Histoplasmosis is a systemic fungal infection caused by dimorphic fungus *Histoplasma capsulatum*, which is widely distributed throughout the world, but the greatest endemicity is reported in the Americas, especially along the Mississippi and Ohio river valleys.\(^1,2\) Its mycelial form is found in soil rich in bird and bat droppings.\(^3\) Airborne conidia enter into the human lungs by inhalation, where they germinate into yeast form.\(^4,5\) The host response to infection depends upon the size of the infective inoculum, the underlying health of the patient, and host immune status.\(^1\) Most infections remain asymptomatic or mild respiratory symptoms may occur in immunocompetent individuals, but in immunodeficient patients, dissemination may occur to involve various organs including the oropharynx, lymph nodes, liver, spleen, skin, and adrenal glands.\(^2,4–11\) Reactivation of latent infections may complicate recipients of solid organ transplants and patients receiving immunosuppressive therapy for other reasons.\(^12,13\) Symptoms depend upon organ involvement; fever and weight loss are common features,\(^4–11\) and the clinical presentation often mimics tuberculosis.\(^6\) Diagnosis depends on identification of the organism in culture or...
Histopathological examination findings of tissue biopsy samples or serological tests. In Bangladesh, one-fifth of the population exhibited positive skin sensitivity reaction to histoplasmin, with the first case of histoplasmosis reported in 1982. Cases were infrequent but in recent years, a good number of cases, mostly disseminated forms, have been reported in immunodeficient and immunocompetent patients. In this systematic review, we describe the sociodemographic characteristics, clinical features, diagnostic proofs, treatment, and outcome of histoplasmosis in Bangladesh.

**METHODS**

We systematically searched to identify all previously published English literature containing information regarding histoplasmosis in/or from Bangladesh. Searches were conducted via “PubMed” using the keywords “Bangladesh”, “Histoplasma capsulatum”, and “histoplasmosis”. We also systematically searched through Bangladesh Journals Online (BanglaJOL) for articles published in local journals. The search engine “Google” was also used to identify articles. All literature searches were conducted up to 31 December 2017. Searches were conducted by the first two authors individually and then cross-checked by all the authors. Unpublished but well-documented cases (seven cases) were added. Cases mentioned elsewhere with inadequate information and possible repetitions were excluded [Figure 1].

Histoplasmosis cases were analyzed for selected sociodemographic characteristics including age and sex, immune status, endemicity, travel history, site(s) of disease, proof of diagnosis, treatment given, and the outcome recorded. Immunodeficiency status included patients with HIV or AIDS, those receiving immunosuppressive drugs, organ transplant recipients, patients with diabetes mellitus, and those with congenital immunodeficiency. Patients were categorized as having localized or systemic histoplasmosis. Systemic disease was characterized as single organ disease or disseminated forms. Disseminated disease was defined when a typical organism was grown in cultures or typical histopathological findings were identified from samples of extrapulmonary sites along with systemic symptoms. Endemicity was labeled where the patient had never traveled outside Bangladesh.

**RESULTS**

Twenty-four articles were identified from published literature including 18 case reports, three research articles, two survey reports, and one conference abstract; and one article was identified from another source (Figure 1, Table 1, case no 22). From them, two cases were excluded because of repetition, three research articles were excluded because of inadequate information for cases (references 7 and 33) and presumptive diagnosis (reference 32), two skin survey reports (references 14 and 15), and one conference abstract was excluded. Finally, a total of 19 cases were eligible for analysis from published literature (total 18 articles) [Figure 1], to which seven unpublished but well-documented cases were added to make the total number of cases 26 [Table 1].

All 26 patients were male with a mean age of 50.9 years (range 8–75) [Table 1 and Table 2]. Nine patients were farmers, and five patients had a history of smoking. Five patients had a history of traveling outside Bangladesh [Table 2].

Among the patients, one was a known case of AIDS, and disseminated histoplasmosis was the presenting feature of AIDS in another three cases [Table 2]. The CD4 counts in one patient with AIDS was 19/μL and 4/μL in another patient [Table 1]. Seven patients had diabetes, one was a...
| Patient number | Journal, Year/Reference | Age/Sex/Occupation | Immune status | Clinical presentation | Physical signs | Important laboratory and imaging findings | Diagnostic test and form of histoplasmosis | Treatment and outcome |
|----------------|-------------------------|--------------------|---------------|----------------------|---------------|------------------------------------------|------------------------------------------|----------------------|
| 1/             | BMRC Bull, 1982          | 69 years/ Male     | Not known     | Nodular lesion in oral mucosa | Submandibular lymphadenopathy | Histopathology from oral nodule. | Disseminated histoplasmosis. | Amphotericin B. Anti-TB prescription. Cured with relapse at 16th month. |
| 2/             | JBCPS, 2005             | 41 years/ Male     | Positive anti-HIV | Fever Weight loss Anorexia Sore throat Loose motion | Anemia Oral moniliasis Dehydration Cervical lymphadenopathy Hepatosplenomegaly | Hb = 7.7 gm/dL WBC = 3800/cmm Platelets = 150 000/cmm | Bone marrow study. Disseminated histoplasmosis. | Itraconazole. Expired in hospital due to septic shock. |
| 3/             | Transpl Infect Dis, 2010 | 60 years/ Male     | T2DM Renal transplant recipient | Fever Sore throat | Skin nodules | Hb = 11.1 gm/dL WBC = 3100/cmm LDH = 256 IU/L Abnormal chest imaging (nodules) | Biopsy and culture from skin nodule, broncho-alveolar lavage, and transbronchial biopsy. Epiglottic biopsy. Disseminated histoplasmosis. | Lipid amphotericin B. Itraconazole for an indefinite period. History of INH prophylaxis. Cured, no recurrence up to 2 years. |
| 4/             | BSMMUJ, 2010            | 45 years/ Male     | HIV-negative  | Fever Weight loss Abdominal pain | Anemia Generalized lymphadenopathy Growth in the oral cavity Asites | Hb = 9.1 gm/dL ESR = 40 mm in first hour | Biopsy and histopathology from tongue growth and lymph node. Disseminated histoplasmosis. | Amphotericin B. Itraconazole (planned for one year). Improved up to six weeks. |
| 5/             | JHPN, 2010              | 32 years/ Male     | Diagnosed AIDS | Fever Weight loss Anorexia | Cervical lymphadenopathy Splenomegaly Maculopapular rash | Hb = 9.6 gm/dL Esophageal candidiasis CD4 = 19/ul | Histopathology from lymph node. Disseminated histoplasmosis. | Amphotericin B (0.7 mg/kg/d for 21 days). Itraconazol (200 mg 12-h). Anti-TB Not known |
| 6/             | J Med, 2010             | 56 years/ Male     | HIV-negative  | Fever Cough Shortness of breath Disorientation | Anemia | Hb = 9 gm/dL ESR = 60 mm in first hour Serum creatinine = 2.3 mg/dL Abnormal chest X-ray (infiltrates) | Bone marrow study. Disseminated histoplasmosis. | Amphotericin B. Anti-TB (presumptive). Expired due to aspiration pneumonia. |
| 7/             | J Med, 2010             | 57 years/ Male     | Not known     | Fever Back pain | Anemia Generalized lymphadenopathy Hepatomegaly Spastic paraparesis | Hb = 8.9 mg/dL ESR = 90 mm in first hour | Open biopsy from paravertebral tissue. Disseminated histoplasmosis. | Not known Not known |
| Patient number/Reference | Age/ Sex/ Occupation | Immune status | Clinical presentation | Physical signs | Important laboratory and imaging findings | Diagnostic test and form of histoplasmosis | Treatment and outcome |
|--------------------------|-----------------------|---------------|----------------------|----------------|------------------------------------------|--------------------------------------|----------------------|
| 8/ Unpublished, 2010*  | 8 years/ Male/ Unknown | Not known     | Fever                | Anemia          | Hb = 8.3 gm/dL WBC = 5300/cmm ESR = 89 mm in first hour | Lymph node culture. Disseminated histoplasmosis. | Anti-TB Expired |
| 9/ J Med, 2011  | 65 years/ Male/ School teacher | HIV-negative  | Fever                | Anemia          | ALT = 81.9 IU/L AST = 83.2 IU/L Abnormal chest X-ray (reticulonodular shadow). Bilateral adrenal masses. | FNAC from adrenal gland. Partial adrenal insufficiency. Disseminated histoplasmosis. | Anti-TB for eight months. Not known |
| 10/ JBCPS, 2011  | 75 years/ Male/ Farmer | HIV-negative  | Fever                | Anemia          | ERS = 41 mm in first hour. Bilateral adrenal masses. | FNAC and culture from adrenal gland. Partial adrenal insufficiency. Disseminated histoplasmosis. | Amphotericin B (five doses) Itraconazole (one year). Cured, no recurrence up to 27 weeks of follow-up. |
| 11/ J Med, 2012  | 60 years/ Male/ Not known | HIV-negative  | Hoarseness of voice | Ulcerative growth in vocal cord | Abnormal chest X-ray (diffuse patchy opacity). | Histopathology from vocal cord specimen. Primary vocal cord histoplasmosis. | Amphotericin B (0.5 mg/kg EAD for 14 doses). Itraconazole (200 mg 12-h for 12 weeks). Anti-TB (two times). Improved and advised for follow-up. |
| 12/ JAFMC, 2012  | 30 years/ Male/ Brick field worker | HIV positive  | Fever                | Anemia          | Pancytopenia ALT = 103 IU/L Alkaline phosphatase = 527 IU/L LDH = 1003 U/L Abnormal chest imaging (consolidation). | PBF and bone marrow study. Disseminated histoplasmosis. | Anti-TB for nine months (presumptive). Expired in hospital due to aspiration pneumonia. |
| 13/ JBCPS, 2012  | 42 years/ Male/ Painter | HIV-negative  | Oral ulcer Dysphagia Poor general health Diarrhea | Anemia          | Histopathology from oral ulcer. Localized to the oral cavity. | Itraconazole (200 mg 12-h for three weeks then maintenance dose). Cured, no recurrence up to 2 months of follow-up. |
### Table 1: Cases of histoplasmosis in/or from Bangladesh (N = 26).

| Patient number/ Journal, Year/ Reference | Age/ Sex/ Occupation | Immune status | Clinical presentation | Physical signs | Important laboratory and imaging findings | Diagnostic test and form of histoplasmosis | Treatment and outcome |
|----------------------------------------|----------------------|---------------|-----------------------|---------------|------------------------------------------|-------------------------------------------|----------------------|
| 14/ JBCPS, 201226                      | 65 years/ Male/ Farmer | HIV-negative  | Oral ulcer            | Anemia        | Histopathology from oral ulcer.           | Itraconazole (200 mg BID for 4 weeks then maintenance dose). Cured, no recurrence up to 2 months of follow-up. |
| 15/ J Gen Pract, 201327               | 32 years/ Male/ Farmer | HIV-negative  | Fever                  | Hepatomegaly  | FNAC from adrenal gland. Disseminated histoplasmosis. | Anti-TB Not known |
| 16/ Bang J Med. 201328                | 45 years/ Male/ Not known | T2DM HIV positive | Fever, Cough, Weight loss, Orogenital ulcers | Anemia, Rash, Crepitation in lung, Hepatomegaly | FNAC from adrenal gland. Disseminated histoplasmosis. Bone marrow study. | Amphotericin B Expired |
| 17/ J Med, 2013\(^9\)                 | 62 years/ Male/ Farmer | HIV-negative  | Fever, Back pain, Paraplegia, Bowel-bladder incontinence | Anemia, Generalized lymphadenopathy, Spastic paraplegia | Lymph node biopsy, CT-guided FNAC from paraspinal soft tissue, Disseminated histoplasmosis. | Amphotericin B Itraconazole Neurosurgical exploration. Improved (up to one month of follow-up). |
| 18/ Mymensingh Med J, 2014\(^9\)     | 60 years/ Male/ Farmer | HIV-negative  | Fever, Cough, Weight loss, Sore throat, Voice change | FBG = 12 mmol/L, Patchy opacity in chest X-ray | Histopathology from vocal cord punch biopsy specimen (ulcer), Vocal cord histoplasmosis. | Amphotericin B (0.5 mg/kg/d for six weeks). Itraconazole (200 mg for 12 weeks). Anti-TB Improved up to three months of follow-up. |
| 19/ Unpublished, 2014*                | 60 years/ Male/ Farmer | Not known     | Weight loss, Anorexia, Weakness | Increased pigmentation | CT-guided FNAC from adrenal gland, Gum biopsy, Anti-histoplasma antibody, Disseminated histoplasmosis. | Itraconazole Hydrocortisone Improved up to five months of follow-up. |
| Patient number/Journal, Year/Reference | Age/Sex/Occupation | Immune status | Clinical presentation | Physical signs | Important laboratory and imaging findings | Diagnostic test and form of histoplasmosis | Treatment and outcome |
|---------------------------------------|--------------------|---------------|----------------------|---------------|------------------------------------------|-------------------------------------------|----------------------|
| 20/Unpublished, 2014*                 | 42 years/Male/Farmer | Not known     | Weight loss          | Anorexia Weakness | Hb = 10.6 gm/dL, WBC = 9700/cmm, Platelets = 230,000/cmm, ESR = 53 mm in first hour, ALT = 65 IU/L, ACTH stimulation test: partial adrenal insufficiency, Bilateral adrenal enlargement | CT-guided FNAC from the adrenal gland, Anti-histoplasma antibody, Disseminated histoplasmosis. | Itraconazole, Hydrocortisone, Improved up to three months of follow-up. |
| 21/Unpublished, 2014*                 | 59 years/Male/School teacher | T2DM HIV-negative | Fever Weight loss Anorexia | Anemia Jaundice Hepatoplenomegaly | Hb = 9.1 gm/dL, WBC = 3900/cmm, Platelets = 89000/cmm, ESR = 85 mm in first hour, Bilateral adrenal enlargement | FNAC from the adrenal gland, Disseminated histoplasmosis. | Discharged against medical advice, Not known |
| 22/BSM Bull, 2015                     | 40 years/Male/Not known | HIV-negative | Fever Weight loss Cough Anorexia Weakness | Anemia Pigmentation Hepatomegaly | Hb = 8.9 gm/dl, Bilateral adrenal mass | USG guided FNAC from adrenal gland, Disseminated histoplasmosis. | Lipid formulation of amphotericin B (0.5 mg/kg/d for two weeks), Itraconazole (200 mg 12-h for 12 months), Anti-TB, Not known |
| 23/Unpublished, 2015*                 | 72 years/Male/Retired government employee | T2DM HIV-negative | Fever Weight loss Anorexia | Anemia | Hb = 9.6 gm/dl, WBC = 6700/cmm, Platelets = 165,000/cmm, ESR = 67 mm in first hour, HbA1c = 8.3%, Bilateral adrenal enlargement | FNAC from the adrenal gland, Disseminated histoplasmosis. | Amphotericin B, Itraconazole, Improving |
| 24/Unpublished, 2015*                 | 62 years/Male/Retired government employee | T2DM HIV-negative | Fever Anorexia Weight loss Cough Convulsion | Anemia | Hb = 8.7 gm/dl, WBC = 4100/cmm, Platelets = 153,000/cmm, ESR = 45 mm in first hour, HbA1c = 7.9%, Bilateral adrenal enlargement | FNAC from the adrenal gland, MRI of brain, Disseminated histoplasmosis. | Amphotericin B, Itraconazole, Recurrence with CNS histoplasmosis (later expired). |
| 25/Unpublished, 2016*                 | 42 years/Male/Service holder | HIV-negative | Fever Anorexia Weight loss | Hepatosplenomegaly | Hb = 12 gm/dl, WBC = 5600/cmm, Platelets = 222,000/cmm, ESR = 78 mm in first hour, Bilateral adrenal enlargement | FNAC from the adrenal gland, Disseminated histoplasmosis. | Itraconazole, Anti-TB, Not known |
HIV was negative in 15 cases and another had AIDS. No other history suggestive of immunosuppression was found among the patients. Fever (n = 20) and weight loss (n = 17) were the two most common clinical presentations. Other features were oral ulcer, anorexia, skin rash and nodules, cough, abdominal pain, diarrhea, and bleeding [Table 2]. Common physical findings included anemia, lymphadenopathy, and abnormal lung findings [Table 2].

| Patient number/ Journal, Year/ Reference | Age/ Sex/ Occupation | Immune status | Clinical presentation | Physical signs | Important laboratory and imaging findings | Diagnostic test and form of histoplasmosis | Treatment and outcome |
|-----------------------------------------|----------------------|---------------|----------------------|---------------|------------------------------------------|------------------------------------------|-----------------------|
| 26/ BIRDEM Med J, 2018**1**            | 42 years/ Male/ Not known | T2DM HIV-negative | Fever Anorexia Weight loss Pigmentation | Hb = 12.4 gm/dl. WBC = 8300/cmm Platelets = 426 000/cmm ESR = 40 mm in first hour ALT = 91 IU/L AST = 82 IU/L ASTA = 62 IU/L | FNAC from the adrenal gland. ACTH stimulation test: no adrenal insufficiency. Disseminated histoplasmosis. | Amphotericin B (14 days). Itraconazole (planned for 18 months). | Improved up to last (six month) visit. |

**Note:** Unpublished cases were recruited from three teaching hospitals, BIRDEM General Hospital (cases 8, 21, 23 and 25), Bangabandhu Sheikh Mujib Medical University (cases 19 and 20), and Dhaka Medical College (Case 24), Dhaka, Bangladesh. Missing data: physical signs (cases 18 and 26) and value/important laboratory and imaging findings (cases 1, 13, 14 and 17).

The first histoplasmosis survey was done in Bangladesh in 1961 (then East Pakistan), which was carried out by the team of the Institute of Public Health, Dhaka, Bangladesh, as part of a study on opportunistic infections. The study included patients from three teaching hospitals, BIRDEM General Hospital, Bangabandhu Sheikh Mujib Medical University, and Dhaka Medical College. The study included 26 cases, of which 15 were HIV-negative and one had AIDS. The remaining cases were not tested for HIV.

**Table 1:** Cases of histoplasmosis in/or from Bangladesh (N = 26)

**DISCUSSION**

The histoplasmosis survey revealed that the disease is common in Bangladesh, particularly among patients with HIV-negative status. The study also highlighted the importance of early diagnosis and treatment, as indicated by the outcomes of the cases. The study was limited by the small sample size and the absence of systematic follow-up of patients. Further research is needed to better understand the epidemiology and clinical presentation of histoplasmosis in Bangladesh and to develop effective strategies for prevention and control.

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*Note: Unpublished cases were recruited from three teaching hospitals, BIRDEM General Hospital (cases 8, 21, 23 and 25), Bangabandhu Sheikh Mujib Medical University (cases 19 and 20), and Dhaka Medical College (Case 24), Dhaka, Bangladesh. Missing data: physical signs (cases 18 and 26) and value/important laboratory and imaging findings (cases 1, 13, 14 and 17).*

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Table 2: Selected sociodemographic, clinical, and laboratory characteristics of Bangladeshi patients with histoplasmosis (N = 26).

| Characteristics                          | Frequency | Percentage | Mean | Range |
|------------------------------------------|-----------|------------|------|-------|
| Age, years                               | -         | -          | 50.9 | 8–75  |
| Sex, male                                | 26        | 100        | -    | -     |
| Occupation, farmer                       | 9         | 34.6       | -    | -     |
| Habit, smoker                            | 5         | 19.2       | -    | -     |
| History of traveling outside Bangladesh  |            |            |      |       |
| No                                       | 21        | 80.8       | -    | -     |
| Yes                                      | 5         | 19.2       | -    | -     |
| Underlying condition                     |            |            |      |       |
| Diabetes mellitus                        | 7         | 26.9       | -    | -     |
| Kidney transplant recipient             | 1         | 3.8        | -    | -     |
| HIV/AIDS status                          |            |            |      |       |
| Positive                                 | 4         | 15.4       | -    | -     |
| Negative                                 | 15        | 57.7       | -    | -     |
| Not known                                | 7         | 26.9       | -    | -     |
| Clinical presentation                    |            |            |      |       |
| Fever                                    | 20        | 76.9       | -    | -     |
| Weight loss                              | 17        | 65.4       | -    | -     |
| Anorexia                                 | 14        | 53.8       | -    | -     |
| Cough                                    | 7         | 26.9       | -    | -     |
| Oral ulcer                               | 8         | 30.8       | -    | -     |
| Hyperpigmentation                        | 3         | 11.5       | -    | -     |
| Anemia                                   | 15        | 57.7       | -    | -     |
| Cervical lymphadenopathy                 | 5         | 19.2       | -    | -     |
| Generalized lymphadenopathy              | 4         | 15.4       | -    | -     |
| Skin rash/nodule                         | 4         | 15.4       | -    | -     |
| Hepatomegaly                             | 3         | 11.5       | -    | -     |
| Hepatosplenomegaly                       | 7         | 26.9       | -    | -     |
| Spleenomagly                             | 1         | 3.8        | -    | -     |
| Major organ involvement                  |            |            |      |       |
| Lung                                     | 6         | 23.1       | -    | -     |
| Liver/spleen                             | 9         | 34.6       | -    | -     |
| Adrenal glands                           | 11        | 42.3       | -    | -     |
| Skin                                     | 7         | 26.9       | -    | -     |
| Gastrointestinal tract                   | 8         | 30.8       | -    | -     |
| Bone marrow                              | 4         | 15.4       | -    | -     |
| Lymph nodes                              | 9         | 34.6       | -    | -     |
| Form of histoplasmosis                   |            |            |      |       |
| Disseminated histoplasmosis              | 22        | 84.6       | -    | -     |
| Localized oropharyngeal disease          | 4         | 15.4       | -    | -     |
| Treatment                                |            |            |      |       |
| Amphotericin B (initial)                 | 14        | 53.8       | -    | -     |
| Itraconazole (continuation/only)         | 17        | 65.5       | -    | -     |
| Anti-TB treatment, empiric              | 9         | 34.6       | -    | -     |
| Follow-up and outcome                    |            |            |      |       |
| Cured/improving up to the last follow-up | 14 (recurred in 2) | 53.8       | -    | -     |
| Death                                    | 6         | 23.1       | -    | -     |
| Recurred                                 | 2 (1 later expired) | 7.7       | -    | -     |
| Not known                                | 6         | 23.1       | -    | -     |

HIV: human immunodeficiency virus; AIDS: acquired immunodeficiency syndrome; TB: tuberculosis.
revealed that 12–23% of people had a positive skin reaction to histoplasmin.\textsuperscript{14} A second survey among patients attending different clinics revealed almost similar results in 1968–1969.\textsuperscript{15} We also found similar results reported among people living along the banks of the river Jamuna near Delhi, India, in a survey in 1960.\textsuperscript{16} In endemic areas, more than half of the population exhibit positive skin reaction to histoplasmin.\textsuperscript{1} The first histoplasmosis case in Bangladesh was reported in 1982\textsuperscript{17} and the second case in 2005.\textsuperscript{18} Cases are increasingly reported nowadays.\textsuperscript{17–31} All were males, reflecting that males are possibly more at risk of exposure to soil due to occupational or recreational activities. A male predominance of histoplasmosis cases was also reported from India\textsuperscript{6,7} and Brazil.\textsuperscript{37}

Common presenting features were fever, weight loss, oropharyngeal ulcer, lymphadenopathy, and hepatosplenomegaly. Bilateral adrenal enlargement was also common. Similar findings were reported among patients from Panama,\textsuperscript{3} Brazil,\textsuperscript{7} Australia,\textsuperscript{10} Europe,\textsuperscript{11} Africa,\textsuperscript{8} South-East Asia\textsuperscript{1}, and India\textsuperscript{6,7} irrespective of patients’ immune status. Disseminated forms were more common than the localized disease in the current study, even in immunocompetent patients. In immunocompetent patients, adrenal enlargements were more common as was seen in an Australian series\textsuperscript{10}, but less than two Indian series.\textsuperscript{6,7} Increased steroid concentration within the adrenal glands promotes the growth of \textit{H. capsulatum}.\textsuperscript{38}

Cytopenias, elevated hepatic enzymes, and LDH are established features of disseminated histoplasmosis in HIV infected patients.\textsuperscript{5,28} Among the three patients in whom LDH reports were available, two had raised LDH, and both had HIV/AIDS. Among the 26 cases reported here, only in the first case authors reported the possibility of histoplasmosis during diagnostic work-up. Among the seven unpublished cases (cases 8, 19–21, 23–25) reported here, in six (except case 8) adrenal histoplasmosis was a deferential diagnosis during diagnostic work-up (primary data; by personal communication); but few other cases reported here were diagnosed incidentally (cases 6, 7, 9, 11, 16, 17 and 26 by personal communication with the corresponding authors) when tissue samples were sent for histopathological examination or culture. A similar observation was reported in a South-East Asian series.\textsuperscript{5}

Treatment of reported histoplasmosis cases consisted mostly of amphotericin B followed by oral itraconazole. In localized oral cases, itraconazole can be curative. Regarding the outcome of histoplasmosis cases, six patients with disseminated disease died, and 14 patients improved with relapse in two cases. Treatment monitoring is important. Urine antigen can be used for treatment monitoring and possible disease recurrence.\textsuperscript{39,40} In Bangladesh, currently there is no facility for such a test.

As histoplasmosis is an uncommon diagnosis in Bangladesh, diagnostic work-up and management strategies varied widely among the cases reported. We do not have any definite working diagnostic algorithms for many diseases, including histoplasmosis, and diagnostic work-ups are performed on a case-by-case basis and also depend upon the availability of diagnostic facilities. The 2007 Update by the Infectious Diseases Society of America recommends initial amphotericin B treatment followed by itraconazole in moderately severe to severe progressive disseminated histoplasmosis cases and in less severe cases oral itraconazole.\textsuperscript{41} Patients with HIV may require life-long therapy depending upon CD4 counts and the status of anti-retroviral therapy.\textsuperscript{42} Physicians should adhere to standard protocols\textsuperscript{43} for managing histoplasmosis cases and as the cases are increasing in Bangladesh, especially in the last two decades [Table 1], it should be evaluated for possible “emerging disease” and also whether it should be considered a “notifiable” one.

Our literature search was confined to “PubMed,” “BanglaJOL,” and “Google” and we did not search through other databases. Treatment detail and outcome data were not available for all the cases reported.

**CONCLUSION**

Despite high skin sensitivity test results, only a small number of cases (mostly from 2010 and onwards) were reported over a three-decade period in Bangladesh. It may indicate that a good number of cases remain asymptomatic or minimally symptomatic. There may be cross-reactivity to some other fungus with histoplasmin. Under-reporting of cases and improper diagnosis, especially tuberculosis, is not impossible. Clinicians should be aware of the condition and histoplasmosis should be suspected in an appropriate clinical setting. A further survey may be done in farm areas and among persons working on poultry farms.
Disclosure
The authors declared no conflicts of interest. No funding was received for this study.

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