HYPOALBUMINEMIA AS A PREDICTOR OF DIARRHEA CAUSED BY *BLASTOCYSTIS HOMINIS*

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Abstract. *Blastocystis hominis* is an intestinal protozoan found worldwide, particularly in developing countries, that may cause gastrointestinal symptoms, including diarrhea. We conducted a hospital-based study to identify clinical factors predictive of diarrhea caused by *B. hominis*. We studied patients with positive stool samples for *B. hominis* by formalin ethyl acetate concentration technique at Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand between 2003 and 2010. Patients were divided into diarrhea and non-diarrhea groups. Diarrhea patients were categorized if the diarrhea was associated with *B. hominis* only. In total, 81 patients with isolated *B. hominis* infection were studied. Of those, 17 patients (21%) had diarrhea associated with *B. hominis* infection. Eight variables were included in the final model predicting diarrhea caused by *B. hominis* on multiple logistic regression analysis. Only serum albumin level was significantly associated with diarrhea cases in this study with an adjusted OR of 0.162 and a 95%CI of 0.027- 0.957. Hypoalbuminemia is associated with diarrhea associated with blastocystosis.

Keywords: *Blastocystis hominis,* predictors, diarrhea, blastocystosis

INTRODUCTION

Blastocystis hominis is an intestinal protozoan found worldwide, particularly in developing countries. *B. hominis* is common in patients with gastrointestinal symptoms (Wang *et al*, 2010; Arques *et al*, 2011; Vahedi *et al*, 2011; Zuel-Fakkar *et al*, 2011). It is associated with several symptoms, including abdominal pain, constipation, diarrhea (Davis *et al*, 2010), irritable bowel syndrome, bowel habit changes and fatigue (Qadri *et al*, 1989; Davis *et al*, 2010). Non-gastrointestinal symptoms, such as urticaria, may also occur in patients with *B. hominis* infection (Zuel-Fakkar *et al*, 2011).

Diarrhea is a common symptom in blastocystosis and it can be severe (Kulik *et al*, 2008). Predictors of diarrhea in *B. hominis* infected patients are unclear. We conducted a hospital-based study to identify factors predictive of diarrhea caused by *B. hominis*.

MATERIALS AND METHODS

We enrolled patients with stool samples positive for *B. hominis* using

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the formalin ethyl acetate concentration technique (FECT) at Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand. The study period was between 2003 and 2010. Patients who had co-infection with other intestinal parasites or bacterial infection were excluded from the study. A chart review was done and the clinical features and laboratory findings of each patient were recorded.

The definition of diarrhea was the passage of unusually loose stools, at least three times in a 24 hour period (WHO, 2005). Diarrhea persisting more than 14 day was defined as chronic diarrhea.

Clinical features were compared between those presenting with diarrhea and those without diarrhea using descriptive statistics. Univariate logistic regression analysis was used to determine the crude odds ratio (OR) and *p*-value of each variable for those having diarrhea. All variables with a *p*-value <0.25 or clinically suspected variables were included in the multivariate logistic regression model. Variables with *p*-value <0.15 will retained in the final model. Analytical results were presented as adjusted OR, and 95% confidence interval (CI). Analysis was performed with STATA version 10.1 (Stata Corporation, College Station, TX).

RESULTS

In total, 81 patients were included in the study. Of those, 17 patients (21%) had diarrhea, 15 had acute diarrhea. More patients with diarrhea were male with a lower education, were farmers, lived in a rural area, contracted the infection during the rainy season and had an HIV infection (Table 1). Peripheral eosinophils and serum albumin levels were lower in patients in the diarrhea group (Table 2). On univariate analysis, the number of patients without diarrhea with an underlying disease was greater than those in the diarrhea group (*p*-value = 0.028). Eight variables were included in the final model predictive of diarrhea (Table 3). On multiple logistic regression analysis only serum albumin level was significantly associated with diarrhea (OR 0.162; 95% CI 0.027- 0.957).

DISCUSSION

Humans contract *B. hominis* infection by fecal-oral route. Diarrhea is a common intestinal symptom in blastocystosis. The prevalence of blastocystosis among the general population in developing countries is 20-50% (Hill, 2007). The prevalence and symptoms of blastocystosis may vary by country. The prevalence of diarrhea in our study was 21%. In Mexico, *B. hominis* was found to be a causative agent of diarrhea in children but at a lower rate than our study (7%) (Diaz *et al*, 2003).

The clinical characteristics in those with blastocystosis with and without diarrhea were comparable aside from the diarrhea (Tables 1 and 2). Underlying diseases were significantly more common among patients with diarrhea but were not predictors of diarrhea on multiple logistic regression analysis. After adjusting for other variables, only serum albumin was a significant protector of diarrhea in blastocystosis. A serum albumin increase of 1 g/dl was associated with an 84% lower chance of having diarrhea.

Hypoalbuminemia has been reported to be a predictor of several conditions, including acute heart failure, acute coronary syndrome, acute pancreatitis or stroke (Arques *et al*, 2011; Dao *et al*, 2011; Vahedi *et al*, 2011). It is also a significant risk factor for death in children with persistent

Table 1
Baseline characteristics of those with and without diarrhea infected by *B. hominis.*

Baseline characteristics, *n* (%)	Diarrhea *n* = 17	Non-diarrhea *n* = 64	*p*-value
Mean age (years)	47.47 ± 19.2	45.24 ± 18.3	0.660
Male	9 (52.9)	27 (42.2)	0.424
Education: primary school or lower[a]	10/16 (62.5)	24/53 (45.3)	0.434
Farmer or laborer[a]	8/14 (57.1)	31/59 (52.5)	0.982
Rural	14 (82.4)	50 (78.1)	0.752
Rainy season	12 (70.6)	41 (64.1)	0.777
Have an underlying disease	12 (70.6)	60 (93.8)	0.028
Type of underlying diseases			
Hematologic malignancy	3 (17.6)	13 (20.3)	1
Other malignancy	2 (11.8)	12 (18.8)	0.723
Autoimmune disease	1 (5.9)	11 (17.2)	0.444
Rheumatologic disease	1 (5.9)	4 (6.3)	0.378
HIV infection	2/6 (33.3)	0/14 (0)	0.079
Radiation therapy	2 (11.8)	3 (4.7)	0.631
Chemotherapy	3 (17.6)	22 (34.4)	0.247
Steroid treatment	3 (17.6)	23 (35.9)	0.243

[a]Missing data

Table 2
Laboratory results in those with and without diarrhea infected by *B. hominis.*

Laboratory results	Diarrhea *n* = 17 Median (min-max)	No diarrhea *n* = 64 Median (min-max)	*p*-value
Hemoglobin (g/dl)	11.6 (7.9-13.8)	10.6 (4.8-16.6)	0.524
Hematocrit (%)	35 (23-41.9)	32.8 (12.9-50.6)	0.497
Total white blood cell count (cells/mm^3)	9.6 (4.6-78)	9.5 (0.8-49.1)	0.721
Neutrophils (%)	69.4 (35.4-92.6)	61.4 (0-96.1)	0.441
Lymphocytes (%)	24.8 (5-50.8)	21 (0-53.5)	0.690
Monocytes (%)	5.5 (1-22.9)	6.4 (0-12.7)	0.801
Eosinophils (%)	0.7 (0-10.3)	3.35 (0-31.7)	0.101
Absolute eosinophil count (cells)	46.8 (0-5,850)	282.9 (0-3,995)	0.129
Serum sodium (mEq/l)	135 (122-143)	137 (120-144)	0.126
Serum potassium (mEq/l)	4.1 (2.6-5)	4 (2.9-5.0)	0.845
Serum chloride (mEq/l)	97 (93-105)	101 (87-111)	0.012
Serum HCO_3 (mEq/l)	26.1 (13.9-30.3)	26.1 (14.9-31)	0.734
Serum albumin (g/dl)	2.9 (1.6-4.2)	3.5 (2.4-4.5)	0.158
Serum globulin (g/dl)	3.7 (2.7-3.9)	3.8 (1.8-6.1)	0.263

Table 3
Variables in the final model on multivariate logistic regression analysis of those having diarrhea caused by *B. hominis*.

Variables	Adjusted odd ratios	95% Confidence interval
Female gender	3.467	0.255 - 47.053
Age	1.007	0.957 - 1.059
Receiving chemotherapy	0.315	0.030 - 3.277
Receiving steroid therapy	0.659	0.071 - 6.114
Receiving radiation therapy	6.605	0.231 - 188.704
Season	0.668	0.071 - 6.215
Serum albumin (g/dl)	0.162	0.027 - 0.957
Absolute eosinophil count	1.000	0.999 - 1.001

diarrhea (Umamaheswari *et al*, 2010). This may indicate that blastocystosis patients with malnutrition have a higher risk of developing diarrhea. Serum albumin is an important protein having an osmotic effect, anti-inflammatory effects and it can bind molecules and drugs (Arques and Ambrosi, 2011). *B. hominis* itself may damage the intestinal mucosa and hypoalbuminemia aggravates the poor mucosal absorption. Another possible explanation is the hypoalbuminemia may be caused by chronic diarrhea from blastocystosis. Two patients have been reported to have hypoalbuminemia associated with *B. hominis* infection (Levy *et al*, 1996; Nassir *et al*, 2004).

A limitation of this study is the formalin ethyl acetate concentration technique may not be the best technique to detect *B. hominis*, which could affect the results of mulitivariate logistic regression analysis. Some of the data was missing due to the retrospective design of the study. However, hypoalbuminemia was associated with diarrhea in blastocystosis.

ACKNOWLEDGEMENTS

This work was supported by a Higher Education Research Promotion and National Research University Project of Thailand, Office of the Higher Education Commission, and the Faculty of Medicine, Khon Kaen University, Thailand. Wanchai Maleewong was supported by a TRF Senior Research Scholar Grant, Thailand Research Fund (Grant no. RTA5580004).

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