ESTIMATION OF THE BURDEN OF SERIOUS MYCOSES IN INDONESIA

Retno Wahyuningsih

1Department of Parasitology, Universitas Indonesia, Faculty of Medicine, Jakarta,
2Department of Parasitology, Universitas Kristen Indonesia, School of Medicine, Jakarta,
Indonesia

- Tropical islands
- Rich biodiversity
- Pathogenic fungi
INDONESIA: A LARGE COUNTRY WITH ±17,000 ISLANDS

Medical mycology facilities limited in big cities
Source of data

- Estimation of Indonesia fungal burden based on laboratory data, manuscripts, publications and the health profile 2013 (government)
- High number of AIDS patients: 52348, so that opportunistic infection in this group must be considered
- High number of TB cases
1. Candidiasis
Invasive Candidiasis

- Prevalence of candidemia
  - in neonates 63%,
  - in adult 12.33%
  - in leukemia children with fever 8%

- Candidemia prevalence in adults, children & neonates during 5 years: 12% (data Dept. Parasitology – FKUI)

- Estimation of the candidemia prevalence in Indonesia
  - in general 8 -12.3%,
  - in neonates 63% specifically

- Causes: *C. tropicalis, C. albicans & C. parapsilosis*

- Concl.: the rate is 8 – 63×10^{-4}/100 000 population

Wahyuningsih et al Maj Kedok Indon 2008; Rusli, thesis 2013; Kalista, thesis 2015,
Candidosis – HIV infection

- Prevalence of oral candidiasis among HIV infected patient in Cipto Mangunkusumo hospital
  - 50% in 2004
  - 57% in 2014
- The main cause is *C. albicans*, followed by
  - *C. tropicalis*
  - *C. glabrata*
  - *C. parapsilosis*
  - *C. nivariensis*
  - *C. ethanolica*
- Concl.: $50 - 47 \times 10^{-4}/100,000$

Wulandari et al. manuscript, Wahyuningsih et al. JCM 2008
2. Cryptococcosis

India ink – spinal fluid
Cryptococcosis – HIV infection

- Based on culture and microscopy of spinal fluid
- Prevalence among AIDS patients (2003-2014):
  - Jakarta 16-26.8%
  - Bandung 29.8%
- Based on cryptococcal serum antigen (CrAg) among ambulatory patient
  - Jakarta 6.4%
  - Bandung 7.1%
- The highest prevalence in HIV infected patients with cerebral involvement
  - ranges between 16-30 ×10⁻⁴/100 000 population
Cryptococcal meningitis among HIV infected patients in Jakarta, Indonesia

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Cryptococcus meningitis

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Cryptococcosis–non HIV

- Cryptococcosis was also detected in non HIV infected patient in Jakarta & Sumatera
  - Patient with CD4 lymphocytopenia
  - Lung tumors in a diabetic patient
  - Skin infection in Hodgkin lymphoma
  - Meningitis in malnourished child
  - Pericarditis in a child
  - Adult with meningitis (2 patients)
  - A male with bronchial problem
Cryptococcosis (AIDS): origin of cases

Places where cryptococcosis were diagnosed; underestimate
Cryptococcus: the species-var

- The most prevalent is *C. neoformans* var *grubii*
- Maldi-TOF analysis of isolates derived from HIV & non-HIV patients reveals:
  - *C. neoformans* var *grubii*: 265 isolates
  - *C. neoformans* var *neoformans*: 6 isolates
  - *C. neoformans*: 3 isolates
  - *C. neoformans* intervariety hybrid (AFLP3): 16 isolates
  - *C. neoformans* var *grubii* x *C. gattii* (AFLP 9): 1 isolate

3. Aspergillosis

Aspergillus head – KOH wet slide
The prevalence of invasive pulmonary aspergillosis in critically ill patients Jakarta is 7.65% and mostly caused by *A. flavus*; ca. $8 \times 10^{-4}$/100 000 population.

In the world, Indonesia is rank 4 for TB.

Regarding TB, WHO estimates in Indonesia (2013):
- the 1-year-post-treatment survivors: 1, 297 047
- those develop chronic pulmonary aspergillosis: 26,935
- Estimation based on statistical analysis, but in real?

Rozaliyani et al, manuscript; WHO report on TB- Indonesia 2013
Post TB patient with chronic cavitary pulmonary aspergillosis

Wahyuningsih et al., Advance Asp. Istanbul 2012
Aspergillus susceptibility

Resistant *A. fumigatus*

- SLE with retro-bulbair mass
- Aspergilloma
- Pulmonary mass

Susceptibility study

Wahyuningsih et al., Advance Asp, Madrid 2014
4. Pneumocytosis
Pneumocystosis

- *Pneumocystis jirovecii* prevalence among 55 AIDS patients with pneumonia (PJP): 14.5%.
- co infection with TB
- Five-year prevalence data on the examination of induced sputum and broncho-alveolar lavage: 28% (HIV infected patient, COPD & ICU patients with lung disease)
- Prevention of PCP among HIV infected patients starts immediately after diagnosis makes determining prevalence of PCP difficult.

Rozaliyani et al., thesis; data Dept. Parasitology FKUI
5. Histoplasmosis

Result of touch biopsy:
Cutaneous histoplasmosis
Histoplasmosis

- Mostly male
- Before the arrival of AIDS pandemic, histoplasmosis was diagnosed in children and adult
- The increasing number of AIDS in Indonesia resulted in an increase in the number of histoplasmosis cases
- Cutaneous and disseminated forms of histoplasmosis have been diagnosed in AIDS (last 10 years) and disseminated form in non HIV (since 1932)
Histoplasmosis

- 1953-55: histoplasmin skin test on 2542 people; positive in
  - 2.7% in student of elementary school
  - 9-12% in adult (mostly male)
  - Radiology on 2311 people: 1.5% have pulmonary calcification (mostly male)
    - Adult 1.5% with calcification
    - Mostly in patients with tuberculin positive have histoplasmin positive

- Suggesting Indonesia as endemic area

Delima I. Medika 1988
Histoplasmosis: clinical spectra

- Hematology malignancy (bone marrow examination)
- Chronic lung disease
- Tuberculosis
- Carcinoma of the palate
- Ulcer
- Hepatitis
- Fever of unknown origin
- Skin infection (dissemination of systemic infection)
Cases of histoplasmosis

Java: Jakarta, Tanggerang, Bandung, Sukabumi, Jatibarang, Surabaya,
Sumatera: Riau
Celebes: Manado
6. Penicilliosis

Culture of *P. marneffei*
Penicilliosis

- Very limited data
- Diagnosed in
  - 2 HIV infected patients
  - A male with bronchomalacia using bronchial prosthesis
  - Sinusitis
  - 2 patients with lung disorders

- From one HIV infected patient, *P. marneffei* was isolated from the lung & liver of a (house) rat caught in his house. Source of infection in Jakarta?
Almost all serious mycoses is found in Indonesia. These data does not describe the actual condition (underestimate). To address (2), it is necessary to spread diagnostic capabilities throughout the country. Getting insight into Indonesia’s fungal burden will help policy makers and clinicians making decisions in the absence of data.
# Collaborators

**Indonesia**
- J. Prihartono
- R. Adawiyah:
- R. Syam
- A. Rozaliyani
- Mulyati
- E. A. T. Wulandari
- D. Imran
- F. E. Siagian

**England, The Netherlands**
- D. Denning
- T. Boekhout
- J. F. MG. Meis
Thank you