Histoplasmosis in Africa: A disease hiding in plain sight

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Africa

- Africa is the world's second largest and second most-populous continent.
- At about 30.3 million km including adjacent islands.
- it covers approx 6% of Earth's total surface area and 20% of its total land area.
- Largest city: Lagos, Nigeria
- Population: 1.216 billion (2016)
- GDP per capita: $1,820 (2017)

Wikipedia

HIV and Africa

- In 2016, 36.7 million people were estimated to be living with HIV.
- An estimated 25.5 million people in sub-Saharan Africa are living with HIV.
- Approx 30% are AHD
- 35 million people have been estimated to have died of AIDS related illnesses.
- In 1987, Histoplasmosis was classified as an AIDS defining disease.

UNAIDS Data 2017

Global and Multi-National Burden of Fungal Diseases - Estimate Precision

F Bongomin, S Gago, RO Oladele & DW Denning

J. Fungi 2017, 3(4), 57

Histoplasmosis and TB

- In 2016; an estimated 1.3 million TB deaths among HIV-negative people (down from 1.7 million in 2000) and an additional 374 000 deaths among HIV-positive people. (WHO, 2017. Global TB report)
- How many were smear negative TB?
- Histoplasmosis is commonly misdiagnosed as TB(Wheat LJ 2006 Mycoses)
- Africa has a significant number of people living with HIV/AIDS - greatest attributable risk factor for histoplasmosis.

Summary of major features associated with tuberculosis and disseminated histoplasmosis in context of HIV infection

Parameters	Tuberculosis	Histoplasmosis
Immune suppression	**	↑↑
Pancytopaenia	**	↑↑
Renal function	––	––
High liver function tests (AST, ALT, γGT, ALP, LDH)	**	↑↑
Hepatosplenomegaly (clinical and ultrasound)	**	↑↑
Inflammatory markers (CRP >70)	––	––
Ferritin and triglyceride	**	↑↑
Systemic involvement (GIT, bone marrow, liver and peripheral blood)	**	↑↑
Disseminated disease	**	↑↑
Respiratory system (clinical and laboratory)	↑↑	**
Central nervous system involvement (clinical and investigation)	––	––
Skin	**	↑↑

Indian J Chest Dis Allied Sci. 2000 Oct-Dec;42(4):271-7.

Histoplasmosis in Africa: a review.

Gugnani HC[1].

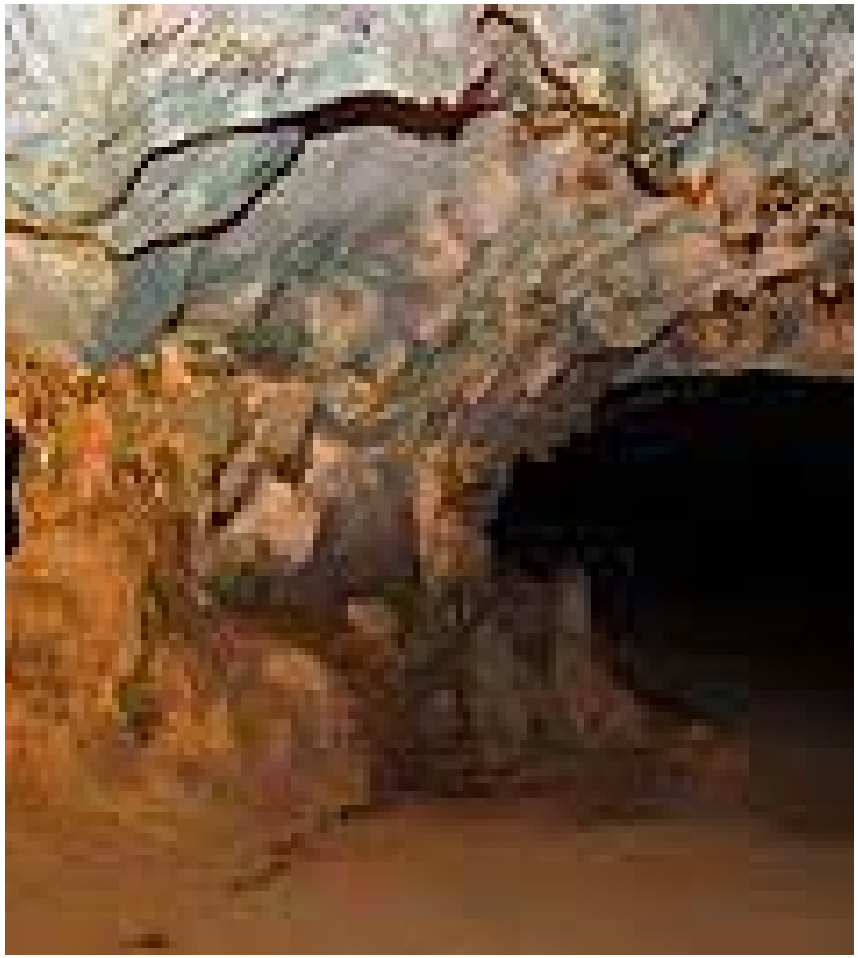
⊕ Author information

Abstract

Classical histoplasmosis caused by Histoplasma capsulatum var. capsulatum, and African histoplasmosis caused by H. capsulatum var duboisii are both endemic in Africa. In South Africa, only classical histoplasmosis caused by Histoplasma capsulatum var. capsulatum is known to occur and cases are seen frequently. It occurs sporadically in several other African countries. Histoplasma capsulatum var. capsulatum is known to occur naturally in caves inhabited by bats in some parts of South Africa, namely, Transvaal and Cape province, Zimbabwe and Tanzania. Outbreaks of histoplasmosis have been reported in cave explorers. Surveys of histoplasmin skin sensitivity

Outbreaks

- Three in South Africa (different regions
- Uganda
- Cave explorers



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Histoplasmosis in Africa: An emerging or a neglected disease?

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Joseph M. Vinetz, Editor

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Abstract

Go to:

Histoplasmosis in Africa has markedly increased since the advent of the HIV/AIDS epidemic but is under-recognised. Pulmonary histoplasmosis may be misdiagnosed as tuberculosis (TB). In the last six decades (1952–2017), 470 cases of histoplasmosis have been reported. HIV-infected patients accounted for 38% (178) of the cases. West Africa had the highest number of recorded cases with 179; the majority (162 cases) were caused by *Histoplasma capsulatum* var. *dubuosii* (Hcd). From the Southern African region, 150 cases have been reported, and the majority (119) were caused by *H. capsulatum* var. *capsulatum* (Hcc). There have been 12 histoplasmin skin test surveys with rates of 0% to 35% positivity. Most cases of Hcd presented as localised lesions in immunocompetent persons; however, it was disseminated in AIDS patients. Rapid diagnosis of histoplasmosis in Africa is only currently possible using microscopy; antigen testing and PCR are not available in most of Africa. Treatment requires amphotericin B and itraconazole, both of which are not licensed or available in several parts of Africa.

Histoplasmosis in Africa

- 470 cases in six decades (up from 250cases reported by Gugnani *et al* 2000)
- Both Hcd (247) and Hcc (185) reported
- Most diagnosis – culture & histology
- Only 4 countries used serology (3 processed in Western countries)
- No PCR (Histoplasmosis) in Africa
- HIV-infected patients accounted for 38% (178) cases

Oladele et al 2018 PLOS NTD

Histoplasmosis in Africa

- Histoplasmin skin sensitivity rates of 0 -35%
- Recent multicentre screening in Nigeria – 4.4% (Oladele et al 2018 PLOS)
  - Benin city highest rates despite no reported cases
- 20 countries in Africa – no data
- Challenges:
  - Lack of awareness amongst clinicians
  - Lack of skilled personnel
  - Diagnostic facilities

Oladele et al 2018, PLOS NTD

Distribution of reported cases of Histoplasmosis in Africa (1952 – 2017)

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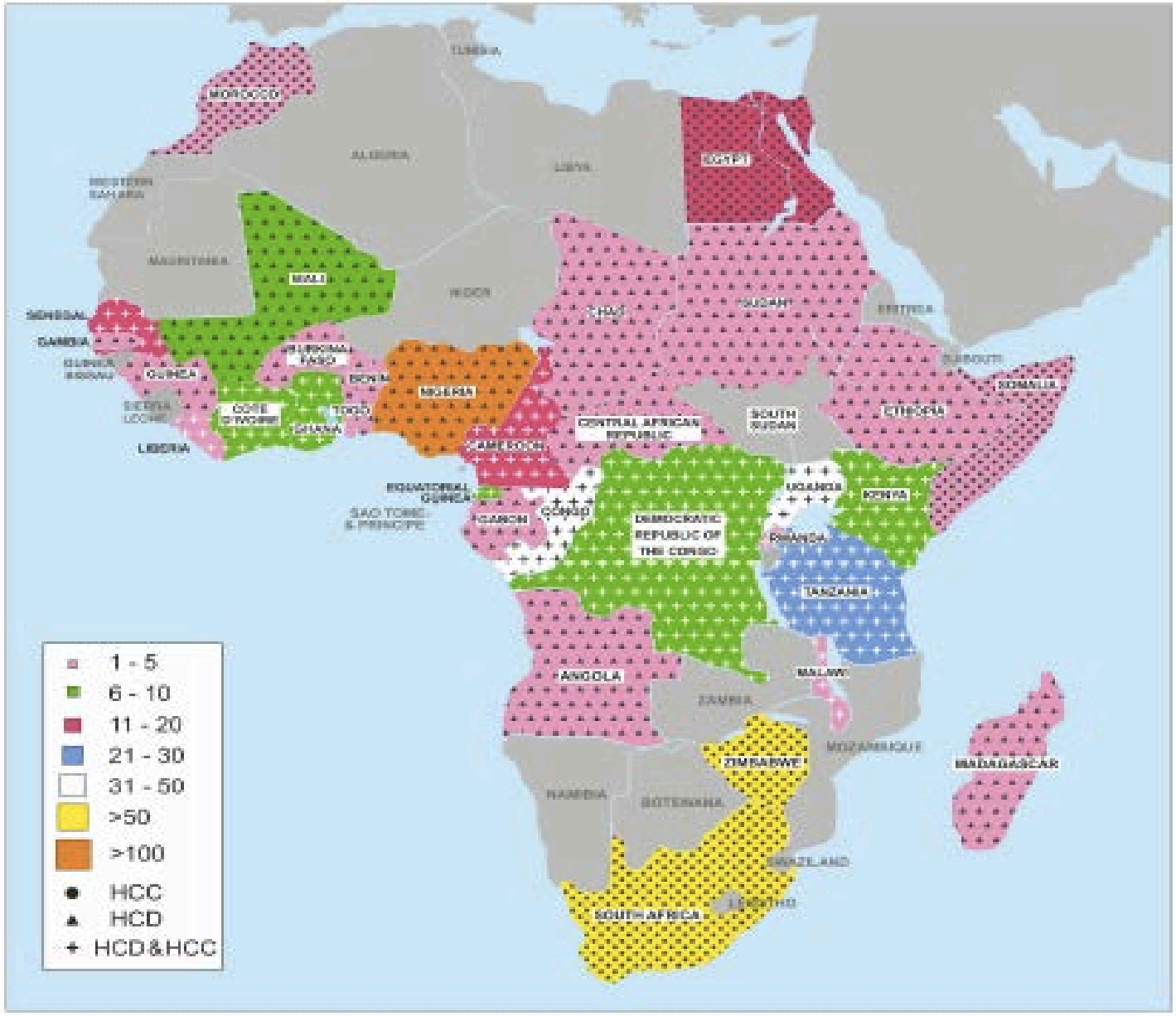

Fig 1. Distribution of reported cases of histoplasmosis in Africa (1952–2017). HCC, *Histoplasma capsulatum* var. *capsulatum*; HCD, *H. capsulatum* var. *duboisii*.

Neglected or an emerging disease?

- Histoplasmosis is a neglected disease in Africa.
  - because histoplasmosis in Africa has increased markedly , but is under-recognised.
  - Histoplasmosis may be misdiagnosed as tuberculosis.

- Africa has a significant number of people living with HIV/AIDS. – **need a high index of suspicion**
- The ongoing health agenda for Africa has to acknowledge the lack of skilled personnel and facilities to make the diagnosis of histoplasmosis in Africa.
- There is limited accessibility and availability of antifungal agents on the African continent.

Situation now: hiding in plain sight

On-going survey in Nigeria

- 30% AHD
- No report of histoplasmosis amongst PLHIV in Nigeria since advent of HIV epidemic
- Multicenter study – 10 sites
- AHD population
- Urinary antigen test
- Sample per patient with one week interval
- 705 samples ran so far, 47 positives -6.7%
- PCR to confirm cases – more or less

SN	SITE	No of participants	No positive
1	MARKURDI (NORTH CENTRAL)	121	9
2	SOKOTO (NORTH WEST)	100	6
3	CALABAR (SOUTH – SOUTH)	59	6
4	BIDA (NORTH CENTRAL)	105	5
5	JOS (NORTH CENTRAL)	111	3
6	LAGOS (SOUTH WEST)	52	1
7	BENIN (MID WEST)	27	0
8	IBADAN (SOUTH WEST)	50	9
9	PORT HARCOURT (SOUTH – SOUTH)	58	7
10	ENUGU (SOUTH EAST)	23	0

Another just concluded study in Calabar, Nigeria

- Presumptive TB population
- 213 patients
- TB-94; HIV -75; co-infection HIV/TB-, 34; and previously treated TB patients -13
- Urinary antigen and sputum PCR
- Urinary antigen -23(10.7%)
- 18(8.45%) – sputum PCR positive
- 2(11.11%)- HIV and TB co-infection, 11(61.11%) were negative for both TB and HIV, 5 (27.78%) were infected by TB, 4(22.22%) were infected by HIV, 2(11.11%) were previously treated for TB, none were MDR TB patients

Ekeng Bassey 2020

What next?

- Epidemiological studies are needed to help determine true burden of the problem in Africa.
- It will be interesting to know if all reported cases from Africa are really *Histoplasma spp*. ?
- ➢ other species among these cases;??*Emergomyces spp.*
- Training and retraining of clinicians managing the at risk population
- Histoplasma antigen detection tests needed especially for AHD population in Africa

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