Evaluating the use of pathology in improving diagnosis in rural Malawi

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Introduction
Limited data exists on histologically confirmed cancers and tuberculosis in rural Malawi, despite the high burden of both conditions. One of the main reasons for the limited data is the lack of access to pathology services for diagnosis. We reviewed histopathology results of patients in Neno District, one of the poorest rural districts in Malawi, from May 2011 to July 2017, with an emphasis on malignancies and tuberculosis.

Methods
This is a retrospective descriptive study reviewing pathology results of samples collected at Neno health facilities and processed at Kamiza Pathology Laboratory. Data was entered into Microsoft Excel and cleaned and analysed using Stata 14.

Results
A total of 532 specimens were collected, of which 87% (465) were tissue biopsies (incision or core biopsies), and 13% (77) were cytology samples. Of the diagnostic results, 7% (40) were non-diagnostic results. Among the results that were diagnostic (n=492), 37% (183) were malignancies, 33% (122) were inflammatory and infectious conditions other than tuberculosis, 20% (97) were benign tumours, 7% (34) were tuberculosis, 4% (21) were pre-malignant lesions, 4% (21) were normal samples, and 4% (22) were cytology samples. A total of 87% (n=465) were histology samples and 13% (n=67) were cytology samples.

Conclusion
Histopathology services at a rural hospital in Malawi provides useful diagnostic information on malignancies, tuberculosis and other diagnoses, and can inform management at the district level.

Key words: malignancies, Tuberculosis, Malawi, Neno, pathology

Introduction
Pathological confirmation of some of the major chronic communicable and chronic non-communicable diseases (NCDs) is essential in low and middle-income countries to facilitate early diagnosis and treatment of these conditions. The accessibility and availability of pathology in Malawi should be prioritised, particularly as Malawi begins to face a double burden of communicable and chronic NCDs. This study evaluates pathology services in Malawi and examines patient and laboratory turnaround times for suspected extra-pulmonary TB and/or malignancies in this rural district. Therefore, we describe here the results obtained from pathology examination of specimens obtained in Neno District, Malawi, from May 2011 to July 2017, with an emphasis on malignancies and TB. Specifically, we aim to contribute to the knowledge gap regarding the significant burden of malignancies and extra pulmonary TB in Malawi. We present data from a rural setting which may be one of the first districts in Malawi to have extensive pathology resources. We explore the sample turnaround time, diagnostic yield, sample types, and results obtained from all the pathologies during this period.

Methods
This is a retrospective descriptive study conducted in the rural district of Neno, in the southwest zone of Malawi. With an estimated population of 165,000 in 2017, Neno has two hospitals and 12 primary health facilities. Most of the malignancies and TB in this study were collected at two hospitals, given that the hospitals had qualified staff, materials, and resources to routinely collect and send samples for pathological examination. The two hospitals are public and therefore free for all at the point of care.

Sample collection
Since 2011, the district has routinely collected and sent samples to Kamiza Pathology Laboratory for pathological examination. Kamiza Pathology Laboratory is a Blantyre-based private laboratory located at least two hours—just over 100 kilometres—away from Neno District. The type and sources of samples were recorded on a standardized laboratory form at the hospital level. Upon collection of the samples, 7% (n=34) were sent to Kamiza Pathology Laboratory depending on the next available transport. Currently, single specimens cost 17,820 Malawian Kwacha (MWK) (equivalent to 24 USD in October 2017) and 11,000 MWK (equivalent to 15 USD in October 2017) for histology and cytology examination, respectively. At the laboratory, samples were accessioned with a unique histology or cytology number. The histology samples were processed, paraffin embedded, and Haematoxylin and Eosin (H&E) stained. The cytology samples were also fixed in formalin, air dried and stained with Pap or Diff Quick stain, at appropriate. The slides were read, and reports generated. After pathological processing of the samples and interpretation of the slides, all results were sent to Neno as soft copies through email to facilitate quick decision making. Hard copies were then collected by the Neno staff weekly.

Data management, outcomes, and analysis
All results from May 2011 to July 2017 were retrieved from pathology laboratory forms and entered into a Microsoft Excel database, with demographic characteristics of the patients, sample turnaround time, site and specimen types, and final diagnosis of the pathology examination. As there can be variations in the definition of turnaround time, we defined turnaround time as the time the sample was collected in Neno to the time the result was reported back from the laboratory. This turnaround time combined times from sample collection by the health workers, temporary storage at Neno laboratory, transportation to Kamiza pathology, laboratory examination, and the time to results being reported back by the laboratory. We categorized sample types at either histology or cytology. Histology samples included open and core needle biopsies. Cytology samples included fine needle aspiration and liquid based examination of the specimens.

All results were classified as either diagnostic or non-diagnostic. Non-diagnostic results were where the samples were not representative, were inadequate, or were not useful to make the diagnosis and required repetition of the examination. Diagnostic results were defined as diagnostic results and were further sub-classified as malignant, premalignant, benign lesion, tuberculosis, other infectious conditions, and normal results. With specific emphasis on malignancy and tuberculosis samples, we describe sample site and type, gender, and age category (0-14 years, 15-60 years, and over 60 years) of the cases.

All data were entered into Microsoft Excel. Data cleaning and analysis occurred in Stata 14 by StatCorp LP. We used descriptive statistics to describe our outcomes.

Ethical considerations
The study was covered by the National Health Sciences Research Committee #1216 and the local Ministry of Health.

Results
Between May 2011 and July 2017, 532 specimen results were reviewed. The average turnaround time for results was 3.7 days (N=531, range: 0.35 days). Of all specimens, 87% (n=465) were histology samples and 13% (n=67) were cytology samples.

Among 9% (n=42) of all samples were diagnostic. Among diagnostic results, 37% (n=183) were malignant, 23% (n=112) were infections and inflammatory conditions, 20% (n=107) were normal samples, 4% (n=22) were premalignant, 4% (n=22) were due to other miscellaneous conditions, and 4% (n=21) were normal results. Among the diagnostic samples, 66% (n=28) were histology and 35% (n=14) were cytology.

Of the diagnostic results that were identified as premalignant lesions (n=21), 76% (n=16) were lesions from the cervix, followed by atypical endometrial dysplasia (14%, n=3) and dysplasia of skin (10%, n=2).

The most common sample collection sites for malignancies were skin (30%, n=55), cervix (27%, n=50), lymph nodes (16%, n=30), breast (5%, n=9), and penis (5%, n=6). The most common sample collection sites for malignancies were also tuberculomas (30%, n=27) and breast (5%, n=9) were the most common cancers (Table 1). By age category, 75% of all cancers occurred in patients between the ages of 15-60 years. Females accounted for 65% (n=114) of all cancer patients.
Cervical cancer was the most common cancer in females, contributing to nearly half of all cancers (43%, n=49). The next most frequent cancers in females were Kaposi sarcoma (14%, n=16) and skin cancer (9%, n=10). Breast cancer was not a common cancer, contributing to less than 10% of all cancers in females. In contrast, Kaposi sarcoma was the most common cancer in males, contributing to over 10% of all cancers in males. The most common cancers in males were squamous cell cancers, lymphoma, secondary lymph node cancers, and other cancers contributing to less than 10% of all cancers in males.

For cervical cancers, the most common subtypes were squamous cell carcinoma (9%, n=2) and adenocarcinoma (n=2) respectively. Squamous cell carcinoma was the most common type of secondary lymph node cancer, contributing to half of all cancers (50%, n=5). Breast carcinoma (9%, n=2) was the least common. Squamous cell carcinoma was the most common type of cervical cancer (9%, n=2). A total of 11 female patients were biopsied and sent for pathological examination, to ensure an accurate diagnosis and hopefully impact treatment decisions. As much as possible, we would encourage abandoning clinical suspicion on cervical cancers in favour of pathological confirmation to allow for accurate cancer and TB diagnosis. It is therefore essential that district hospitals in Malawi have access to high-quality and timely pathological services to achieve this goal. Based on the high yield of results in this study, we recommend that clinicians consider this as a routine service and refer cases for further evaluation. A TB diagnosis was made in 34 samples, or 7% of the total cancers in females. Only two samples were not sent for pathological analysis. By adding pathological diagnosis of the TB samples to all biopsies in the study, we speculate that most cancers were not diagnosed at the local district hospitals. This is therefore an important area of future study and intervention.

In this study, cancers alone contributed to 4 out of 10 samples that were sent for pathological analysis. By adding pathological diagnosis of the TB samples to all biopsies in the study, we speculate that most cancers were not diagnosed at the local district hospitals. This is therefore an important area of future study and intervention.
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**Author contributions**

CK conceptualized the study and performed data cleaning and analysis. AP and FM collected and entered the data. CK wrote the first draft. All authors contributed to the study and approved the final version for publication.

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**References**

1. Fleming KA, Naidoo M, Wilson M, Flanigan J, Harton S, Kuti M, et al. An essential pathology package for low- and middle-income countries. Am J Clin Pathol. 2017;147(1):15-32. doi:10.1093/AJCP/AQW143.

2. Morhason-bello IO, Odedina F, Rebbeck TR, Harford J, Dangou J, Denny, L, et al. Challenges and opportunities in cancer control in Africa: a perspective from the African Organisation for Research and Training in Cancer. Lancet Oncol. 2013;14:e141-151. doi:10.1016/S1470-2045(12)70482-5.

3. Government of the Republic of Malawi. Health Sector Strategic Plan II 2017-2022: Towards Universal Health Coverage. Lilongwe: Government of the Republic of Malawi; 2017.

4. Rubinstein P, Aboulafia D, Zloza A. Malignancies in HIV/AIDS from Epidemiology to Therapeutic Challenges. AIDS. 2014;28(4):553-465. doi:10.1002/wrna.1178.

5. Shiels MS, Engels EA. Evolving epidemiology of HIV-associated malignancies. Curr Opin HIV AIDS. 2017;12(1):6-11. doi:10.1097/COH.0000000000000327.

6. Cundale K, Wroe E, Matanje-Mwagomba BL, Muula AS, Gupta N, Berman J, et al. Reframing noncommunicable diseases and injuries for the poorest Malawians: The Malawi national NCDI poverty commission. Malawi Med Journal. 2017;29(2):194-197. doi:10.4314/mmj.v29i2.9.

7. Wroe EB, Cundale K, Kasomekera N, Masamba L, Gopal S, Crampin M, et al. Prioritizing Non-Communicable Diseases and Injuries Amongst the Poorest in Malawi: Where’s Cancer? Second Malawi Cancer Consortium; 2017, 28-29 August; Lilongwe: Malawi cancer consortium; 2017

8. Gopal S, Krysiak R, Liomba NG, Hornm S, Shores CG, Alide, N et al. Early Experience after Developing a Pathology Laboratory in Malawi, with Emphasis on Cancer Diagnoses. PLoS One. 2013;8(8):6-13. doi:10.1371/journal.pone.0070361.

9. Rudd P, Gorman D, Meja S, Mtonga P, Jere Y, Chidothe I, et al. Cervical cancer in southern Malawi : A prospective analysis of presentation , management , and outcomes. Malawi Med J. 2017;29(2):124-129. http://dx.doi.org/10.4314/mmj.v29i2.9.

10. Masamba L, Mtonga P, Kalilani-Phiri, Bychkovsky B. Cancer Pathology Turnaround Time at Queen Elizabeth Central Hospital, the Largest Referral Center in Malawi for Oncology Patients. J Glob Oncol. 2017:1-6. doi: 10.1200/JGO.2015.000257

11. National Statistical Office. Integrated Household Survey 2010-2011: Household and Social Economic Characteristics Report. Zomba: National Statistical Office; 2012

12. Msyamboza K, Dzamalala C, Mdokwe C, Kamiza S, Lemerani M, Dzowela T et al. Burden of cancer in Malawi; common types, incidence and trends: National population-based cancer registry. BMC Res Notes. 2012;5(1):149. doi:10.1186/1756-0500-5-149.

13. Mukhula V, Sibale D, Tarmahomed L, Dzamalala C, Msyamboza K, Chasimpha S. Characterising cancer burden and quality of care at two palliative care clinics in Malawi. Malawi Med J. 2017;29(2):130-135. http://dx.doi.org/10.4314/mmj.v29i2.10.

14. Msyamboza KP, Manda G, Tembo B, Thambu C, Chitefe C, Mindiera C, et al. Cancer survival in Malawi: A retrospective cohort study. Pan Afr Med J. 2014;19:234. doi:10.11604/pamj.2014.19.234.4675.

15. National Statistical Office. Malawi population and housing census. Zomba: National Statistical Office; 2008.

16. Msamba LPL, Jere Y, Brown ERS, Gorman DR. Tuberculosis Diagnosis Delaying Treatment of Cancer: Experience From a New Oncology Unit in Blantyre, Malawi. J Glob Oncol. 2016;2(1):26-29. doi:10.1200/JGO.2015.000299.

17. Moses A, Mwafongo A, Chikase M, Kafantenganji L, Staney C, Chimzukira E, et al. Risk factors for common cancers among patients at Kamuzu Central Hospital in Lilongwe, Malawi: A retrospective cohort study. Malawi Med J. 2017;29(2):136-141 http://dx.doi.org/10.4314/mmj.v29i2.11.

18. Mtonga P, Masamba L, Milner D, Shulman LN, Nyirenda R, Mwafulirwa K. Biopsy case mix and diagnostic yield at a Malawian central hospital. Malawi Med J. 2013;23(3):62-64.

19. Mabedi C, Kendig C, Liomba G, Shores C, Chimzimu F, Kampani C, et al. Causes of cervical lymphadenopathy at Kamuzu Central Hospital. Malawi Med J. 2014;26(1):16-19.

20. Purohit M, Mustafa T. Laboratory diagnosis of extra-pulmonary tuberculosis (EPTB) in resource-constrained setting: State of the art, challenges and the need. J Clin Diagnostic Res. 2015;9(4):EE01-EE06. doi:10.7860/JCDR/2015/12422.5792.

21. Adebamowo CA, Casper C, Bhatia K, Mbulaiteye SM, Sasco AJ, Phipps W, et al. Challenges in the Detection, Prevention, and Treatment of HIV-Associated Malignancies in Low- and Middle-Income Countries in Africa Clement. J Acquir Immune Defic Syndr. 2015;67(1). doi:10.1097/QAI.0000000000000255.

22. Hüb K. HIV-Associated Malignancies. Oncol Res Treat. 2014;40:80-81. doi:10.1159/000456716.

23. National Statistical Office Malawi and ICF. Malawi Demographic and Health survey 2015-2016. Zomba, Malawi and Rockville, Maryland,USA: National Statistical Office and ICF. 2017.

24. Herce ME, Kalanga N, Wroe EB, Keck JW, Chingoli F, Tengatenga M, et al. Excellent clinical outcomes and retention in care for adults with HIV-associated Kaposi sarcoma treated with systemic chemotherapy and integrated antiretroviral therapy in rural Malawi. J Int AIDS Soc. 2015;18 doi:10.7448/IAS.18.1.19929.

25. Herce ME, Elmore SN, Kalanga N, Chingoli F, Tengatenga M, et al. Assessing and responding to palliative care needs in rural sub-Saharan Africa: Results from a model intervention and situation analysis in Malawi. PLoS One. 2014;9(10). doi:10.1371/journal.pone.0110457.

https://dx.doi.org/10.4314/mmj.v30i3.6