

REVIEW ARTICLE

The role of medical mycology societies in combating invasive fungal infections in low- and middle-income countries: A Nigerian model

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Summary

The discipline of medical mycology has become increasingly relevant in the face of the rising incidence of invasive fungal infections (IFI), which pose diagnostic and therapeutic challenges for contemporary medical practice. While firmly established in developed countries, medical mycology remains obscure in many low- and middle-income countries (LMICs). With a teeming vulnerable populace and an incidence rate of 11.8%, Nigeria has one of the highest estimated burdens of invasive fungal infections (IFIs) in the world. Regardless, the scourge of IFIs has remained silent due to a combination of factors principal amongst which are a lack of awareness and dearth in personnel skilled in diagnosis. The present narrative examines the status of medical mycology practice in Nigeria and chronicles the journey to change the status quo spurred by the Leading International Fungal Education (LIFE)-facilitated burden estimate paper and culminating in the birth of the Medical Mycology Society of Nigeria (MMSN), the pioneer national medical mycology society in Africa. The prospects of tackling the IFI challenge are highlighted from the perspective of the nascent society.

KEYWORDS

diagnostics, invasive fungal infections, low- and medium-income countries, medical education, medical societies, Nigeria

1 | INTRODUCTION

In the last few decades, the incidence of invasive fungal infections (IFI) has risen due to an increase in the populations at risk.^{1,2} According to recent global estimates, more than 15 million cases of fungal infections occur annually.³ More than 1.6 million people die of fungal diseases each year: 500 000 of these are AIDS-related and a further 450 000 are due to chronic pulmonary aspergillosis.^{4,5} These figures are likely an underestimation because autopsy rates have declined universally and successful ante-mortem diagnosis of IFIs does not exceed 50% even with the best diagnostic tools.^{6,7} Moreover, most countries lack a surveillance system for fungal infections.² In the few countries where active surveillance networks exist, reporting is voluntary and only for specific conditions, notably candidaemia.⁸

In Nigeria, as in many other low- and middle-income countries (LMIC), IFIs receive little or no public health attention despite possessing a mortality rate comparable to that of tuberculosis and greater than threefold that attributable to malaria.³ There is no government resource allocation for surveillance, diagnostic facilities, outbreak response, epidemiological study and control of IFIs. Yet established risk factors for invasive fungal infections (IFIs) abound in Nigeria: an HIV epidemic thought to be the second largest globally; a ranking of sixth amongst nations with the highest burdens of tuberculosis; a rising number of tertiary hospitals with intensive care units; increasing incidence of malignancies and the introduction of solid organ and stem cell transplant facilities in the country.^{9,10} Furthermore, Nigeria possesses the unique geopolitical and socio-economic character that makes LMICs hotspots for IFIs: location in the tropics where fungal pathogens thrive; over-the-counter abuse of antibiotics and steroids; unprotected construction activities in hospitals; economic deprivation and malnutrition.¹¹ Nigeria, with an estimated population size of 172 million and an estimated gross domestic product of \$2178 per capita in 2016, is the largest economy in Africa but a recent report by the World Poverty Clock ranked Nigeria first amongst countries with the largest number of people living in extreme poverty.¹²

Against this backdrop, a burden estimate of IFIs was conducted and published in 2014 yielded results which were shocking yet not illogical: Nigeria has one of the highest estimated incidences of IFIs the world over. Recent findings have demonstrated that some of these figures, specifically cryptococcal meningitis and CPA, were underestimated.^{13,14}

An indirect but important dividend of this burden estimate assessment has been the birth of the Medical Mycology Society of Nigeria (MMSN), a society borne out of need for training, research and advocacy. In this report, we chronicle the landscape of medical mycology practice in Nigeria over the years with the Leading International Fungal Education (LIFE)-facilitated estimation of disease burden as a landmark inflection point and conclude with a discourse on the plans of MMSN to bring about a renaissance in medical mycology practice in Nigeria.

2 | HISTORICAL BACKGROUND OF MEDICAL MYCOLOGY IN NIGERIA PRIOR TO THE BURDEN ESTIMATE

H.C Gugnani is the principal documented source for the history of twentieth-century medical mycology practice in Nigeria.^{15,16} The discipline began in University College Hospital, Ibadan, in the late 1950s, under the supervision of Dr B.M Clark.¹⁵ The centre was selected in March, 1967, as the venue for the international Ciba symposium on systemic mycoses, a testament to the quality of work that went on there.¹⁷ Dr Clark contributed to the literature on rhinotomophthoromycosis, histoplasmosis and other deep mycoses.¹⁷ Her departure in 1976 caused services to dwindle. However, the University of Nigeria, Nsukka, and University of Nigeria Teaching Hospital, Enugu, both established in 1973 quickly filled the void, and the bulk of medical mycology services was hitherto domiciled in the laboratories within these facilities.¹⁵ Although the range of services was limited to conventional microscopy and culture with no provisions for antifungal susceptibility testing and non-culture based diagnostics, the laboratory personnel were able to apply creative strategies to their low budget practice. For instance, rice flour was substituted for corn meal agar.¹⁵ Research publications during this period revolved largely around *Candida*, dermatophytes, subcutaneous mycoses and case reports of African histoplasmosis.¹⁶

There have been no attempts at formally assessing or describing medical mycology services in the 21st century, but there has been little improvement in the ensuing years. Instead, the brain drain brought about by migration of skilled healthcare professionals to Western countries and the Middle East in the 1990s resulted in a decline in diagnostic capability, the situation made more dire by the tremendous growth in population and increase in risk for serious fungal diseases that occurred over time.¹⁸ Surprisingly, the advent of HIV/AIDS, which sparked global interest in invasive mycoses, failed to catalyse medical mycology practice and research in Nigeria. The APIN-PEPFAR partnered with Harvard University to train laboratory personnel for the AIDS control programme but failed to provide a single mycology bench in any of the centres, despite fungi accounting for a significant proportion of opportunistic infections in the HIV/AIDS population. The scant epidemiological data on HIV/AIDS-related mycoses such as cryptococcal meningitis and *Pneumocystis pneumonia* bear witness to this claim.

3 | BURDEN ESTIMATE OF IFIS IN NIGERIA

The value of research often resides in its ability to bring about societal change. One such research endeavour can be said to have sparked a series of changes with the potential to alter the bleak picture painted in the preceding paragraph and is therefore cited

as a landmark inflection point for medical mycology practice in Nigeria.

In 2014, Oladele and Denning estimated that a serious fungal infection afflicts over 11.8% of Nigerians each year.¹⁹ Besides Senegal and Portugal with estimates of 12.5% and 16%, this is the highest incidence reported in the literature.^{20,21} Seventy-five thousand patients with AIDS are expected to develop *Pneumocystis pneumonia* (40% rate in children) annually.¹⁹ In a recent global estimate of AIDS-related cryptococcal meningitis, Nigeria alongside South Africa is estimated to have an annual incidence of 25 000 cases of cryptococcal meningitis.¹³

Burden estimates in the presence of diagnostic limitations and in the absence of surveillance systems are bound to be significantly inaccurate.⁸ For instance, a later study on CPA (Oladele et al¹⁴) demonstrated an incidence of 44 930 cases, substantially greater than the estimate of 19 000 predicted by Oladele and Denning. Burden estimates thus require validation by local epidemiological studies. This statement that concluded the burden assessment effort served a dual purpose: it was a caveat as well as a challenge to the medical community.

Poor awareness drives the under-recognition of IFIs in developing countries.¹⁶ As a corollary to the burden estimate assessment, therefore, Oladele et al evaluated the knowledge and awareness of IFIs amongst trainee doctors.²² They discovered that a number of these doctors had poor knowledge and awareness of IFIs. This knowledge gap could be traced to deficiencies in medical mycology training in both undergraduate and postgraduate medical curricula.^{16,23} Dearth of epidemiological data also contributed substantially to this lack of awareness. To control the scourge of IFIs, it became clear that this cognitive hurdle would have to be surmounted.

4 | THE INVASIVE FUNGAL INFECTION FORUM AND ESTABLISHMENT OF MEDICAL MYCOLOGY SOCIETY OF NIGERIA

In 2014, the invasive fungal infection forum (IFIF) was set up with the aim of bridging the knowledge gap and driving the awareness of IFIs

in Nigeria. Annually, the forum organised training events targeted at specialist doctors who routinely manage patients at risk of serious fungal infections. The Global Action Fund for Fungal Infections (GAFFI) partnered with IFIF to facilitate these trainings online with logistic support provided by PFIZER pharmaceuticals.

In 2017, GAFFI partnered with IFIF to organise a 3-day training course onsite with hands-on laboratory and radiological training sessions. The course was attended by 35 specialist doctors (including clinicians, radiologists and laboratory physicians), five laboratory scientists, eight postgraduate students and other professionals from across Nigeria. Professor Malcolm Richardson and Prof David Denning were amongst the faculty and handled all practical sessions themselves. At the conclusion of the event, the Medical Mycology Society of Nigeria (MMSN) was inaugurated under the supervision of the then president of the International Society for Human and Animal Mycology (ISHAM), Prof Malcolm Richardson.

The formation of professional societies has, in the past, facilitated the establishment of medical mycology as a specialty in developed countries.²⁴ Likewise, we believe the collective professional effort spearheaded by a national medical mycology society will create a strong presence for the discipline in the healthcare system and ultimately stem the morbidity and mortality associated with IFIs in Nigeria.

MMSN is a non-governmental, interdisciplinary body comprising health professionals with interest in various aspects of human fungal pathogens. The foundational aims of the society include research and dissemination of research findings, hands-on training, advocacy and health policy development in Nigeria. The overarching mission is to improve awareness of IFIs and to advocate for the mainstreaming of diagnostics and drugs necessary for the management of these infections in the Nigerian healthcare system. Since inception, four study groups have been commissioned (Table 1) and the fifth IFI Forum has been organised under the aegis of the society. MMSN has also succeeded in providing free training on cryptococcal meningitis for healthcare providers in 10 institutions across Nigeria, an initiative funded by the United States Centre for Disease Control foundation, Atlanta.

TABLE 1 Study Groups of MMSN and activities

MMSN Study Group	Activities
Histoplasmosis Study Group	Completed a multicentre histoplasmin skin sensitivity survey Survey found a skin sensitivity rate of 4.4% in 750 participants across the country. Rates varied with location ranging from 0 to 15% Findings presented at 8th Trends in Medical Mycology (TIMM) 2017; published in a peer-reviewed journal ²⁵
<i>Aspergillus</i> Study Group	Ongoing multicentre study to standardise <i>Aspergillus</i> IgG levels and determine cut-off values for Nigerians.
<i>Cryptococcus</i> Study Group	Ongoing multicentre study for cryptococcal antigenaemia screening and cost-effectiveness of screening and pre-emptive therapy
Paediatric <i>Pneumocystis Pneumonia</i> Study Group	Designed a protocol and presently sourcing funding

National medical mycology societies are certainly not lacking in LMICs: the Aspergillus & Aspergillosis Website indicates the existence of at least 15 such organisations.²⁶ The MMSN was, however, the first in Africa. Although a Pan African Medical Mycology Society (PAMMS) was inaugurated in 2005, holding three conferences with the support of ECMM and ISHAM (the third biennial conference was held in Abuja, the capital of Nigeria, in 2009), activities have not been sustained beyond 2011 and the impact on medical mycology in Nigeria vis-a-vis IFIs and patient management has not been felt. This may have resulted from the effort being dissipated across too wide a region and the number of persons with interest in the subject not reaching a critical mass. In the same vein, there exists a Mycological Society of Nigeria (MYCOSON) which caters to all branches of mycology. Again, this only scratches the surface of the thriving problem of IFIs in Nigeria due to a scope that is too broad. This is evident in the themes from the annual conferences held so far which consistently focus on fungi in relation to the economy, agriculture and biotechnology. We believe the focus of the MMSN, first on medical mycology and secondly on Nigeria, make it doubly suited over these older professional bodies to impact health needs of the nation as it relates to IFIs.

4.1 | Prospects

A vibrant community with consistent activities and focused goals is necessary if the MMSN is to bring about the much needed renaissance in medical mycology practice in Nigeria.

4.2 | Community

The MMSN will continue to work to build up its membership to include clinical microbiologists and PhD diagnostic scientists, infectious disease physicians, respiratory disease physicians, radiologists, surgeons, pathologists, pharmacists and also other medical specialties including dermatologists, paediatricians, intensivists, oncologists and public health physicians. This is because IFIs are best researched and managed by multidisciplinary teams which integrate diagnostic and therapeutic decision making in a timely manner.²⁷

Local interactions will be achieved by regular scientific conferences and meetings: The society will also serve as a platform to build and maintain affiliations with international bodies like ISHAM and the European Confederation of Medical Mycology (ECMM) as well as other local professional societies. These local and international interactions are necessary for the sustainability of medical mycology as a discipline.²⁸

4.3 | Activities

The activities undertaken by MMSN such as educational meetings, hands-on trainings, research, gap analysis surveys and development of guidelines will serve as tools to improve medical mycology practice in Nigeria and impact on outcome in management of the patient population at risk of these life-threatening IFIs.

Epidemiological studies to map disease distribution represent one of the first tasks of national medical mycology societies and are already a core mission of MMSN. Emphasis will be placed on nationally relevant IFIs as exemplified by the study groups of MMSN (Table 1). Data derived from these studies can facilitate the development of evidence-based diagnostic and therapeutic guidelines that are country-specific. They will also be needed to advocate for greater attention from government and support from multilateral agencies. Furthermore, dissemination in peer-reviewed journals will help drive awareness and clinical index of suspicion about IFIs amongst clinicians in Nigeria.

MMSN originated from focused educational programmes to address the knowledge gaps amongst practicing physicians and these will continue to be organised annually. Hands-on training to build laboratory diagnostic capacity will continue. The society plans to take up the responsibility of identifying and securing opportunities for training in established institutions and facilities such as the National Institute for Communicable Diseases in South Africa. Funding will be provided for training scholarships for short periods to learn and take home-specific laboratory skills. This will require intense fund raising efforts by the MMSN. Essential skills to develop include appropriate use of laboratory information management systems (LIMS), workflow practices, monitoring of quality indicators such as turnaround time, external quality assurance, resistance surveillance, updates on new technologies and forward planning.

The MMSN will engage in gap analysis surveys which are particularly useful for systematic documentation of the deficiencies in mycological diagnostic services, clinical management and medical education. Based on these analyses, recommendations can be made to relevant stakeholders to advocate for change.

Diagnostic algorithms and management guidelines designed in developed countries often do not consider the unique challenges in LMICs. MMSN will come up with suitable alternatives that are country-specific and supported by local evidence to guide patient management. This will require the participation of medical representatives from the Ministry of Health and other relevant national professional bodies to ensure "buy in" and adoption across the country. MMSN can contribute these unique evidence-based perspectives to global guidelines with worldwide applicability such as the ECMM-led initiative which aims at stratifying guidelines for high- and low-resource countries.²⁹

4.4 | Goals

While improved awareness and capacity building are essential goals (Figure 1), the greatest dividends can perhaps be achieved with successful efforts at advocacy. MMSN intends to target advocacy efforts at the administrators of academic institutions, specialist physicians and most importantly the government.

With the results of gap analyses surveys in undergraduate and postgraduate training, recommendations will be made to administrators of universities and postgraduate training colleges to better emphasise mycology training in their respective curricula. This is a



FIGURE 1 Essential components and key requirements

long-term goal. Likewise, surveys of local practices can inform the development of unified clinical management guidelines. Activism will be required to encourage specialists to adopt these guidelines. We will also advocate that there is need for standardisation of medical mycology curriculum and training which should be driven internationally by ISHAM and ECMM.

Members of the MMSN are professionals from different specialties currently drawn from various parts of the country. Each is expected to function as an advocate for medical mycology at their various hospitals and institutions of practice. This will lower the threshold for suspicion of fungal infections amongst specialist physicians. For example, a mycoses research group has been formed and is currently headed by a member of MMSN in the University College Hospital Ibadan.

Political will is crucial to tackling the menace of IFIs in any country. Recognition of the need to establish a mycology section at the National Institute of Health (NIH) by the federal government of the United States was fundamental to the development of medical mycology in that country.³⁰ Similarly, in Britain, funds provided by the Medical Research Council in 1943 were instrumental to the firm establishment of the specialty.²⁴ Thus, a prime goal of MMSN is to organise advocacy visits to the Federal Ministry of Health to impress upon government health officials the importance of IFIs. Such advocacy efforts need to be backed up by evidence (epidemiological surveys and gap analysis surveys of mycological services) because resources are scarce. Position papers clearly stating the areas requiring government input will be provided and recommendations will prioritise judicious use of scarce funds. To cut costs, for instance, the agenda for IFIs can be integrated into already existing national public health programmes for HIV, tuberculosis, diabetes and blindness as proposed by Cole et al.⁴ Specifically, MMSN will advocate for:

- The establishment of a reference mycology laboratory in at least three regions in Nigeria to serve both diagnostic and capacity-building needs. Extant facilities can be equipped to serve as

reference centres. For instance, in Nigeria, a mycology reference section can be created in the microbiology department of the Nigerian Institute for Medical Research (NIMR) that currently has provisions for human virology, tuberculosis research and parasitology but no facility for the diagnosis of fungal diseases. MMSN will also advocate for the government to partner with international bodies to facilitate the establishment and running of these reference laboratories, a model of which is the mycology reference laboratory in Chandigarh, India, which serves as a WHO collaborating centre.

- Training programmes for personnel to oversee diagnostic laboratories.
- Adoption of the essential fungal diagnostics for advanced AIDS and fungal diseases proposed by the GAFFI-led expert panel in a recent consensus meeting in Kampala, Uganda. These tests include cryptococcal antigen, *Histoplasma* antigen, *Pneumocystis* PCR, *Aspergillus* antibody and therapeutic antifungal drug monitoring.³¹
- Procurement and distribution of low-cost, high-quality antifungal medicines on the WHO Model Lists of Essential Medicines
- Accessing of funds for mycology research

5 | CONCLUSION

Poor awareness, lack of skilled personnel and dearth of diagnostic facilities are principal contributors to the scourge of IFIs in Nigeria. This report has provided an account of the inauguration of the first national society dedicated to medical mycology practice in Africa, the achievements so far and the plans to bring about a renaissance of medical mycology in Nigeria.

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