25 . RUT demonstrated H.pylori infection in 74 patients (Table 2). Esophageal lesion was significantly higher among the older patients aged ≥ 40 years ($p=0.032$) than the younger and the diabetic than the non diabetic patients ($p=0.009$). Esophageal lesion was more

common among the female than male (25.8% Vs 15.6%) and in the alcoholic than nonalcoholic (28.6% Vs 17.0%), but these differences were not statistically significant. The proportion of esophageal lesion was remarkably lower in the GERD patients having BMI < 25 than the other two groups of patients with BMI 25-299.9 and ≥ 30 . But Patient's BMI was not correlated with esophageal lesion. H.pyloric infection and smoking/tobacco consumption were not significantly associated with esophageal lesion (Table 2).

Table 3 Multiple logistic regression analysis: effects of age and diabetes mellitus to develop esophageal lesion in GERD

Variables	Adjusted odds ratio [95% confidence interval (CI)]	P value	Prevalence of the variable (%)
Age		0.03	
< 40 years ^a	1		128.7
40 years and above	3.77 (0.80-17.80)		71.3
Diabetes Mellitus		0.024	
Diabetic	3.25 (1.17 9.05)		30.56
Non-diabetic ^a	1		69.44

^aReference group

In Multivariate analysis, older age (Adjusted OR, 3.77; 95%CI, 0.80-17.80; $P < 0.03$) and diabetes mellitus (Adjusted OR, 3.25; 95%CI, 1.17-9.05; $P < 0.024$) were identified as risk factors to develop esophageal lesion (Table 3).

Discussion

Gastro esophageal reflux disease is the highly prevalent disease of western and affluent society. The typical symptoms of GERD includes heartburn, regurgitation and epigastric pain and all enrolled patients were carrying these symptoms. In fact UGI endoscopy is the important tool for evaluating GERD patient widely. Aste H et al. found esophageal abnormalities on endoscopy in 33% cases who are having typical GERD symptoms.⁹ Another study showed 40 to 60 % patients with typical reflux symptoms do not have any endoscopic lesion and considered as endoscopy negative disease (ENRD).⁶ In our study we found about more than one fifth of patient exhibit some sort of gastroduodenal lesions. Our findings are making the conformity that gastroduodenal lesions were quite high in patients with typical GERD symptoms. The findings suggested that peptic disease might be an underlying cause for GERD. This study depicted high prevalence of H pylori infection and about two third (68.5%) of patients were RUT positive which consistent with the Lee CS et al. findings in Bangladesh.¹⁰ They found 69.7% RUT test positive in dyspeptic patients. There is a notion that H. pylori infection in stomach protect GERD symptoms. The explanation is that if H pylori infection is associated with predominant corpal gastritis and gastric atrophy that leads to reduced gastric secretion and minimize symptoms of GERD. On the contrary antral predominant H Pylori related gastritis is associated with high acid secretion & worsen GERD symptoms. The present study findings agreed with the 2nd hypothesis. It is clear that despite of all patients had GERD symptoms but about one quarter of cases were gastro duodenal lesions and it is higher than esophageal lesions. From this observation It can be assumed that such findings may be most likely due to high prevalence of PUD and H. Pylori infection. This observation suggested that we need to do UGI endoscopy in patient of GERD like symptoms particularly in our perspective. Though is not supported by

many guidelines or studies.^{7,11} However, it is needed to do further study to verify the association between PUD and GERD particularly in those countries where the prevalence of PUD and H Pylori infection is very high.

The frequency of GERD complications, such as erosive esophagitis, esophageal stricture, Barrett's esophagus, and esophageal cancer is significantly higher in older patients.¹² Collen et al. found an increase of esophagitis and Barrett's esophagus in patients over 60 years of age compared to those younger, 81% versus 47%.¹³ Huang et al¹⁴ found more severe esophageal lesions in elderly patients, as compared to younger patients. Hence, elderly patients with GERD are at greater risk than younger patients for developing serious complications of GERD. In this study, older age was also identified as a risk factor for esophageal lesions like, erythema, erosions, hiatus hernia, barrett's esophagus, GERD patients = 40 years had a risk more than 3 times to develop esophageal lesion than the younger patients <40years.

Male gender has also been reported to be an independent risk factor for esophagitis.¹⁵⁻¹⁷ Moreover, different parietal cell mass, lower esophageal function or body mass index between genders have been proposed as possible causes to explain the gender effect.¹⁸ However, in our study, the proportion of male gender was not significantly different between patients who had esophageal lesion and those who did not. Similarly, we could not find any significant effect for gender to be considered as a risk factor for esophageal lesion.

Over weight and obesity are risk factors for symptoms of GERD.¹⁹⁻²¹ Thought in this study Over weight and obesity (BMI =25) was not significantly associated with esophageal lesion but esophageal lesion were higher among the over weight and obese patients than the GERD patients having BMI <25. Most of the type 2 diabetes patients are over weight or obese, it seems to make sense

that GERD and its complications are more common in these individuals.²² So overweight might be explained part of high frequent symptoms of GERD and its complications like esophageal lesion in type 2 diabetes patients. But most of the studies suggested that diabetic neuropathy is the responsible for the GERD and its complications in diabetes patients.^{22,23} The present study findings also suggested that Type 2 diabetes had an independent role for developing esophageal lesion in GERD patients.

Gastroduodenal lesions may be an important underlying cause for GERD in Bangladesh. UGI endoscopy should be performed routinely in GERD patients. Special consideration should be taken during the management of GERD in elderly and diabetic patients.

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Bardet Biedl syndrome: a case report

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Abstract

Bardet-Biedl syndrome is rare genetic disorder, characterized by gross physical abnormalities like postaxial polydactyly or syndactyly, obesity, visual disturbances, mental retardation, hypogonadism. Diagnosis based on a group of clinical features. Here I am reporting a case of 14 years old boy presenting with obesity, difficulty in vision and hypogonadism. Bardet-Biedl syndrome was diagnosed and appropriate counselling and symptomatic treatment was discussed with his parents.

Key words: Bardet-Biedl syndrome, obesity.

Introduction

The Bardet-Biedl syndrome (BBS) is a rare ciliopathic human autosomal-recessive disorder, characterized by cardinal symptoms of marked central obesity, retinal dystrophy, polydactyly, mental retardation and hypogonadism and renal dysfunction.¹ Its prevalence varies from 1:160,000 to 1:13,500, respectively, in northern Europe and in some communities in Kuwait.² Higher incidence in Arab populations can be due to the fact of marriage being usual between relatives.³ BBS is part of a group of human genetic disorders of cilia function, and mutations of 17 genes are reported to be responsible for more than 80% of clinically diagnosed cases.⁴

The diagnosis of Bardet-Biedl syndrome (BBS) is established by clinical findings. Beales et al have suggested that the presence of four primary features or three primary features plus two secondary features is diagnostic. Primary features are: Rod-cone dystrophy, Polydactyly, Obesity, Genital anomalies, Renal anomalies, Learning difficulties and Secondary features are : Speech delay, Developmental delay, Diabetes mellitus, Dental anomalies, Congenital heart disease, Brachydactyly/ syndactyly, Ataxia/ poor coordination, Anosmia/hyposmia. Four primary features or three primary features and two secondary features are required for a clinical diagnosis of Bardet Biedl syndrome.^{5,6}

Case reports

Abdur Rashid, 14 years old boy, non diabetic, normotensive hailing from Bagmara, Rajshahi was admitted in RMCH on 01.01.2016 through emergency with the complaints of Difficulty in vision and Progressive weight gain for 6 years. According to the statement of the mother of the patient, he was reasonably well 7 years back then he developed difficulty in vision both near and distant. She also complains of difficulty in vision at night. There was no history of pain, watering or redness of eyes. She also complains of progressive weight gain for the last 6 years. She gives a history of excess food intake with increase appetite. There was no history of cold intolerance, proximal muscle weakness, headache, constipation, excessive sleep, taking any drugs like steroids. None of the family members were suffering from such type of illness. On examination, patient was obese involving more on central part of the body. Face is rounded but not plethoric. Height-150 cm, weight-91 kg, BMI-40 kg/m². No anemia, jaundice, clubbing, koilonychia, leukonychia or oedema. No thyromegaly or lymphadenopathy. There are multiple linear striae involving abdomen, thigh and shoulder. No bruise present. No proximal myopathy. Both breasts are enlarged, soft and non tender (bilateral lipomastia). Postaxial Polydactyly present on both hands and feet. Pulse-80b/min, BP-120/80 mmHg, respiratory rate-14/min, temperature-98 F.

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Cite this as:
BMCJ 2018;4(1): 23-25

Received : 9 October 2017
Accepted : 7 December 2017



Figure 1: Obesity and small penis.

Higher psychic function revealed normal. Visual acuity reduced to finger counting. Bilateral reduction of temporal field of vision. Color vision normal. Fundoscopy revealed arteriolar narrowing, perivascular bone specule pigmentation and waxy optic disc pallor. Other cranial nerves were normal. Motor and sensory functions were intact. Abdomen distended, flanks full, soft, nontender, bowel sound present, hernial orifices intact. Bilateral small testes (4ml on orchidometer bilaterally) with small external genitalia (4cm). His serum testosterone was 2.78 nmol/l (lab ref. level of serum testosterone of 12-15 years boy : 3.46-11 nmol/l). Other lab investigation reports CBC, RBS, Liver and Renal function tests were normal. Chest X-ray P/A view and Ultrasonography of abdomen reveal no abnormalities. Thyroid hormones and ECG report were also normal. Our patient had four primary features of Bardet-Biedl syndrome retinal changes, obesity, hypogonadism and polydactyly as suggested by Beales et al.^{5,6}



Figure 2: Polydactyly involving hands



Figure 3 : Polydactyly involving leg

Discussion

Laurence and Moon in 1866 at the Ophthalmic Hospital in South London first described LaurenceMoonBiedlBardet syndrome, but now a days BardetBiedl syndrome and LaurenceMoon syndrome is usually considered a separate entity.⁷ In 1920 Bardet described the three of the five cardinal features of the syndrome, polydactyly, obesity and pigmentary retinopathy.⁸ Later Biedl in 1922 added mental deficiency and genital hypoplasia. In 1925, Solis-Cohen and Weiss coined the name 'LaurenceMoonBiedlBardet syndrome'.⁸

Major clinical features are pigmentary retinopathy, poor visual acuity, low vision, and/or blindness caused by an impaired photoreceptor transport mechanism in the retina.⁸ Loss of, or reduced sense of, smell (anosmia). Some patients claim extra-sensitive sense of smell.⁹ Polydactyly (extra digits) or syndactyly (webbing of fingers and toes). Hypertrophy of interventricular septum and left ventricle and dilated cardiomyopathy. Hypogonadism, renal failure, urogenital sinuses, ectopic urethra, uterus duplex, septate vagina, and hypoplasia of the uterus, ovaries, and fallopian tubes. Developmental delay, especially of fine and gross motor skills. A wide variety of socialization and social interaction problems have been identified with BBS. Obesity, possibly related to a decreased sensory function that would normally indicate satiation. Hyperphagia in some patients.¹⁰

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Squamous cell carcinoma misdiagnosed and treated as tubercular consolidation of lung two case reports.

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Abstract

Carcinoma of lung can be covered up as pulmonary tuberculosis even in endemic areas like Bangladesh. Due to similarity of clinical presentation many patients with lung cancer may be wrongly treated as pulmonary tuberculosis. This case was presented because it was wrongly treated as pulmonary tuberculosis whereas he had lung cancer. We came to a definitive diagnosis of squamous cell carcinoma depending upon USG guided FNAC.

Key words : squamous cell carcinoma, pulmonary tuberculosis, Bangladesh.

Introduction

There are a good number of tuberculosis cases in Bangladesh annually. Higher prevalence of tuberculosis and overlapping its clinical presentation and radiological findings with lung cancer creates a scenario where a significant number of early lung cancer patients may be misdiagnosed as tuberculosis. The radiological findings of tuberculosis of lung is in the form of cavity, fibroproductive, exudative, acinary, micro and macro nodular and miliary. Radiological appearance may mimic pathological lesions of lungs and may cause clinical diagnosis difficult.

Case summary

Case No.1: Mr. Robiul, 60 years old nondiabetic, normotensive, nonasthmatic, smoker, muslim male farmer by occupation hailing from Horipur, Kansat, Shibgonj, Chapainobabgonj. Presented with low grade fever for > 6 months. The fever was evening rising, comes with shivering and goes away with sweating after taking antipyretics like

paracetamol. He also complained of chronic cough for 6 months and Hemoptysis for the last 1 month. Along with these he also had respiratory distress and progressive weight loss and generalized weakness. He gave no history of trauma or bleeding disorder. On general examination patient was co-operative with below average body built and poor nutritional status, anemic but cyanosis, jaundice, clubbing, koilonychia, leukonychia, edema and dehydration was absent. His temperature was 99.4° F and hemodynamic status was within normal limit. On systemic examination, all the system revealed normal finding except respiratory system. On inspection no gross abnormality was visible in chest wall on respiratory movement. Breath sound was vesicular with prolonged expiration but diminished in right upper zone, rhonchi absent but crepitation was present in right side in that region. Percussion note was dull in right upper zone of lung. Vocal fremitus and resonance was also increased. So, clinically there was consolidation of lung was established.

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Cite this as:
BMJ 2018;4(1): 26-30

Received : 20 November 2017
Accepted : 14 December 2017



Figure 1: X-ray chest



Figure 2: X-ray chest

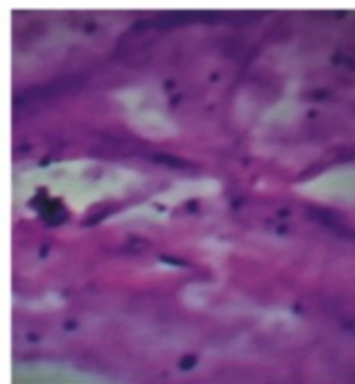


Figure 3: FNAC

Due to these reasons he visited Upazilla Health Complex. There he was investigated initially by chest X-ray, (Figure 1) the finding was right lung upper zone including apical region consolidation. Then sputum for AFB was done where sputum found blood stained and LED 4/L with 1+. Based on these he was prescribed Category 1 anti TB regimen and continued for 2 months. Finding no clinical improvement he again underwent X-ray chest (Figure 2) and sputum for AFB. At this time lung lesion persisted rather increased in size but sputum was negative for tubercle bacilli but clinically no improvement was observed. Then patient was referred to Chest Disease Hospital, Rajshahi for his proper management. In this hospital the patient underwent X-ray chest, the finding was as previous and sputum for AFB, Gene X-pert both the results were negative for tubercle bacilli. Then Ultrasonography guided Fine Needle Aspiration Cytology (USG guided FNAC) was performed (Figure 3). The FNAC findings are Smears are cellular. It reveals anaplastic squamous cells arranged in groups, nests, sheets and singly. Some of the cells are large, have large hyperchromatic nuclei and ample eosinophilic cytoplasm. Background shows dense acute inflammatory cells, necrotic material and red blood cells. Features are suggestive of squamous cell carcinoma.

Case No.2: Mr. Abdul Mojib, normotensive, non-diabetic, smoker, muslim male hailing from Bagmara, Rajshahi presented to us with the complaints of progressive loss of weight, low grade fever, nausea, vomiting and abdominal pain for > 3 months. He also complained of respiratory distress as well. At first, the patient developed productive cough along with respiratory distress which was

progressively deteriorating despite treatment. His weight was lost significantly during the period of last one month. He has malaise, fever, loss of appetite for the last 3 months and along with this abdominal pain started due to chronic cough. Due to these complaints he visited the local village doctors and last of all to the upazilla health complex and under gone X-ray Chest (Figure 4) with the finding of collapsed of left lung with mediastinal pulling mostly due to lung neoplasm and compensatory emphysematous change in right lungs. He underwent sputum for AFB where the first smear showed 2/L and second smear showed no organism. Then anti-tubercular therapy was started since 16th of September 2017 and continued for one and half months. No subjective and objective improvement was observed rather he developed mild jaundice. Then he was referred to RMCH for better management. There he underwent chest X-ray (Figure 5), USG guided FNAC which revealed chronic granulomatous inflammation consistent with tuberculosis. On complete blood count the ESR was 120 mm in first hour. Then anti-tubercular drugs were continued and the patient was referred to Chest Disease Hospital Rajshahi. In this hospital he was thoroughly evaluated clinically and found that the patient is ill looking, below average body built and nutrition. He is anemic with mild jaundice and hemodynamically stable. On systemic examination all the system revealed normal except respiratory system. On examination of the respiratory system, breath sound on the right side was absent with increased vocal fremitus and resonance and respiratory distress was present. So clinically lung consolidation was established.



Figure 4: X-ray chest

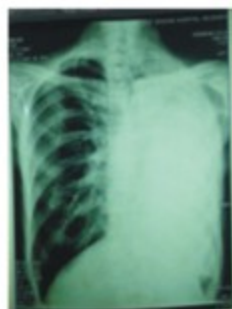


Figure 5: X-ray chest

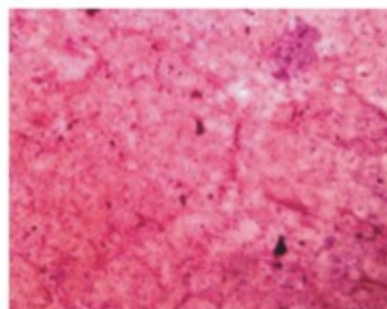


Figure 6: FNAC

He was being treated as a case of tubercular lung consolidation. But no improvement was observed. Then he was again evaluated with ultrasonography guided FNAC (Figure 6). At this time the findings were anaplastic squamous cells arranged in groups, nests, sheets and singly. Some of the cells are large, have large hyperchromatic nuclei and ample eosinophilic cytoplasm. Background shows dense acute inflammatory cells, necrotic material and red blood cells. Features are suggestive of squamous cell carcinoma.

Discussion

It is very difficult to diagnose a benign lesion from a malignant one in case of lungs. Because of high prevalence of pulmonary tuberculosis and similarity of clinical findings with carcinoma of lung and several other factors like lack of awareness, inadequate infrastructure and socio-economic factors in developing countries, a large number of lung cancer patients initially get wrongly treated for TB. But no above reasons can be self-satisfactory on our part of diagnosis because the treatment for both is entirely different and has tragic consequences. Lung cancers are clinically and genetically distinct. Small cell carcinoma of lungs is best treated by chemotherapy, because almost all of them are metastatic when patients presents clinically. The non-small cell lung cancers may be curable by

surgical intervention if it is limited to the lung. The overall, 5-year survival rate is only 16% despite surgical excision, radiotherapy and chemotherapy. The 5-year survival rate is 52% for localized lung lesions, 22% when there is regional and only 4% with distant metastases¹. Early-diagnosis of lung cancer enhances the chance of surgical resection and timely chemo-radiotherapy may provide better outcome. Although Pulmonary tuberculosis and lung cancer have similarity in clinical presentation, a careful history and clinical examination can be helpful in differentiating in between the two. History of cigarette smoking is usually present in cases of lung cancer while it may or may not be present in cases of pulmonary tuberculosis. The common symptoms of lung cancer at presentation are gradually deteriorating chronic cough, hemoptysis, dyspnea, hoarseness of voice, chest pain, unexplained weight loss and loss of appetite, non-resolving pneumonia and superior vena cava syndrome if it is involved. Fever is low grade with evening rise in case of tuberculosis whereas in lung cancer it is non-specific. Sudden and significant weight loss indicates malignancy rather than pulmonary tuberculosis where weight loss is gradual². The overall Sensitivity of various investigations in the diagnosis of Lung Cancer is as follows³(Table No.1).

Table 1. Investigations and their sensitivity

Investigation	Overall sensitivity
Sputum cytology	66%
Flexible Bronchoscopy	88% in central, Endo-bronchial lesions
R-EBUS (radial Endo-bronchial ultrasound)	73%,
EMN (electromagnetic navigation bronchoscopy)	71%,
TTNA(Transthoracic needle aspiration)	90%,
Pleural fluid cytology	72%,
Closed pleural biopsy	38% to 47%
Image-guided closed biopsy	75% to 88%
Thoracoscopic biopsy of the pleura	95% to 97%.

From the above table one can assume that none of the available investigations have 100% accuracy in the diagnosis of lung cancer. A sensible combination of the available modalities is very important in avoiding misdiagnosis between pulmonary tuberculosis and lung cancer. Sputum cytology may be the initial cost effective test, followed by CXR and CECT (Contrast Enhanced Computer Tomography) chest. As tuberculosis is prevalent and having radiological similarity with lung cancer, many of lung cancer bearing patients initially get treatment for tuberculosis wrongly depending on radiological picture only. So, cytohistopathological evidence is must be reported to make a definitive diagnosis of lung cancer. There are a series of investigations commonly obtainable now a days. The most important one is Flexible bronchoscopy with or without Brush biopsy or Bronchioalveolar lavage. The sensitivity of traditional Flexible bronchoscopy is high for Endo-bronchial disease and poor for small peripheral lesions less than 2 cm in diameter. Adding more sensitivity, in the recent years several guided-bronchoscopy techniques like electromagnetic navigation bronchoscopy (ENB), virtual bronchoscopy (VB) combined with narrow band imaging, radial Endo-bronchial ultrasound (R-EBUS) guided trans-bronchial needle aspiration, ultrathin bronchoscope have been developed^{4,6}. A meta-analysis in 2012 showed that the diagnostic produce of such guided bronchoscopic techniques is definitely better than that of traditional transbronchial biopsy⁷. So, guided bronchoscopy has been suggested as an alternative to or be complementary to TTNA (Transthoracic needle aspiration) for tissue sampling of Endo-bronchial Pulmonary Nodule and even in the evaluation of peripheral pulmonary lesions⁷. Laser induced fluorescence endoscopy and spectrofluoremetry can also be done for detection of lung cancer earlier. The gold standard against which bronchoscopic

modalities are compared is Transthoracic needle aspiration cytology⁷. The sensitivity of TTNA is excellent for diagnosis of lung cancer but has a higher rate of pneumothorax.

Conclusion

Opacity in lung field in the chest X-ray should not be considered as tuberculosis all the times even in endemic zone. Based only on radiological findings one should not stamp a case as smear negative tuberculosis. Image guided fine needle aspiration cytology namely ultrasonography guided FNAC can be a very important tool in making a definitive diagnosis. As occurred in our case. Other diagnostic tools must be considered also. We presented this case because it could be an important lesion for the physician of Bangladesh in treating patients with such kind of chest X-ray findings. So that lung cancer may not be mistaken as pulmonary tuberculosis.

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Acknowledgments

The author should acknowledge only those people and their institutions that have made significant contributions to the study.

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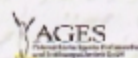
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