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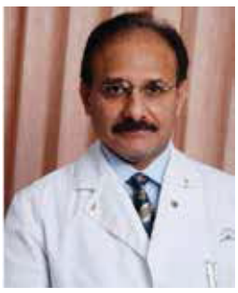















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**Editorial**

# Inequities in Healthcare: Human Rights and Wrongs

Access to healthcare is a fundamental right of every citizen and is explicitly enshrined in the Constitution of Kenya (Section 43) (1). Yet, millions of Kenyans are denied this right every day due to issues of accessibility and affordability as well as poor governance, manifesting as inequity in distribution of healthcare facilities, under-funded and ill-equipped healthcare facilities and de-motivated health professionals (2,3).

Thus, access to basic healthcare in Kenya remains a pipe dream for the majority poor and low income earners who daily struggle in a losing battle against runaway inflation, rampant corruption and ever-rising cost of living. For them, the right to health remains a cruel joke, since they can't even afford the basic food to maintain their health and keep body and soul together (4). When health emergencies strike—and they always wait until it's a real emergency, otherwise they simply soldier on and hope for the best—they solely depend on the goodwill and contributions of well-wishers (5). Otherwise they resort to self-medication with possible dire consequences, sometimes leading to death (6).

As in many parts of the world, healthcare inequities in Kenya occur as a consequence of multitude of interrelated factors (7). Healthcare disparities in Kenya are exacerbated by huge differentials based on location, poverty level, education level, gender and age (8).

Granted, the journey towards equity for health is a complex process that even the most developed countries are yet to achieve. While the Government of Kenya continues to invest in health, the sector suffers perennial shortages of funds, forcing hapless citizens to pay to access healthcare. This is sometimes termed as 'out-of-pocket payment' for health services (9). This regressive form of healthcare financing means that the poorest and the most vulnerable end up bearing the greatest burden.

This entrenched inequity presents an almost intractable paradox. On the one hand, there exists a situation of too few doctors and hospital beds per capita in the main public sector which means that, with wide disparities and inequities in access, distribution and affordability, many people simply have no way of getting the level and quality of healthcare they need (10). On the other hand, however, is the opposite situation of "one patient, too many doctors" in the private healthcare facilities (11). That is not necessarily a good thing: too many doctors can be bad for the patients' health (12). It has been shown that if many physicians see one patient, there is a correspondingly greater chance of miscommunication and over-treatment. This undesirable situation is all-too-common in most high-end private health institutions. In fact, when it comes to the wellbeing of patients, less is often more. The combination of over-treatment and poor coordination of care by physicians in many private hospitals in Kenya is a clear and rising threat with the growing number of practitioners consulting in many private hospitals.

The situation is worse for the chronically ill who may exhibit medication problems where different physicians are prescribing for the same patient. It is not unusual to run across a duplication of medication with many specialists seeing the same patient in an uncoordinated manner (13). One may easily come across long-suffering patients who are already on multiple medications being prescribed the same drugs all over again! Quite clearly, the likelihood of being on too many drugs increases with the number of consultants seeing a patient (14,15). This clearly calls for streamlining of the number of physicians seeing one patient at any one time. Too many doctors on one patient will lead to too many tests, and it is not uncommon for a doctor to order a test that another doctor had just had done. And with the enthusiasm borne of consultation, even minor abnormalities or incidental findings are often over-investigated, subjecting the patient to a battery of diagnostic tests of doubtful utility. In the end, the patient is saddled with ballooning healthcare costs even as their health may not be noticeably improved as a result (16).

That is not to say that genuine medical problems should be ignored or dealt with perfunctorily, no. The plain truth however remains that over-treatment and too many tests take away precious time from more fundamental, if less glamorous, interventions. This may also elicit doubt and stress in the patient due to frequent tests, the anxious wait for results waiting and, above all, trying to make sense of conflicting opinions among the many attending physicians. Often times, the end result of such excessive tests are invasive procedures that may result in serious complications that are best avoided than remedied.

Having many doctors can help the patient get the best care if the effort is seamlessly coordinated, but

it can also cause serious problems if poorly managed. When doctors attending to the same patient fail to talk to each other, confusion ensues for both doctor and patient and, in such circumstances, the end result can only be less than optimal.

It must be pointed out that a healthcare system is a complex combination of technology, process, professionalism and diverse stakeholders. Even so, the crux of the matter must always hinge on health in general, and the health and well being of the patient in particular. For optimal operations and outcomes, the entire system and its constituent parts must be properly incentivized.

Too much medical care can be dangerous: all medical tests carry some degree of risk, including side effects, 'false positives' and 'false negatives'. It is always possible, probable even, that most patients will have some abnormalities that will turn up with sufficient probing, leading to a potentially vicious cycle of increased testing and treatment. In short, all procedures and treatment carry some degree of risk and come with a price tag, both of which are not always in the 'best interest' of the patient or their wallets.

This is especially a concern for tests involving radiation such as CT scans since exposure to radiation is dangerous in cumulative doses (17). The quest for diagnosis may lead doctors to order further tests just to be sure or rule out other possibilities (18).

We realize that this kind of situation is not always or necessarily physician-driven: the patient may often ask for or even demand for tests just to give them the peace of mind that nothing serious is wrong or ask for medication after procedures in the hope of feeling better faster. This, combined with the brief time allocated for medical consultation, may lead physicians to perform or consent to tests and procedures they do not need.

A special situation arises in doctor-owned medical, diagnostic and surgical centers, where a sort of 'perverse incentive' may kick in, pushing the doctor to conduct or encourage medical tests and procedures because of financial incentives (19).

When all is said and done, the quest for equity remains a persistent challenge for healthcare systems in Africa and most of the developing world. Achieving equitable, comprehensive, and integrated health services will require important transformations in the model of care and in the organization of health care delivery (20). The countries of the region agree that models of care based on the values and principles of primary health care strategy should govern health care organizations or networks to provide integrated, quality, people- and community-centered services. For that to happen, certain changes will be essential, including more equitable health financing, new or adjusted regulatory frameworks, innovative approaches to human resources development and allocation, and strong leadership by the national health authorities.

In the meantime, health systems in Kenya struggle with the dichotomy of a declared policy intention to move toward universal health and people- and community-centered models of care based on the values and principles of primary health care, juxtaposed against the reality of stubborn structures and practices of the old biomedical model (21). In curative services–oriented systems, a preponderance of funds is allocated to in-patient care. This is the present situation, as borne out by the fact that the Ministry of Health continues to allocate the lion's share of its budget to hospital services that are inequitably distributed nationwide.

In light of the above, the country urgently needs to accelerate the transformation of the health system with universal health as a deliberate goal. Comprehensive strategic actions implemented in a progressive and sustained manner are required to build health services that are responsive to the needs of all segments of the population. As democratic processes in the country mature and greater decision-making power is transferred to counties, people and their communities, the social demand for universal health can be expected to grow, supported by increasingly well organized advocacy efforts (7).

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**Original paper**

# Prevalence and Risk Factors for Hypertensive Retinopathy at Moi Teaching and Referral Hospital, Eldoret, Kenya

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## Abstract

**Background:** Hypertensive retinopathy (HTNR) is a recognized complication of hypertension. Early diagnosis is crucial for the mitigation of more severe complications such as retinal detachment and loss of vision by the timely institution of appropriate management strategies. In addition, HTNR findings are a useful risk stratification tool for acute coronary events and strokes, two leading causes of Disability Adjusted Life Years (DALYs) worldwide. Paucity of data exists on the prevalence and associated risk factors for HTNR in Sub-Saharan Africa (SSA).

**Objectives:** To determine the prevalence and associated risk factors for HTNR at Moi Teaching and Referral Hospital (MTRH).

**Design:** This was a cross-sectional study.

**Methods:** The study was conducted among patients with hypertension attending the Medical Out-Patient Clinic (MOPC) at MTRH between January and April 2018. The study population included 640 patients on follow up for hypertension over the study period. Systematic random sampling was used to select 240 participants. Structured interviewer administered questionnaires were utilized to collect socio-demographic, anthropometric, clinical and laboratory data. Low Density Lipoproteins-Cholesterol (LDL-C) measurement was performed using enzymatic colorimetric method and fundoscopic examination performed using an ophthalmoscope, with all measurements taken on the same visit. Grading of HTNR was done using Mitchell-Wong classification. STATA version 15 was used for analysis and appropriate statistics used to analyze various variables in line with the study objectives. Categorical variables were summarized in frequency tables, percentages and bar graphs. Continuous variables were summarized using means, standard deviations, frequencies, medians and interquartile ranges (IQR). Medians were compared using Wilcoxon-rank sum test. Univariate and multivariate logistic regression models were used to assess associations of the variables with HTNR.

**Results:** The median age was 59 years (IQR:52,69) with a female preponderance at 185 (77%). The prevalence of HTNR was 23.3% (95% CI: 18.13-29.20) representing 54 participants. Of these, 47 (84%) had Grade 1, 7 (13%) had Grade 2 and 2 (3%) had Grade 3. Chi square p values for age (p=0.001), blood pressure control (p=0.004) and duration of hypertension (p=0.017) showed association with the occurrence of HTNR. On multiple logistic regression, age had an Odds Ratio (OR) of 1.3 (95% CI: 1.026-1.086), Stage 2 HTN had OR 3.66 (95% CI: 1.40-9.50) and duration of HTN of more than 15 years had OR 3.69 (95% CI: 1.10-12.28). Body Mass Index (BMI) and LDL-C measurements did not show any association with HTNR.

**Conclusion:** HTNR is common among patients attending MOPC at MTRH with its mild form (Grade 1) predominating. Longer duration after diagnosis, advanced age and uncontrolled BP were strongly associated with its occurrence.

**Key words:** Hypertension, Hypertension retinopathy

## Introduction

Hypertensive retinopathy refers to the retinal changes that are caused by elevated systemic blood pressures (1). Hypertension continues to be a major global health issue with approximately one billion people affected worldwide (2) and prevalence projected to be as high as 30% by 2025 (3).

The prevalence of hypertension will keep rising as life expectancy increases (4). However, challenges in the awareness, management and control means recognition and adequate treatment remains sub optimal (5). These challenges translate to poor control of blood pressure with a concurrent increased risk for development of complications such as hypertensive retinopathy. The burden of complications will therefore continue to rise as many patients with hypertension remain undiagnosed and those who are diagnosed remain poorly controlled with subsequent increased occurrence of complications.

Hypertensive retinopathy is a recognized complication of hypertension associated with reversible loss of vision. However, persistent elevation of blood pressures can cause even more adverse effects with permanent loss of vision through retinal detachment and optic nerve atrophy (1).

HTNR occurrence can also be used in projecting the risk for the development of even more serious complications of hypertension such as strokes, coronary heart diseases and heart failure. Cerebral and coronary circulation share similar anatomical and physiological properties with retinal circulation (6 ) and fundoscopy therefore provides a reflection of these vasculature which are ordinarily inaccessible (7).

Numerous studies have found ophthalmoscopy to be a useful clinical tool in the risk stratification for the development of strokes and coronary heart disease (8). A study done in Nigeria showed prevalence rates of HTNR of up to 19.4% among 903 hypertensive patients (9) but there is paucity of data in the larger Eastern Africa region despite worsening burden of hypertension. Approval to conduct the study was received from Moi University/Moi Teaching & Referral Hospital ethical review board.

## Materials and methods

A cross-sectional hospital based study was conducted in the general medical outpatient clinic at Moi Teaching and Referral Hospital, Eldoret, Kenya. The sample size was calculated to be 240 respondents derived by the Fishers formula and based on a prevalence of 19.4% obtained from a Nigerian study (9). Recruitment was by systematic random sampling with exclusion of patients with diabetes mellitus, conditions precluding fundoscopy such as cataracts, ocular trauma or pregnant women – because mydriatics has a potential risk of fetotoxicity.

The Principal investigator (RMO) and the research assistant reviewed the files and screened for those who met the inclusion criteria on every clinic day. Screening for diabetes from the charts was conducted by a random blood sugar performed (using an Accu-Chek Aviva Plus glucometer) followed by blood pressure measurement (three readings at least one minute apart with the average of the last two being recorded) performed by a digital blood pressure machine Omron M2 blood pressure machine (Omron Healthcare, Inc., 1200 Lakeside Drive, Bannockburn, Illinois 60015) and anthropometric measurements taken from consenting participants. A standardized questionnaire was subsequently administered for collection of information on socio-demographics. A drop of the mydratic agent, tropicaimide was instilled in both eyes and after fifteen minutes a fundoscopic examination was performed (using a Welch Allyn™ 3.5V standard ophthalmoscope) by the principal investigator and findings confirmed by an ophthalmologist (OCO).

Features of HTNR were examined for and the findings classified as per the Mitchell Wong classification into mild (Grade 1), moderate (Grade 2) and malignant (Grade 3) HTNR and the findings documented for analysis. A blood sample was then drawn for measurement of Low Density Lipoproteins (LDL) levels at the MTRH International Organization for Standardization (ISO) accredited laboratory facility.

Validation of the data was done before being entered into the computer, data analysis was subsequently performed using SPSS Version 24. Descriptive statistics such as the median and corresponding interquartile range were used to summarize continuous variables such as age, BMI, serum and LDL-C levels. Frequencies and the corresponding percentages were used to summarize categorical variables such as gender, level of education, and marital status.

The prevalence of HTNR was expressed as a percentage of the study population who were diagnosed to have hypertension as per the operational definition. The second objective of the study explored association between hypertensive retinopathy and categorical independent variables assessed using Pearson's Chi Square Test, Fisher's Exact Test and Wilcoxon Rank Sum Test.

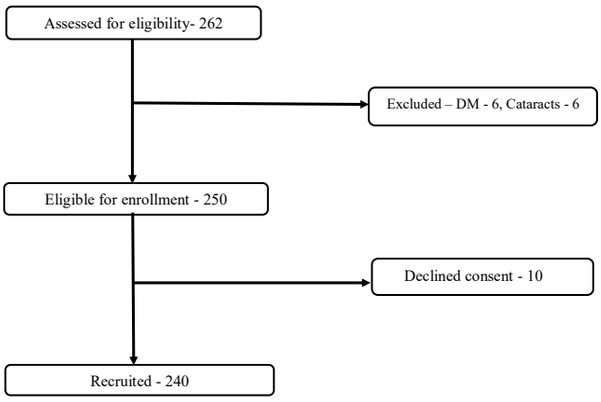
Logistic regression model was used to assess the variables associated with hypertensive retinopathy. Bivariate logistic regression model was used to calculate the unadjusted Odds Ratios (OR), and the multivariate logistic regression model was used to calculate the adjusted odds ratios. In the multivariate model, the variables that were significantly associated with hypertensive retinopathy in the bivariate analysis were included.

The univariate analysis that showed significant relationships ($p < 0.020$) between exposure variables and hypertensive retinopathy were included in the multivariate analysis. These variables were age, duration of hypertension and elevated BP reading. Odds ratio and the corresponding 95% confidence intervals were reported. Results were presented using tables, pie charts and bar graphs. The sample size calculated was powered to explore these associations.

## Results

Two hundred and forty participants were enrolled (Figure 1).

**Figure 1**: Recruitment schema




The median age was 59 years (IQR:52,69). Of the 240 participants, 185 were females representing 77% and 55 males being 23% of the participants. Demographic data is illustrated in Table 1.

**Table 1:** Socio-demographic characteristics

| Variable | Freq/Median | %/ IQR |
|---|---|---|
| Age in years | 59 | (52,69) |
| Gender | | |
| Female | 185 | 77% |
| Male | 55 | 23% |
| Level of education | | |
| None | 50 | 20.8% |
| Primary | 107 | 44.6% |
| Secondary | 66 | 27.8% |
| Tertiary | 17 | 7.1% |

One hundred and fifty one participants had been hypertensive for less than 5 years representing 62.9% of the participants. On the other end of the spectrum 18 (7.5%) and 17 (7.1%) of the participants had been hypertensive for 11-15 years and more than 15 years respectively. One hundred and nine (45.4%) participants were overweight, defined as a BMI of between 25.0 to 29.9kg/$m^2$ while 71 (23.3% were obese- defined as a BMI of more than 30 kg/$m^2$. A normal BMI of 18-24 kg/$m^2$ was only observed in 56 participants (23.3%) with a further 4 (1.7%) being underweight. One hundred and twenty three (51.2%) participants were on two antihypertensive agents with the rest being on either one agent (32.9%) or at least 3 (15.8%) combination therapies. CCBs were the most prescribed class of anti-hypertensive agents with 107 (44.6%) being on them as either mono or combination therapy. Fifty eight participants (24.2%) were on ARBs, 44 (18.3%) were on ACEI, 30 (12.5%) were on a thiazide diuretic and 4 (1.7%) were on beta blockers. Two hundred and two participants were found to have normal LDL – C levels with 38 participants having hypercholesterolemia.

The prevalence of hypertensive retinopathy was 23.3% (95% CI: 18.1, 29.2). Of these 47 (84.5%) had grade 1 HTNR. Grade 2 HTNR was found in 7 (12.5%) while Grade 3 HTNR was observed in 2 (3%) of participants with HTNR. The median age for participants with HTNR was 64 which was higher than the mean of persons without HTNR at 57 years with a significant P-value of 0.0002. There was no preponderance of sex for the development of HTNR.

The duration of hypertension (P-0.004) and blood pressure (P-0.017) was associated with the occurrence of HTNR. BMI, waist circumference and LDL measurements had no association with HTNR. Variables with a P-value of less than 0.05 were subjected to multiple logistic regression analysis. These results of the univariate analysis are illustrated in Table 2.

**Table 2:** Univariate analysis of the variables

| | HTNR | | |
|---|---|---|---|
| | No | Yes | |
| Variable | Freq (Row%) | Freq (Row%) | P-value |
| Age in categories | | | |
| Median (IQR) | 57 (50,58) | 64 (59,75) | 0.0002 |
| Sex | | | 0.431[2] |
| Female | 144 (77.8) | 41 (22.2) | |
| Male | 40 (72.7) | 15 (27.3) | |
| Duration of HTN (years) | | | |
| Less than 5 | 121 (80.1) | 30 (19.9) | 0.004[3] |
| 6- 10 | 43 (79.6) | 11 (20.4) | |
| 11-15 | 13 (72.2) | 5 (27.8) | |
| More than 15 | 7 (41.2) | 10 (58.8) | |
| BMI | | | 0.162[3] |
| Underweight | 4 (100) | 0 (0) | |
| Normal | 42 (75) | 14 (25) | |
| Overweight | 89 (81.7) | 20 (18.3) | |
| Obese | 49 (69) | 22 (31) | |
| LDL | | | 0.372[2] |
| Normal | 157 (77.7) | 45 (22.3) | |
| Hypercholestrolemia | 27 (71.1) | 11 (28.9) | |
| BP control | | | 0.017[2] |
| Normal | 63 (86.3) | 10 (13.7) | |
| Grade1 | 74 (77.1) | 22 (22.9) | |
| Grade2 | 47 (66.2) | 24 (33.8) | |

[1] Wilcoxon rank sum test [2] Chi square test
[3] Fishers' exact test

On the multiple regression, age, duration of hypertension of more than 15 years and Grade 2 hypertension remained significant. Significance was assigned for a value of less than 0.020. Grade 2 hypertension is a BP reading of more than 160mmHg systolic and a diastolic BP reading of more than 110mmHg or both. The results of the multiple logistic regression analysis are expressed in Table 3.

**Table 3:** Outcomes of significant variables on multiple logistic regression model

| Variable | Odds Ratio | P-value | [95% Conf. | Interval] |
|---|---|---|---|---|
| Age in years | 1.056 | 0.000 | 1.026 | 1.086 |
| Duration of HTN (years) | | | | |
| Less than 5 | 1.000 | | | |
| 6-10 | 1.147 | 0.751 | 0.492 | 2.672 |
| 11-15 | 1.356 | 0.620 | 0.407 | 4.511 |
| More than 15 | 4.050 | 0.020 | 1.246 | 13.162 |
| Hypertension control | | | | |
| Normal | | | | |
| Grade1 | 2.195 | 0.091 | 0.883 | 5.456 |
| Grade2 | 3.961 | 0.005 | 1.529 | 10.262 |

## Discussion

The prevalence of HTNR was 23.3%. Grade 1 HTNR was the most common among those with HTNR representing 83.9%. Grade 2 was found in 12.6% with Grade 3 found in 3.5% of the participants.

These findings were similar to the findings of Oluleye *et al* (8) conducted in Nigeria which found an overall prevalence of 19.4%. Of these, 93.14% were grade 1, 5.7% were grade 2 and 1.1% with Grade 3 while Mondal *et al* (9) in India found a prevalence of 29.4% among 313 participants. Some studies however found a significantly lower prevalence. A study done in Bangladesh by Akhter *et al* (10) found a much lower prevalence of 5.4%. This could be attributed to the relatively younger age of the study population, whose mean age was 46 years against 59 years in our study. Studies with a younger average age also tended to have a lower prevalence of HTNR which would suggest age related changes and possible longer duration of hypertension.

Grade 3 HTNR was consistently an uncommon occurrence with most studies having a prevalence of less than 3% as seen in this study, for example the study by Mondal *et al* (9) had only 1.1% and Oluleye *et al* (8) also had 1%. In Netherlands Ong *et al* (11) with n=2907, only one participant had grade 3 HTNR. In as much as adequate control remains elusive, earlier diagnosis and initiation of management helps to mitigate for the extremely high blood pressures required for Grade 3 HTNR (2).

The median age for participants with HTNR was 64 years which was higher than the mean of persons without HTNR at 57 years with a significant P-value of 0.0002, and was significant when subjected to multiple logistic regression. Other studies have found age to be strongly associated with the occurrence of HTNR, similar to the findings of other studies (12-14). In all these studies, the average age of persons with HTNR was significantly higher than the participants found not to have HTNR.

The study performed in Malawi by Kayange *et al* (15) however did not find an association of age with the occurrence of HTNR. This is likely due to the distribution of age in this study as the ages between the population of those with HTNR and those without HTNR were similar, 56 years and 57 years respectively. This minimal difference in the ages may therefore explain the lack of statistical association of age with HTNR.

The duration of hypertension was strongly associated with the occurrence of HTNR and remained significant when subjected to multiple logistic regression as found in other studies. This is thought to result from the prolonged duration of stress on the vasculature from prolonged duration of hypertension (9,13).

In the early stages of hypertension, most of the fundus blood vessels are normal. However, with the development of the disease, the formation of atherosclerotic plaques gradually increases the thickness and decreases the diameter of blood vessels, followed by the development of arteriosclerosis and the corresponding retinopathy (16). Some studies however did not show an association between HTNR with the duration of hypertension (15). This is likely because the stratification of duration of hypertension was not long enough to determine it as a factor of the development of HTNR as the categorization was less than 3 years, 3-4 years and more than five years. In addition, a limited sample size of 104 participants may have contributed to the lack of association.

Blood pressure control was associated with the occurrence of HTNR (P-0.017) and was significant on multiple regression analysis. This was similar to other studies done which found that the control of HTN had a strong correlation with the occurrence of HTNR (13,14). Poorly controlled blood pressure subjects the retinal vasculature to increased arterial wall stress which causes reflex vasoconstriction and subsequent arteriolar attenuation. At higher blood pressures, exudative processes lead to retinal haemorrhages and cotton wool spots (17). The study by Kayange *et al* (15) however found no association in the occurrence with the development of HTNR. In this study, up to 83% of the participants however were poorly controlled and this may have weakened the potential association between BP control and development of HTNR.

BMI was not associated with the occurrence of HTNR in this study. Studies have revealed inconsistent associations between increased BMI and the development of HTNR. Some studies have shown that increased BMI could be associated with HTNR by the action of leptin (3). Leptin is an endocrine hormone synthesized from adipocytes and its main function is glucose and lipid metabolism. Leptin levels are elevated in persons with increased BMI, which in turn increases its associated angiogenic properties on the retina (18). In addition obesity leads to obesity related microangiopathy (19). Studies that found no association between BMI and the occurrence of HTNR seem to have had a lower sample mean and the population was generally leaner. These findings corroborated with the findings of Chao *et al* (13) which had a mean of 23kg/$m^2$ and Van Leiden *et al* (20) in the Netherlands found a mean of 25.9kg/$m^2$. In our study, the sample mean for BMI was 28.2kg/$m^2$. Studies that found an association also had higher BMI levels, an example is Kotsis *et al* (22) who found an average BMI of 34 kg/$m^2$.

LDL was not associated with the occurrence of HTNR. These findings are similar to the findings of the study done in China by Zhang *et al* (16) on 228 patients which did not find an association between HTNR and levels of LDL. LDL is hypothesized to lead to atherosclerosis or thickening of the arterial walls. This occurs when LDL seeps into the arterial walls through damaged junctions of the endothelial cells that line the arterial wall. The residual thickening narrows the channel and decreases blood flow through the vessel, which can lead to ischemia and other HTNR changes. Studies by Akhter *et al* (10) in Bangladesh on 836 participants and Adhikari *et al* (21) on 240 participants in India both found an association of elevated LDL with the occurrence of HTNR. This is likely because in both studies the percentage of the participants with an elevated LDL was 70% and 89% respectively and thus could explain the association with HTNR. Only 28% of the participants had a high LDL and this could explain the lack of association reported. The association between levels of LDL and HTNR have been inconsistent in numerous studies (3).

Of the 240 patients sampled from the MOPC at MTRH only 30.4% were found to be well controlled. Forty per cent were found to have Grade I hypertension and 29.5% having grade 2 hypertension. Good control of hypertension remains a challenge in many clinical units. A study in Kenya by Mohamed *et al* (5) found only 51.7% to be well controlled. The poor BP control in our study could possibly be explained by the high percentage of participants who were obese and overweight, representing 75% of the study population, a factor known to predict poor BP control (22). Poor control of hypertension is frequently associated with non-compliance to medications. Serial surveys show an increasing prevalence of hypertension in developing countries, possibly caused by urbanization, aging of population, changes to dietary habits and social stress. High illiteracy rates, poor access to health facilities, bad dietary habits, poverty and high costs of drugs could also contribute to poor blood pressure control (7).

Our study limitations include the fact that we were not able to ascertain the duration of hypertension with certainty since the disease can exist long before a diagnosis is made. Besides we did not measure visual acuity to correlate with the severity of the retinopathy, an aspect that could bear more utility from the patient perspective. While we recommend that routine fundoscopic examination be part of routine evaluation of all hypertensive patients, future longitudinal studies should address the relationship of HTNR with occurrence of hard cardiovascular outcomes such as strokes, acute coronary events and heart failure.

## Conclusions

HTNR is common among patients attending MOPC at MTRH with its mild form (Grade 1) predominating. Longer duration after diagnosis, advanced age and uncontrolled BP were strongly associated with its occurrence.

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**Original paper**

# Cardiovascular Disease Risk Profile of Patients attending Medical Outpatient Clinics in Three Hospitals in Western Kenya

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## Abstract

**Background:** Cardiovascular Disease (CVD) is a leading cause of mortality in people above the age of 30 years in Sub-Saharan Africa (SSA). Multiple modifiable CVD risk factors may be prevalent and clustered in individuals. In this situation CVD risk profiling is an important first step in CVD prevention.
**Objective:** We set out to describe the CVD risk profile of patients attending Medical Outpatient Clinics (MOPCs) in three hospitals in Western Kenya.
**Design:** This was a cross-sectional observational study
**Methods:** The study was done in medical outpatient clinics in Moi Teaching and Referral Hospital, Kitale County Hospital and Fountain Healthcare in two counties in western Kenya. The study included consenting adult patients that resided within the two counties, were not pregnant at time of consenting and did not have a previous diagnosis of stroke or myocardial infarction. The primary outcome measure was cardiovascular risk profile, which was assessed using the INTERHEART-cholesterol risk score. Additional individual CVD risk factors such as dyslipidemia, waist circumference and overweight and obesity were assessed and recorded. Data analysis was done using STATA version 13.
**Results:** A total of 369 patients with a mean age of 55.4 years were enrolled. Of this number, 73% were female, 53% unemployed and 50% were of low socio-economic status. Ten percent of patients had a high CVD risk while 53% had moderate risk. Waist circumference and BMI were associated with CVD risk score. Dyslipidemia was the most prevalent individual CVD risk factor at 87% followed by hypertension at 85%. Central obesity, and overweight and obesity were significantly more prevalent in females than males.
**Conclusion:** Patients attending general medical outpatient clinics do have significant CVD risk with key risk factors being hypertension, dyslipidemia and central obesity. Central obesity may be a useful single indicator for CVD risk in this patient population.

**Key words:** Cardiovascular diseases, Medical outpatient clinics, Western Kenya

## Introduction

Cardiovascular Disease (CVD) is a leading cause of mortality in the world with 80% of CVD deaths occurring in Low and Middle-Income Countries (LMIC) (1). More than half of this CVD burden affects middle-aged population between the age of 45 and 69 years (2). CVD burden is rapidly growing and is the leading cause of mortality in people aged over 30 years in Sub-Saharan Africa (SSA) (3). In addition to the epidemiologic burden, CVD threatens to impose a significant economic burden on LMICs (4,5). In Kenya, variable CVD mortality has been described ranging from 6.1% to 8% (6). Additionally, 13.8% of the general population has three or more CVD risk factors (7).

Hypertension is quantitatively the most important cause of premature cardiovascular disease, being more prevalent than smoking, diabetes, dyslipidemia and obesity in SSA (8). It accounts for an estimated 56% of all strokes and 47% of all Ischemic Heart Disease (IHD) events globally (2). As much as individual risk factors are important contributors to CVD, the co-existence of multiple factors has been found to be more detrimental to cardiovascular health. As a result, all recent guidelines on treatment of hypertension emphasize the importance of risk stratification when starting treatment. Guidelines for diabetes treatment also currently emphasize the role of holistic evaluation and management of all co-existent CVD risk factors (9). Risk scores are useful in quantifying the overall risk of CVD events

in an individual and hence guide the appropriate and commensurate management. The INTERHEART risk score is one of the widely used CVD risk score that included 52 countries from all continents during its development. Its INTERHEART-cholesterol version was also used in Africa amongst other LMIC regions (10).

Kenya like many other developing countries continues to struggle with a growing burden of CVD amongst other Non-Communicable Diseases (NCD) (7). Most hospitals within the country have Medical Outpatient Clinics (MOPC) that are set up to ensure continuity of care for patients with chronic diseases. Patients are followed up in these clinics for varying health problems with a large number being on treatment for hypertension alone or in combination with other conditions (11). Studies done in specialty diabetes clinics in urban slums of Kenya have shown high rates of individual CVD risk factors (12). In order to design contextually relevant prevention interventions, it is important to understand the actual risk factors in this population. Given the frequent interaction of the health system with patients attending MOPCs, this group of patients represents a practical and feasible target for the assessment and potential remediation of CVD risk factors. The study set out to describe the CVD risk profile and prevalence of individual CVD risk factors of patients attending three MOPCs in western Kenya.

## Materials and methods

*Study design:* This was a cross-sectional descriptive study.

*Study site:* The study was conducted in Moi Teaching and Referral Hospital (MTRH), Kitale County Hospital (KCH) and Fountain Healthcare (FHC) MOPCs. The MTRH and FHC clinics are located in Eldoret town and serve the population from Eldoret and its surrounding western Kenya catchment population. The Kitale County Hospital is a secondary care facility that serves mostly a low-income population from Kitale township in Trans Nzoia County and the surrounding Western region counties. MTRH is the second national referral hospital in Kenya serving a catchment population of over 15 million people. Being a national hospital, MTRH has many specialist medical clinics hence the MOPC is reserved for general medical problems and is not as large as Kitale MOPC which serves all conditions. Fountain Healthcare Clinic is a group practice private facility that serves mostly middle and high income clients from Eldoret town. As such it is the smallest of the three clinics selected.

*Human subjects' protection:* This study was reviewed and approved by the MTRH Institutional Review Committee (IREC approval #0001446). All enrolled participants provided individual written informed consent.

*Study population:* This study targeted adult patients attending MOPCs in the three study clinics. We included all consenting patients aged 18 years and above who resided in the study counties. We excluded all pregnant women and persons with documented diagnosis of stroke or myocardial infarction. Data were collected between 1st September 2015 and 31st January 2016.

*Eligibility, sampling and recruitment method:* The target sample size was calculated based on an expected prevalence of diabetes, one of the main CVD risk factor, of 6% based in prior literature (13). We used a 95% confidence level and effect size of 3% which yielded a minimum sample size of 241.

$$n = \frac{[z^2 * p * q]}{E^2}$$

Where:
n= Target sample size
z= Confidence interval at 95% (standard value of 1.96)
p= Estimated prevalence of diabetes mellitus
q= 1-p
E= Margin of error (0.05)

We further adjusted for a dropout of 20% between 1st and 2nd visit, which yielded a total minimum target sample size of 302. This recruitment was stratified for the three clinics and pro-rated for the number of patients registered in each clinic. Files for each clinic were assessed on the day before clinic and all those meeting inclusion criteria were identified for enrollment. Consecutive recruitment of patients with tagged files was done on clinic day as the patients arrived. Eligibility was re-confirmed in a face-to-face interview. Those who were confirmed eligible and consented were then enrolled in study procedures. Recruitment was done on alternate weeks until the desired sample size for each clinic was recruited.

*Study procedure and sources of data*: An interviewer assisted clinical assessment questionnaire, incorporating the CVD risk factors was used to collect data. The clinical assessment questionnaire had questions on all patient demographic, socio-economic and clinical data. Anthropometric and laboratory measurements were also recorded in a table in the questionnaire. The questionnaire was programmed into Research Electronic Data capture (REDCap) database which allowed for direct data entry daily.

Blood pressure was measured using an Omron M2 compact upper arm blood pressure (BP) monitor (Omron Healthcare, Inc., 1200 Lakeside Drive, Bannockburn, Illinois 60015). Weight was measured

with a 762 Dial Bathroom Floor Scale and height measured with a Mechanical roll-up measuring tape (Seca 260) with wall attachment. The standard BMI calculation formula was programmed into the data collection form in REDCap and generated BMI automatically. A constant tension tape measure was used to measure waist circumference. All measurements were done according to the WHO Stepwise survey protocols.

On the recruitment day the participants were consented and study questionnaire filled anthropometric measurements and blood pressure assessments were also done. The patient was then requested to return to clinic in a week's time in a fasting state. On the second clinic visit a venous blood sample was drawn for measurement of fasting lipids and fasting blood sugar. During blood draws, universal safety procedures were observed. Blood sample for lipid profile measurements were centrifuged and transported to the lab within 3 hours in a cooler box. Lipid profiles were done using a Cobas Integra automatic analyzer (Roche) in the AMPATH reference laboratory.

The primary outcome of interest was cardiovascular risk score as calculated using the INTERHEART risk score. The INTERHEART risk score includes data on age, sex, smoking status, diabetes, hypertension, physical activity, family history of heart disease, waist-to-hip ratio, diet and psychosocial factors. Scores range from 0-48, with risk categorized based on total scored as low risk 0-9, moderate risk 10-15, and high risk if more than 16.

The secondary outcome of interest was prevalence of individual CVD risk factors studied. These were:

(i) Hypertension defined as known hypertensive on treatment from the file notes or newly diagnosed hypertension by having 3 or more readings of Systolic Blood Pressure (SBP) >=140, or Diastolic Blood Pressure (DBP) >=90.

(ii) Diabetes mellitus defined as known to have diabetes on treatment, or an initial FBS, over 7.0 mmol/l. or 2 hour post OGTT RBS >11.1mmol/L.

(iii) Dyslipidemia was defined according to the third report of the National Cholesterol Education Program Expert Panel on detection evaluation and treatment of high blood cholesterol in adults (NCEP Adult Treatment Panel 111) as presence of any of: Total cholesterol >6.2mmol/dl (240mg/dl), and or increased LDL cholesterol >2.6mmol/L (100md/dl), and or decreased HDL cholesterol <0.9 mmol/l (35mg/dl).

(iv) Overweight and obesity categorized as overweight, BMI >25-30, obesity BMI >30-40, and morbid obesity BMI>40.

(v) Central obesity defined as per NCEP ATP III as waist circumference > 88cm in women and > 102cm in men.

(vi) Daily intake of fruits and vegetables defined as adequate if taking 5 or more servings per day.

(vii) Physical activity defined as adequate if participant does vigorous intensity activity for at least 10 min daily for 5 days a week.

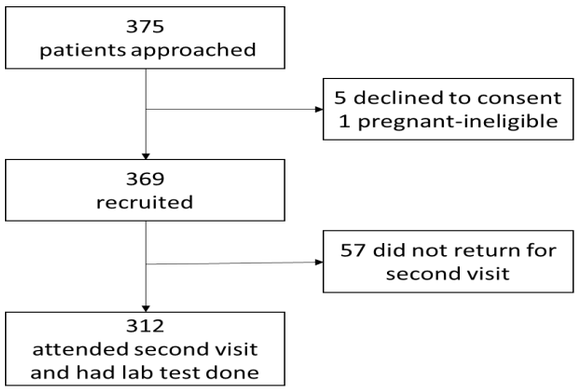
*Data analysis:* Overall description and summaries of the demographic, clinical characteristics and specific risk distribution of the study population were done as well as comparison by site. Group frequencies for categorical variables were compared using chi-square test or Fisher's exact test when counts were less than 5. For the continuous variables, comparison between the sites was done using analysis of variance comparing means. Comparison of medians was done using Kruskal Wallis rank test for variables which had a wide range of possible values including extreme measurements.

The cardiovascular risk score was categorized into three levels; low risk, medium risk and high risk. Comparisons of categorical variables were done using a chi square test. For all the tests done, a p-value less than 0.05 ($p<0.05$) was considered statistically significant. All the analysis was done using STATA® version 13.

## Results

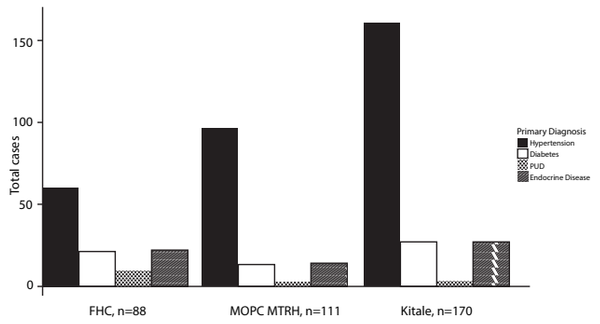
We recruited 369 patients out of the 375 that were approached. Of those approached five declined to give consent and one was excluded, because of pregnancy. Of these 369, a total of 312 attended the second appointment and had their blood samples taken for FBS and lipid profile (Figure 1).

**Figure 1:** Recruitment flow diagram




The distribution of these patients across the three clinics was equitable as planned with 24% being from FHC, 46% from Kitale County Hospital and 30% from MTRH. Majority of the patients were being treated for hypertension, while the rest had diabetes, other endocrine diseases, or peptic ulcer disease (Figure 2).

**Figure 2:** Primary diagnosis of patients in the three clinics




Of the 369 patients recruited, the mean age was 55.4 years, with 74.8% being women. Secondary or tertiary education was reported by only 48%, while 55% were unemployed. Majority of the patients were of low socio-economic status with 55.6% earning less than US$ 50 per month (Table 1). Of note is the fact that 84% of the patients were known to be hypertensive and on treatment.

**Table 1:** Characteristics of study participants

| Characteristics | | |
|---|---|---|
| Age | | |
| Mean (SD) | 55.4 (13.18) | |
| Range | 20 -96 | |
| Variable | Total (N=369) | (%) |
| Sex | | |
| Female | 276 | (74.8) |
| Male | 93 | (25.2) |
| Education | | |
| None | 39 | (10.6) |
| Primary | 153 | (41.4) |
| secondary | 108 | (29.3) |
| Tertiary | 69 | (18.7) |
| Marital status | | |
| Single | 25 | (6.8) |
| Married | 306 | (82.9) |
| Widowed | 38 | (10.3) |
| Current professional status | | |
| Unemployed | 203 | 55.0 |
| Formal Employment | 93 | 25.2 |
| Self-employed | 73 | 19.78 |
| Monthly income (USD) | | |
| 50/month or less | 205 | 55.56 |
| 50.01-200 | 94 | 25.4 |
| 200 and above | 70 | 18.9 |

The mean INTERHEART CVD risk score for the study patients was 10.7 (SD. 4.0) which denotes an overall medium cardiovascular risk. About half the patients studied had a medium risk while 10% had a high risk. MTRH and KCH had very similar distribution of patients into risk categories with most of them having medium risk. FHC had half the patients at low risk, which was comparably fewer than the other facilities (Table 2a).

**Table 2a:** CVD risk score by clinic

| INTERHEART risk level | Location | | | |
|---|---|---|---|---|
| | FHC | MOPC MTRH | Kitale | Total |
| Low risk n (%) | 38 (54.29) | 28 (33.33) | 48 (30.38) | 114 (36.54) |
| Medium risk | 23 (32.86) | 49 (58.33) | 94 (59.49) | 166(53.21) |
| High risk | 9 (12.86) | 7 (8.33) | 16 (10.13) | 32 10.26) |

There was no association found between CVD risk score and gender, employment status, income category, and reported physical activity. Waist circumference and BMI, however, were shown to be associated with the CVD risk score (Table 2b).

**Table 2b**: CVD risk category according to patient characteristics

| Attribute | Low risk | Medium risk | High risk | P-value |
|---|---|---|---|---|
| Total, n | 114 | 166 | 32 | |
| Sex, n (%) | | | | 0.103 |
| Male | 32 (28.1) | 35 (21.1) | 12 (37.5) | |
| Female | 82 (71.9) | 131 (78.9) | 20 (62.5) | |
| Occupation (%) | | | | 0.124 |
| Formally employed in office | 28 (24.6) | 35 (21.1) | 9 (28.1) | |
| Self employed | 28 (24.6) | 27 (16.3) | 6 (18.8) | |
| Casual laborer | 0 (0.0) | 7 (4.2) | 0 (0.0) | |
| Unemployed | 58 (50.9) | 97 (58.4) | 17 (53.1) | |
| Income category USD (%) | | | | 0.304 |
| <50 | 55 (48.2) | 85 (51.2) | 13 (40.6) | |
| >50-200 | 38 (33.3) | 56 (33.7) | 9 (28.1) | |
| >200 | 21 (18.4) | 25 (15.1) | 10 (31.2) | |
| BMI categories (%) | | | | 0.027 |
| Normal | 40 (35.1) | 35 (21.1) | 7 (21.9) | |
| Overweight and obese | 74 (64.9) | 131 (78.9) | 25 (78.1) | |
| Waist circumference (mean (sd) | 93.48 (17.87) | 100.37 (17.21) | 103.91 (12.22) | 0.001 |
| Vigorous physical activity = Yes (%) | 49 (43.0) | 86 (52.1) | 14 (43.8) | 0.286 |

The prevalence of dyslipidemia in this group of patients was high at 83.3%, while 72.9% and 64.8% had overweight/obesity and central obesity respectively. High waist circumference was significantly more prevalent in females than males. Diabetes was prevalent with 16.5% of the participants having confirmed diabetes.

Hypertension was the commonest individual risk factor, with 85% of the participants being hypertensive, with 55% of them being uncontrolled. Only one individual reported smoking cigarettes out of the whole sample (Table 3).

**Table 3:** Prevalence of individual CVD risk factors, overall and by gender

| Attribute | Overall 369 | Female 276 | Male 93 | P-value |
|---|---|---|---|---|
| Uncontrolled hypertension n (%) | 201 (54.5) | 149 (54.0) | 52 (55.9) | 0.747 |
| Diabetes = Yes (%) | 61 (16.5) | 36 (13.0) | 25 (26.9) | 0.002 |
| Dyslipidemia = Yes (%) | 260 (83.3) | 197 (84.5) | 63 (79.7) | 0.322 |
| BMI categories (%) | | | | 0.070 |
| Normal | 100 (27.2) | 68 (24.6) | 32 (34.4) | |
| Overweight and obese | 268 (72.8) | 207 (75.3) | 61 (65.6) | |
| Central obesity = Yes (%) | 239 (64.8) | 206 (74.6) | 33 (35.5) | 0.000 |
| Use tobacco (%) | | | | 0.000 |
| Yes | 1 (0.3) | 0 (0.0) | 1 (1.1) | |
| Never | 351 (95.1) | 270 (97.8) | 81 (87.1) | |
| Stopped | 17 (4.6) | 6 (2.2) | 11 (11.8) | |
| Adequate fruits and vegetables = Yes (%) | 94 (25.5) | 74 (26.8) | 20 (21.5) | 0.310 |
| Adequate vegetables = Yes (%) | 327 (88.6) | 247 (89.5) | 80 (86.0) | 0.362 |
| Adequate fruits = Yes (%) | 98 (26.6) | 78 (28.3) | 20 (21.5) | 0.202 |

## Discussion

This study found a significant number of patients attending medical outpatient clinics in western Kenya have a moderate to high CVD risk. We postulate that hypertension, which was the most prevalent risk factor in these patients is probably a main driver of the CVD risk. This is in keeping with studies done elsewhere in SSA that have shown higher CVD risk in patients with hypertension than in the general population (14).

Both central obesity as measured by waist circumference, and overweight and obesity as measured by BMI were found to be associated with higher CVD risk score. The INTERHEART study in Africa showed similar results but had shown a stronger correlation of central obesity with CVD risk than BMI. We did not power our study to look at these associations and are therefore unable to compare the two measures. A key difference between this study and the INTERHEART study in this respect is that the INTERHEART study group used waist-hip ratios while we used waist circumference to gauge central obesity. The utility of the waist circumference is a significant finding because measuring waist circumference is much simpler than BMI calculation and may be easier to implement in a busy MOPC (10). Almost all the patients in our study sample were non-smokers. Given that the Inter heart risk score gives the highest weight to cigarette smoking which was very rare in our study, in populations like our own, assessment of the other CVD risks was critical.

Dyslipidemia was found to be highly prevalent in this study population with both high LDL cholesterol and low HDL being common. This dyslipidemia prevalence is higher than that described by the National WHO STEP survey that was done in our community at around the same time as this study (7). The difference may be attributed to the nature of our sample and the high prevalence of hypertension in our study. Prevalence of diabetes in our study sample was also found to be higher than in the general population, perhaps because of the fact that our study is hospital based, and most of the participants had hypertension which is a risk factor for diabetes. This has been described similarly in western Africa (14).

Both the mean BMI and waist circumference were found to be high in this group, with both being significantly higher in women than men. This has been described in other studies in the country, including

work done amongst HIV patients in MTRH and the STEP survey (7,15).

The strength of our study is that it included patients from both public and private health facilities, and urban and rural settings. It thus has a good representation of patients in medical care within our region. We also used the cholesterol INTERHEART risk score which was partly developed in Africa with similar population. The INTERHEART score provides an overall picture of the risk category rather than just assessing individual risk factors. Lastly the sample size was adjusted for possible drop outs and hence the 312 patients who got laboratory tests done provided enough power to give valid prevalence estimates.

This study did have certain limitations. The fact that the study setting was in three clinics that all serve as referral sites may have led to sampling of sicker patients and hence reduced generalizability to primary care settings. The fact that majority of the patients in these clinics were being treated for hypertension makes it impossible to generalize these results to non-hypertensive individuals. Additionally, being a hospital based setting, there may have been reporting bias especially in revealing smoking status. Use of self-report to assess physical activity level rather than the more objective assessment of fitness level is also an important limitation of our study which may have led to underestimation of CVD risk.

In conclusion, patients attending MOPC for non-cardiac conditions do have significant CVD risk with key risk factors being hypertension, dyslipidemia and central obesity. Even under medical supervision, the prevalence of uncontrolled blood pressure, excessive body weight, too little exercise, apparently undetected diabetes mellitus, and adverse lipid profiles is striking. We recommend incorporation of CVD risk assessment into routine care in MOPC for early institution of CVD preventive measures in these patients. Additionally, the usefulness of waist circumference in assessing CVD risk should be emphasized to healthcare providers.

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***Declaration of interest:*** None.

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Original Paper

# Electrocardiographic Abnormalities among HIV Infected Adults attending The Comprehensive Care Center at Kenyatta National Hospital: An Analysis

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## Abstract

**Background:** Cardiovascular disease is a growing concern among the Human Immunodeficiency Virus (HIV) infected population. HIV positive individuals have a greater risk of both traditional cardiovascular risk factors and cardiovascular events, than non-HIV individuals. Various Electrocardiogram (ECG) abnormalities have been shown to be predictors for adverse cardiovascular outcomes. Resting ECG testing can be a convenient tool for cardiovascular screening and risk stratification. There is no data in Kenya on the prevalence and types of ECG abnormalities amongst HIV infected adults.

**Objectives:** The primary objective was to identify the prevalence and types of ECG abnormalities among HIV infected adults attending the Comprehensive Care Center at Kenyatta National Hospital (KNH). The secondary objective was to determine the association between the presence of ECG abnormalities and demographic characteristics, selected cardiovascular risk factors (hypertension, diabetes mellitus, smoking, obesity) and HIV related factors (the nadir CD4 cell count and antiretroviral therapy status) of the patients.

**Design:** This was a descriptive cross sectional study.

**Setting:** The study was conducted at the Comprehensive Care Center at Kenyatta National Hospital between April and May 2018.

**Methods:** Two hundred patients were recruited and a resting 12 lead ECG was recorded for each patient by standard procedure. The ECGs were interpreted as per the American Heart Association /American College of Cardiology (AHA/ACC) recommendations for the standardization and interpretation of the electrocardiogram.

**Results:** The average age was 44 years, 69.5% were female. Mean duration (from the time of diagnosis) of HIV infection since diagnosis was 101 months (SD 68.3). Ninety nine percent were on Highly Active Antiretroviral Therapy (HAART) of whom 12.7% were on second line HAART. Mean nadir CD4 cell count was 283.7 (SD 239.8). BMI was 26.3 (SD 5.6). Hypertension and type 2 diabetes were present in 20% and 2.5% respectively. An abnormal ECG was found in 68 (34%) participants. Arrhythmias were seen in 18.5%, T wave abnormalities in 7.5%, LVH and QTc prolongation were both present in 3.5% of participants. Conduction abnormalities were seen in 4.5% of participants. ST segment abnormalities and pathological Q waves were observed in 1.5% and 1% of all participants respectively. No association between any demographic and HIV factors with any ECG abnormality was detected.

**Conclusion:** Thirty four percent of HIV participants had at least one ECG abnormality. Minor abnormalities had the highest prevalence. Clinical significance of these ECG abnormalities among our HIV population still needs to be established.

**Key words**: ECG abnormalities, HIV, HIV prevalence

## Introduction

Sub-Saharan Africa (SSA) carries a huge burden of HIV infection and Kenya has the fourth largest epidemic in the World according to the United Nations Programme on HIV/AIDS (UNAIDS) 2017 report (1).

With the access to antiretroviral therapy, AIDS-related mortality has significantly reduced. HIV positive people live longer and cardiovascular disease has become one of the most common causes of morbidity and mortality. Both traditional cardiovascular risk factors, HIV related risk factors such as viral replication and opportunistic infections, as well as metabolic toxicity of antiretroviral drugs have been implicated in the development of cardiovascular disease (2-5).

It is important to screen these subset of patients due to increased incidence of atherosclerotic cardiovascular disease, more so in Western countries, which may lead to cardiomyopathy, myocarditis, pericardial disease and pulmonary arterial hypertension. Arrhythmias due to autonomic dysfunction or prolonged QT interval are predominant in Africa (6). In developing countries

where the resources are limited, resting ECG has been proposed to be a useful screening tool especially in asymptomatic heart disease. Studies have shown that up to 11% of silent myocardial ischemia among HIV positive patients can be seen on a resting ECG (7).

A large study in Europe of 4,518 HIV infected patients found a prevalence of any ECG abnormalities of 51% (8), is a significant predictor of cardiovascular events. In SSA, a higher prevalence of ECG abnormalities has been noted. In Zambia, a study including 243 asymptomatic HIV patients described a prevalence of 54%. The most common abnormalities were LVH and T wave changes (9). In Nigeria, two other studies documented a prevalence of 72% and 83% respectively and the most frequent abnormalities in both studies were sinus tachycardia, T wave changes and prolonged QTc (10,11). A higher rate of ECG abnormalities was observed among patients with a low CD4 count ≤ 350 (9-11).

Despite suggestions from the literature on the prognostic value of resting ECG testing among HIV positive individuals, it is not routinely done in this population. In Africa, very few studies have looked at the spectrum of electrocardiographic abnormalities in HIV patients and in Kenya none has been done. This study aims to fill this gap by giving a local prevalence and characteristics of ECG changes in our HIV infected population.

This study was approved by the Ethics and Research Committee of Kenyatta National Hospital/ University of Nairobi and it analyzed the ECG findings among ambulatory HIV infected patients in the Comprehensive Care Clinic (CCC) at KNH and their association with selected clinical factors.

## Materials and methods

This was a descriptive cross sectional study carried out at the Comprehensive Care Center, which is an outpatient HIV clinic at Kenyatta National Hospital. The study included HIV patients coming for their scheduled follow up visit who were ≥18 years and had given a written consent. Pregnant women and women in the postpartum period were excluded as they could have cardiac disease related to the peripartum period as well as patients with a known cardiac abnormality prior to the diagnosis of HIV.

The sample size was calculated using Fisher's formula

$$n = \frac{Z^2 \times P(1-P)}{d^2}$$

where n=desired sample size, Z=1.96 for 95% CI, d= desired precision (0.05), P= maximum prevalence of any ECG abnormalities reported in an African study (13.6%) (12). A minimum sample size of 178 was calculated.

After screening, a consecutive sampling was done. A face to face interview was conducted with the participants, to obtain socio-demographic data and their full medical history. Additional data was obtained from the patients' medical records such as selected traditional risk factors and HIV related factors. An anthropometric assessment and a resting ECG were done. The 12 lead ECG was recorded at a paper speed of 25mm/s and voltage gain of 10mm/mv using a 3 channel automated ECG machine, model MEM 3. The British Society for Cardiological Science and Technology (SCST) guidelines was followed (13). ECG findings were interpreted as per the AHA/ACC recommendations for the standardization and interpretation of the electrocardiogram (14-19). Lead II was used as the rhythm strip. Heart rate, P wave (presence, amplitude, duration), frontal plane QRS axis, PR interval, QRS complex (duration), QT interval, Q wave, T wave, R and S wave, ST segment changes were analyzed.

*Study variables:* An abnormal ECG was defined as the presence of the following: arrhythmias, AV conduction defects, ventricular conduction defects, chamber enlargement, QT abnormalities, repolarization abnormalities (ST segment changes, T wave changes), pathological Q waves and abnormal axis deviation. Cardiovascular risk factors were defined as the presence of hypertension, diabetes, smoking and obesity that were documented in the patient's medical records. HIV related factors were a nadir CD4 cell count <200 and exposure to antiretroviral therapy both obtained from the patient's medical records.

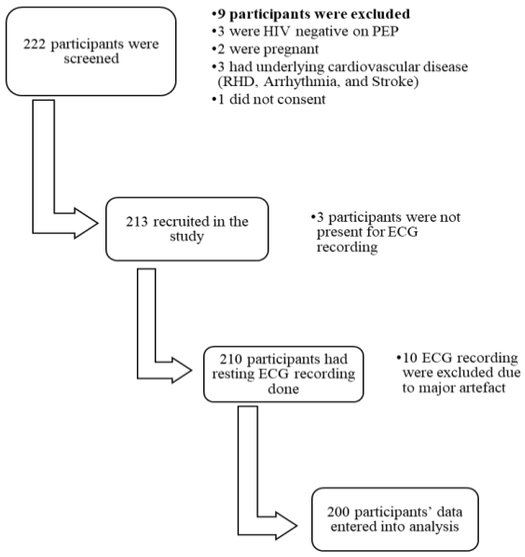
*Data analysis:* The overall prevalence of ECG abnormalities was calculated as the proportion of patients with at least one abnormality on the ECG and presented as a percentage, and 95% confidence interval was determined. The type of ECG abnormalities was calculated as the proportion of patients with abnormal ECG and presented as a percentage. Bivariate analysis was used to test the association between the presence of ECG abnormalities and the demographic characteristics (gender), selected cardiovascular risk factors (hypertension, diabetes, smoking, obesity) and HIV related factors (nadir CD4 cell count, antiretroviral therapy status) respectively. A P-value <0.05 was considered statistically significant.

*Ethical considerations:* The study was undertaken after approval by the Department of Clinical Medicine and Therapeutics as well as the Ethical Committee of Kenyatta National Hospital/University of Nairobi (approval number P14/01/2018). Participation in the study was voluntary and only participants who gave an informed written consent were recruited.

## Results

Between April and May 2018, 222 adults were screened. Two hundred and thirteen participants met the inclusion criteria and were recruited in the study. Two hundred and ten were enrolled for resting ECG recording and the final analysis of the study included 200 participants.

**Figure 1:** Flow diagram of patients' recruitment




*Baseline characteristics of the study participants:* The mean age of all participants was 44.0 years (SD 10.1 years) and ranged from 20 to 73 years. Majority of the participants (64%) were between 30 and 50 years of age. One hundred and thirty nine participants (69.5%) were female (Table 1).

**Table 1:** Baseline characteristics of study participants

| Variable | Total (%) | Female (%) | Male (%) |
|---|---|---|---|
| Mean BMI Kg/m$^2$ | 26.3 (SD 5.5) | 26.9 (SD 5.6) | 25.1 (SD 5.1) |
| BMI category n (%) | | | |
| Underweight (<18.5Kg/m$^2$) | 9 (4.5) | 6 (4.3) | 3 (4.9) |
| Normal (18.5-24.9Kg/m$^2$) | 81 (40.5) | 50 (36) | 31 (50.8) |
| Overweight (25-29.9Kg/m$^2$) | 60 (30) | 46 (33.1) | 14 (23) |
| Obesity (≥30Kg/m$^2$) | 50 (25) | 37 (26.6) | 13 (21.3) |
| Mean duration of HIV infection (months) | 101 (SD 68.3) | 106.2 (SD 65.8) | 89.3 (SD 72.8) |
| Mean duration of HAART (months) | 84.4 (SD 60.4) | 86.7 (SD 56.4) | 79.2 (SD 68.7) |
| Smoking status n (%) | | | |
| Non smoker | 181 (90.5) | 136 (97.8) | 45 (73.8) |
| Former smoker | 16 (8) | 3 (2.2) | 13 (21.3) |
| Current smoker | 3 (1.5) | 0 | 3 (4.9) |
| Alcohol use n (%) | 28 (14.0) | 14 (10) | 14 (22.95) |
| Type 2 diabetes n (%) | 5 (2.5) | 3 (2.15) | 2 (3.3) |
| Hypertension n (%) | 40 (20.0) | 26 (18.7) | 14 (22.95) |
| Recent viral load | 179 | | |
| <1000 | 162 | 118 | 44 |
| >1000 | 17 | 9 | 8 |
| Nadir CD4 cell count | 163 | | |
| <200 | 72 | 46 | 26 |
| ≥200 | 91 | 68 | 23 |
| Current HAART regimen | 197 | | |
| First line | 172 | 119 | 53 |
| Second line | 25 | 17 | 8 |

**Table 2:** Prevalence of ECG abnormalities among 200 HIV infected adults at CCC/KNH

| Variables | Total N=200 (%) |
|---|---|
| Any ECG abnormality | 68 (34) [CI 27.8-40.8] |
| Arrhythmia | 37 (18.5) |
| QRS axis deviation | 7 (3.5) |
| Chamber enlargement | 8 (4) |
| Atrioventricular block | 7 (3.5) |
| Intraventricular block | 2 (1) |
| QTc prolongation | 7 (3.5) |
| T wave changes | 15 (7.5) |
| ST segment changes | 3 (1.5) |
| Pathological Q waves | 2 (1) |

**Table 3**: Types of ECG abnormalities among 68 HIV infected adults with any ECG abnormality

| Type of ECG abnormalities | Category prevalence N=68 | Female | Male |
|---|---|---|---|
| Arrhythmias | 37 (54.4) | 21(56.8) | 16 (43.2) |
| Supraventricular | 32 (47.0) | 18 (56.3) | 14 (43.7) |
| Sinus bradycardia | 29 (42.6) | 15 (51.7) | 14 (48.3) |
| Sinus tachycardia | 2 | 2 | 0 |
| Premature atrial contraction | 1 | 1 | 0 |
| Ventricular (premature ventricular contraction) | 4 | 3 | 1 |
| Junctional | 1 | 0 | 1 |
| Axis deviation | 7 | 3 | 4 |
| Left axis deviation | 3 | 2 | 1 |
| Right axis deviation | 4 | 1 | 3 |
| Chamber enlargement | 8 | 4 | 4 |
| Left ventricular hypertrophy | 7 | 4 | 3 |
| Right ventricular hypertrophy | 1 | 0 | 1 |
| Atrial enlargement | 0 | 0 | 0 |
| AV conduction abnormality | 7 | 3 | 4 |
| First degree AV block | 6 | 2 | 4 |
| Mobitz type II block | 1 | 1 | 0 |
| IV conduction abnormality | 2 | 1 | 1 |
| Bifascular block | 1 | 1 | 0 |
| Left bundle branch block | 1 | 0 | 1 |
| ST segment abnormality | 3 | 1 | 2 |
| ST depression | 1 | 1 | 0 |
| ST elevation | 2 | 0 | 2 |
| T wave abnormality | 15 | 11 | 4 |
| T wave flattening | 7 | 7 | 0 |
| T wave inversion | 8 | 4 | 4 |
| Pathological Q waves | 2 | 1 | 1 |
| QTc prolongation | 7 | 6 | 1 |

**Table 4**: Association of ECG abnormalities with demographics, selected cardiovascular risk factors and HIV-related clinical characteristics

| Variable | ECG abnormal (%) | ECG normal (%) | COR (95% CI) | P-value |
|---|---|---|---|---|
| Gender | | | | |
| Female | 43 (63.2) | 96 (72.7) | 0.65 (0.35 –1.20) | 0.22 |
| Male | 25 (36.8) | 36 (27.3) | | |
| HAART experienced | | | | |
| Yes | 68 (100%) | 129 (97.7) | Undefined | |
| No | 0 | 3 (2.3) | | |
| Lowest CD4 Count | | | | |
| <200 | 26 (38.2) | 46 (43.8) | 1.04 (0.55-1.99) | 1.00 |
| ≥200 | 32 (61.8) | 59 (56.2) | | |
| Diabetes | | | | |
| Yes | 1 (1.5) | 4 (3.0) | 0.48 (0.05 – 4.36) | 0.57 |
| No | 67 (98.5) | 128 (97.0) | | |
| Hypertension | | | | |
| Yes | 10 (14.7) | 30 (22.7) | 0.59 (0.27 – 1.29) | 0.24 |
| No | 58 (85.3) | 102 (77.3) | | |
| Obesity (BMI ≥30.0) | | | | |
| Yes | 15 (22.1) | 35 (26.5) | 0.78 (0.39-1.57) | 0.61 |
| No | 53 (77.9) | 97 (73.5) | | |
| Smoking status | | | | |
| Ever smoked | 7 (10.3) | 12 (9.1) | 1.15 (0.43 – 3.06) | 0.98 |
| Non smoker | 61 (89.7) | 120 (90.9) | | |

## Discussion

Thirty four percent of the participants had at least one ECG abnormality and majority had minor abnormalities: sinus bradycardia, non-specific ST-T changes, LVH and QTc interval prolongation.

Sinus bradycardia was the commonest abnormality at 42.6%. This high prevalence of sinus bradycardia could be either physiologic, drug induced or as a result of cardiac autonomic dysfunction which is common in HIV infected population. However, none of the participants were symptomatic. Major arrhythmias such as atrial fibrillation, atrial flutter, supraventricular and ventricular tachycardia were absent; our population had a low rate of comorbidities and some of these arrhythmias are paroxysmal in nature.

Minor and major ST/T abnormalities have been shown to be a significant predictor of cardiovascular events among HIV population [HR 1.58, 1.91 respectively] (8). Repolarization abnormalities and pathological Q waves represented 29.4% (20/68) of all ECG abnormalities. The most common type of abnormality was non-specific T wave changes (22.1%). ST elevation was found in two participants and this was attributed to early repolarization. Repolarization abnormalities in our study were mostly non-specific and could have also been associated with electrolytes disturbances. There were no abnormalities suggestive of ischemic changes or pericarditis.

Left ventricular hypertrophy, using Sokolow-Lyon criteria, was the most common type of chamber enlargement accounting for 87.5%. Four out of seven participants who had LVH were hypertensive. LVH is significant correlated to hypertension and has been shown to be a strong predictor of cardiovascular events and mortality in the HIV infected population [RR 1.37] (8).

QTc prolongation, using Bazett's formula, represented 10.3% of all ECG abnormalities. QTc prolongation is common in HIV population and it seems to be related to common factors such as female gender, increasing age, hypertension (LVH), diabetes, duration of HIV; with a significant prolongation after the 4$^{th}$ year of HIV infection and medications (20). QTc prolongation has been shown to be an independent risk of ventricular arrhythmias and sudden cardiac death (20).

The prevalence of ECG abnormalities in our study was much lower compared to a study done in Zambia by Kabwe *et al* (9) that evaluated subclinical CVD in 243 asymptomatic HIV infected patients, mean age of the participants was 42 years, females 58.5%, hypertension 16%, diabetes 3%, current smokers 3%, chronic kidney disease 39.5% and dyslipidemia 23%. The prevalence of any ECG abnormalities using the Minnesota code was 54% (major abnormalities 33% and minor abnormalities 21%. There was a correlation between CD4 cell count less than 350 and an increasing risk of ECG abnormalities. Diabetes,

smoking, duration of HIV and exposure to PIs did not show any association. The high prevalence of kidney disease and dyslipidemia in addition to the different methods of ECG analysis (Minnesota code) could explain the higher prevalence of ECG abnormalities compared to our study.

Prevalence of 34% was higher compared to 14.7% found in a study done in south India among 150 HIV positive patients (24). This study had strict inclusion criteria that could explain the low prevalence of ECG abnormalities. The participants were HAART naïve, were aged between 18 and 55 years with no comorbidities as hypertension, diabetes, any heart disease and family history of CVD were excluded. Although age and gender were suggestive of a trend towards a higher risk of having ECG abnormalities, none of the associations were statistically significant. Being a prevalence study, it was not powered enough for associations. This differ from the literature where studies have shown that being either on NRTI especially the older drugs such as stavudine, didanosine and zidovudine or being on a PI based HAART regimen was associated with a significant increased risk of cardiovascular events (21-23) as well as the severity of immunosuppression especially when the CD4 cell count is less than 200 cells/$mm^3$ (3,4).

This is the first study in Kenya describing the prevalence of resting ECG abnormalities among HIV infected adults and will serve as a baseline for future studies. The following limitations were noted in this cross-sectional study: (i) Paroxysmal ECG abnormalities may have been under-reported; (ii) No comparison group for this study to determine the role of HIV infection in increasing the risk of ECG abnormality in this population.

## Conclusions

Thirty four percent of the participants had at least one ECG abnormality. Majority of these abnormalities were minor. There was no factor that was found to be associated with ECG abnormalities. Clinical significance of these ECG abnormalities among our HIV population still needs to be established.

## Recommendations

A prospective study following up cardiovascular adverse events of HIV patients with identified ECG abnormalities is needed to define their clinical significance. The ideal study design would have been to do age/sex matched comparisons between the two groups and is a limitation of the present study. LVH is a well-documented finding in HTN patients and may be incidental. Dyslipidemia should be assessed, as it is a precursor to many cardiac risk factors. A study with serial ECG testing or a 24 hour Holter monitoring might have a role due to the paroxysmal nature of some ECG abnormalities.

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Original Paper

# Burden of Cardiovascular Diseases among Elderly Patients admitted at Moi Teaching and Referral Hospital, Eldoret, Kenya

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## Abstract

**Background:** Cardiovascular Disease (CVD) is the leading cause of global mortality. The elderly bear the highest risk due to their unique age related physiological perturbations of the Cardiovascular System (CVS) that make them vulnerable to quick decompensation and death. This segment of population in Sub-Saharan Africa (SSA) is growing due to improved standards of living.
**Objective:** To determine the prevalence of CVD and associated risk factor profile in patients aged 60 years and above admitted at Moi Teaching and Referral Hospital (MTRH).
**Design:** This was a cross sectional survey.
**Methods:** The study was conducted in MTRH adult wards targeting patients aged 60 years and above recruited using systematic random sampling. Structured interviewer administered questionnaires were used to collect socio-demographic, clinical and laboratory data from 336 consenting adults between May and October 2018. A resting 12-lead electrocardiogram (ECG) and a standard Trans–Thoracic Echocardiogram (TTE) were done. Presence of CV risk factors, Left Ventricular Systolic Dysfunction (LVSD – EF <50%), Primary Valve Disease (PVD), cardiac rhythm abnormalities and presence of pathological Q waves on ECG were all analyzed. Descriptive statistics were calculated for continuous variables and frequency listings used for categorical variables. Interval estimates for primary outcomes were calculated at 95% confidence and association between categorical variables was assessed using the Pearson's Chi Square Test. A P-value of less than 0.005 was considered statistically significant.
**Results:** Fifty percent of the study participants had some form of documented cardiac abnormality. There were 184 cases of different cardiovascular diseases. Males comprised 60% of the participants and the median age was 71 years. The prevalence of LVSD was 17.86% (95% CI: 13.91, 22.38) while primary valve disease was 20.23% (95%CI: 16.62, 25.57). Rhythm abnormalities were frequent with atrial fibrillation predominating at 13.7%. Only 2 (0.59%) participants had pathological Q waves. Traditional CV risks present included hypertension at 44.3%, cigarette smoking at 27.1%, hyperlipidemia at 26.8%, obesity and overweight at 25.6%, Diabetes Mellitus (DM) at 15.5%, chronic kidney disease at 5.4% and family history of sudden cardiac death at 4.5%. Only DM and cigarette smoking were significantly associated with presence of LVSD and PVD.
**Conclusion:** There was a high prevalence of CVD and associated risk factors in elderly patients admitted at MTRH.

**Key words:** Cardiovascular disease, Cardiovascular risk, Elderly, Left ventricular systolic dysfunction, Aortic sclerosis, Atrial fibrillation

## Introduction

Cardiovascular Disease (CVD) is on the rise globally with significant associated morbidity and mortality (1). Most of the CVD mortalities (80%) occur in the low and middle income countries (2). The elderly population has the highest risk of cardiovascular disease as they have unique age-related changes to their physiology. These changes affect structure and function of the cardiovascular system leading to a higher incidence and prevalence of these diseases (3). Sub-Saharan Africa (SSA) is undergoing an epidemiological transition with CVD emerging as a significant cause of morbidity and mortality, especially in the elderly

population (2,4). This has been attributed to the rise in cardiovascular risk factors among the population (5). As the elderly population in SSA tend to be largely dependent on their younger working family members for livelihood and out of pocket healthcare support, this has social and economic implications on families and the nation at large (6). Therefore, it is of utmost importance to highlight the magnitude of the cardiovascular diseases in the elderly population in SSA where access to quality care is not always available (7). This study set out to establish the prevalence of CVD plus associated risk factor profile among elderly patients admitted at Moi Teaching and Referral Hospital (MTRH).

## Materials and methods

This was a descriptive cross-sectional study of elderly patients aged 60 years and above admitted in all the adult inpatient wards of MTRH. We excluded patients with severe chest injuries or burns and those admitted at the Intensive Critical Care Unit (ICU) due to technical challenges with cardiovascular imaging. A sample size of 338 participants was derived using the Fisher's Formula based on projected CVD prevalence of 70% as per Yazdanyar *et al* (8) study with provision for missing data. Systematic random sampling was used to select study participants where the $K^{th}$ case was every $3^{rd}$ patient that met the eligibility criteria between May and October 2018. Approval was received from Moi University/MTRH ethical review committee and the study was conducted according to the Helsinki Declaration. There was linkage to care for the newly identified cases before discharge.

Data was collected on standardized questionnaires from all consenting patients who met the inclusion criteria. We documented participants' socio-demographic information and traditional CVD risk factors including alcohol use, cigarette smoking and family-social history of cardiac disease. A thorough physical examination was then conducted that included measurements of height, weight, waist and hip circumference. Blood pressure was measured using an automatic devise (OMRON M2) by taking three readings, one minute apart, and the average of the last two recorded. A Random Blood Sugar (RBS) was measured (On Call Plus point of care digital devise). Diabetes mellitus was defined as RBS greater than 11.1mmol/L with symptoms of hyperglycemia or being on anti-diabetic drugs. Two milliliters of venous blood was drawn into a plain bottle for lipid profiles assay calorimetrically (COBAS INTEGRA 400 plus) at MTRH International Organization of Standardization (ISO) certified laboratory. The tests done were total cholesterol, triglycerides (TG), high-density lipoproteins cholesterols and Low-Density Lipoprotein cholesterol (LDLc) derived using the Friedewald formula. Hyperlipidemia was defined as LDLc greater than 2.59mmol/L and TG greater than 2.30mmol/L. A standard 12 lead ECG was then done using a portable Philips machine followed by a standard echocardiogram (Philips CX50). All ECG and echocardiogram images were archived on an external hard drive and interpreted with the help of a cardiologist.

Data was analyzed using STATA version 15.0® with descriptive statistics being calculated for continuous and frequency listings used for categorical variables. The 95% confidence interval was used to determine the interval estimate for the primary outcomes. Chi square test was used to assess association between categorical variables while Wilcoxon rank sum test was used for continuous variables. P-values of less than 0.05 were considered to be statistically significant.

## Results

Out of a population of 1044 participants screened 336 were recruited and analyzed. The study population was elderly with a median age of 71(IQR 64, 78) and most participants were male 171 (57%). Half of the patients had a history of alcohol use. Majority of the study population had a normal Body Mass Index (BMI). Sixty three (18.8%) and twenty three (6.8%) were overweight and obese respectively. Among fifty-five participants (16.3%) with pre-existing heart disease, 33 (60%) were in acute decompensated heart failure.

**Table 1**: Socio-demographic and clinical characteristics of the study population

| Socio-demographic parameter | | (n=336) |
|---|---|---|
| Median age – 71; IQR (64, 78) | | |
| Age distribution (years) | Frequency | (%) |
| 60 – 70 | 164 | 49 |
| 71 – 80 | 113 | 34 |
| 81 – 90 | 44 | 13 |
| > 90 | 15 | 4 |
| Gender | | |
| Male | 191 | 57 |
| Female | 145 | 43 |
| Alcohol use | | |
| No use | 168 | 50 |
| Use | 168 | 50 |
| Cigarette smoking | | |
| Use | 91 | 27.1 |
| No use | 245 | 72.9 |
| Pre-existing heart disease | (n = 336) | |
| Yes | 55 | 16.3 |
| No | 281 | 83.6 |
| Acute decompensated heart failure | (n = 55) | |
| Yes | 33 | 60 |
| No | 22 | 40 |
| Wards admitted | (n=336) | |
| Medical wards | 219 | 65 |
| Surgical & gynaecological wards | 117 | 35 |
| BMI | Median BMI 21.5; IQR | (20,25) |
| BMI distribution | (n=336) | |
| Underweight | 19 | 5.7 |
| Normal | 231 | 68.8 |
| Overweight | 63 | 18.8 |
| Obese | 23 | 6.8 |

Traditional cardiovascular risk profile

Hypertension was the most prevalent traditional cardiovascular risk at 44.3%. Ninety one (27.1%) had a significant smoking history. Notably, 52 (15.5%) of the participants had diabetes mellitus. The least common risk factor was a family history of premature cardiac death at 4.5%.

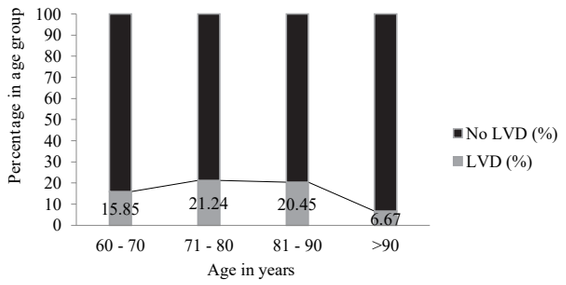
**Table 2:** Traditional cardiovascular risk profile of the study population (n=336)

| Risk factor | Frequency | (%) |
|---|---|---|
| Hypertension | 149 | 44.3 |
| Cigarette smoking | 91 | 27.1 |
| Hyperlipidemia | 90 | 26.8 |
| Obesity/Overweight | 86 | 25.6 |
| Diabetes | 52 | 15.5 |
| Chronic kidney disease | 18 | 5.4 |
| Family history | 15 | 4.5 |

Assessment of the 10 year cardiovascular risk was done using the Multi-Ethnic Study of Atherosclerosis (MESA) without coronary artery calcification scores via an online calculator (UpToDate.Inc). Thirty-one participants were not assessed because they were above the age of 85 years. Three hundred and five participants were assessed. Out of these, 279 (91%) had a 10 year cardiovascular risk of less than 15% whereas 26 (9%) had a high risk of greater than or equal to 15%.

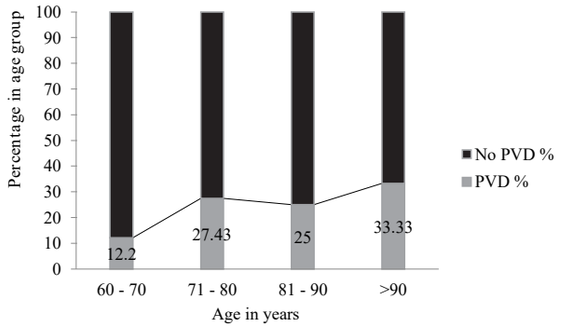
*Prevalence of left ventricular systolic dysfunction (LVSD):* A total of 60 participants (17.9%) had LVSD (95% CI: 13.91, 22.38). There was a variation in the distribution of LVSD across the different age groups with highest prevalence being in the 71 – 80 year age group.

**Figure 1**: Age based proportion of left ventricular systolic dysfunction




*Prevalence and characteristics of primary valve disease:* A total of 68 (20.23%) participants had primary valve disease (95% CI: 16.62, 25.57) with the highest proportion across the age groups being reported in the persons aged above 90 years in whom 33.33% had primary valve disease.

**Figure 2**: Age based proportion of primary valve disease




Aortic valve involvement was seen in 57 (83%) patients while the mitral valve was involved in 5 (7.4%) patients. Involvement of both valves was seen in 6 (8.8%) patients, with features of rheumatic aetiology (World Heart Federation criteria) (9). Haemodynamic assessment using pulsed wave and spectral Doppler flows revealed only 5 (1.49%) lesions to be of significance despite the pooled prevalence of 68 (20.23%). This mainly involved the aortic valve. Twenty-six (7.7%) had sclerosis with no haemodynamic significance and 31 (9.23%) had aortic regurgitation.

*Prevalence of cardiac rhythm abnormalities and pathological Q waves:* Sixty-five (19.3%) participants had abnormal rhythms. Atrial fibrillation was commonest rhythm abnormality, present in 46 (13.7%) participants. Only 2 (0.5%) participants had pathological Q waves.

**Table 3:** Cardiac rhythms identified in the study population (n=336)

| Cardiac rhythm | Frequency | (%) |
|---|---|---|
| Sinus rhythm | 268 | 79.8 |
| Normal sinus | 206 | 61.3 |
| Sinus bradycardia | 56 | 16.7 |
| Sinus tachycardia | 6 | 1.8 |
| Supraventricular rhythm | 54 | 16.1 |
| Atrial fibrillation | 46 | 13.7 |
| Atrial flutter | 6 | 1.8 |
| MFAT*& junctional | 2 | 0.6 |
| Others | | |
| Heart blocks | 11 | 3.3 |
| Ventricular tachycardia | 1 | 0.3 |
| Ventricular paced rhythms | 2 | 0.6 |

*MFAT – Multifocal Atrial Tachycardia

*Association between categorical variables:* Analysis of association using the Pearson's chi square test of the traditional cardiovascular risk factors with left ventricular systolic dysfunction and primary valvular disease found that only DM and cigarette smoking were significantly associated with presence of LVSD and PVD with P-values of 0.024 and 0.033 respectively.

**Table 4:** Cardiovascular risk factor association with left ventricular systolic dysfunction and primary valvular disease

| | Left ventricular dysfunction | | Chi square P-value | Valvular disease | | Chi square P-value |
|---|---|---|---|---|---|---|
| Variable | Absent | Present | | Absent | Present | |
| | Freq (Row %) | Freq (Row %) | | Freq (Row %) | Freq (Row %) | |
| Gender | | | 0.797 | | | 0.304 |
| Female | 120 (82.8) | 25 (17.2) | | 111 (76.6) | 34 (23.4) | |
| Male | 156 (81.7) | 35 (18.3) | | 155 (81.2) | 36 (18.8) | |
| BMI status | | | 0.915 | | | 0.394 |
| Normal | 189 (81.8) | 42 (18.2) | | 177(76.6) | 54 (23.4) | |
| Obese | 20 (87) | 3 (13) | | 20 (87) | 3 (13) | |
| Overweight | 52 (82.5) | 11 (17.5) | | 53 (84.1) | 10 (15.9) | |
| Underweight | 15 (78.9) | 4 (21.1) | | 16 (84.2) | 3 (15.8) | |
| DM | | | 0.024 | | | 0.073 |
| No | 239 (84.2) | 45 (15.8) | | 220 (77.5) | 64 (22.5) | |
| Yes | 37 (71.2) | 15 (28.8) | | 46 (88.5) | 6 (11.5) | |
| Hyperlipidemia | | | 0.73 | | | 0.150 |
| No | 201 (81.7) | 45 (18.3) | | 190 (77.2) | 56 (22.8) | |
| Yes | 75 (83.3) | 15 (16.7) | | 76 (84.4) | 14 (15.6) | |
| HPTN | | | 0.208 | | | 0.424 |
| No | 158 (84.5) | 29 (15.5) | | 151 (80.7) | 36 (19.3) | |
| Yes | 118 (79.2) | 31 (20.8) | | 115 (77.2) | 34 (22.8) | |
| Cigarette use | | | 0.575 | | | 0.033 |
| No | 203 (82.9) | 42 (17.1) | | 201 (82) | 44 (18) | |
| Yes | 73 (80.2) | 18 (19.8) | | 65 (71.4) | 26 (28.6) | |
| Alcohol use | | | 1.000 | | | 0.591 |
| No | 138 (82.1) | 30 (17.9) | | 135 (80.4) | 33 (19.6) | |
| Yes | 138 (82.1) | 30 (17.9) | | 131 (78) | 37 (22) | |
| Family Hx | | | 0.362 | | | 0.935 |
| No | 265 (82.6) | 56 (17.4) | | 254 (79.1) | 67 (20.9) | |
| Yes | 11 (73.3) | 4 (26.7) | | 12 (80) | 3 (20) | |
| CKD | | | 0.259 | | | 0.655 |
| No | 263 (82.7) | 55 (17.3) | | 251 (78.9) | 67 (21.1) | |
| Yes | 13 (72.2) | 5 (27.8) | | 15 (83.3) | 3 (16.7) | |

*CKD-Chronic Kidney Disease

## Discussion

There was a very high prevalence of CVD in our population of elderly patients seeking care at MTRH, some of whom were hospitalized for non-cardiac related morbidities. Majority had advanced age with a median of 71 years. One hundred and eighty-four (50%) cases of structural and rhythm abnormalities were documented with all the individual components of cardiac disease studied being equally represented. Except for the 30 participants who had LVSD with acute decompensation, the vast majority tended to be asymptomatic. The population was equally overburdened with traditional CVD risk factors that may explain many of the documented CVDs.

A prevalence of 17.86% for LVSD in our population was comparable to a study done by Ogah (10) in Nigeria where the prevalence of LVSD among hypertensive patients was found to be 18.1%. Notably however, their study population was younger than our study population (56±12.7). Secondly, they only looked at the prevalence in hypertensive patients. The prevalence of hypertension in our study was 44.3%; slightly less than half of the entire study population. Boonman-de Winter *et al* (11) in Netherlands studied the prevalence of LVSD in diabetic patients who were aged 60 years and above. They found a prevalence of 25.8% which was higher than the one we found. However, only 15.4% of our participants had diabetes. Heart failure with reduced ejection fraction is frequently associated with diabetes mellitus and both atherosclerotic and non-atherosclerotic pathways have been well described in its pathogenesis over the years (12). We also found that the frequency of LVSD tended to increase with advancing age. This finding compares with other studies that have looked at ventricular dysfunction in the elderly. The Meta-analysis Global Group in Chronic Heart Failure (MAGGIC) found that there is a higher prevalence of Left Ventricular Diastolic Dysfunction (LVDD), at almost 60% among heart failure patients. Whereas we did not interrogate LV diastolic dysfunction in our study, LVSD is important as it was shown in their study to be associated with higher mortality.

Primary degenerative valve disease has been described to occur with age with the most common valve affected being the aortic valve. Aortic valve sclerosis without stenosis is common in elderly patients (13). In our study, we found the prevalence of primary valve disease to be 20.23%, with the aortic valve involvement in 83% of the participants. High atherosclerotic risk associated even with asymptomatic cases makes the finding of a prevalence of primary valve disease of 20.23% significant. Comparatively, in the cardiovascular health study, aortic valve sclerosis was present in 29% of participants aged 65 years and above (14). In contrast, another study with a higher mean age of 82 found a prevalence of 42% (15). The prevalence of 1.49% for aortic stenosis in our study was lower than that found in both of these studies. A lower prevalence of aortic valve stenosis has been reported in the Black population than in Caucasians in the United States in a study done by Nkomo (16). It is not clear whether there is a genetic component that makes the Black race less likely to get aortic stenosis. Our study participants were mainly black Africans. Notably, Rheumatic Heart Disease (RHD) was not found to be a major contributor to valve disease in our study.

The prevalence of AF in our study was 13.7%. This was high in comparison to other studies done in Sub-Saharan Africa (SSA). A study done in Tanzania by Dewhurst (17) found a prevalence of 0.7% in persons aged 70 years and above. However, this was a community based survey and reported what they called a strikingly low prevalence of AF among elderly persons in Tanzania. The fact that our study was a hospital based can account for the difference in findings as persons visiting a hospital are likely to be sicker and may have factors predisposing to AF. Secondly, 16.3% of our participants had pre-existing heart disease. Stambler and Ngunga (18) in a review of the epidemiology of atrial fibrillation in Africa reported that the prevalence of AF in SSA is low but is expected to increase. They attributed the low prevalence to diagnostic challenges and poor access to healthcare. They projected that as diagnostic abilities improve and as more patients are able to seek better healthcare, the prevalence would rise. Non-Valvular AF (NVAF) is commonly found in elderly patients than Valvular Atrial Fibrillation (VAF). This was the same finding in our study. A study done in Nairobi, Kenya by Shavadia and Yonga (19) found that NVAF predominated VAF in their study population with hypertension and diabetes being the most common co-morbidities. The mean age of their study population was 67 ± 17 years and mainly recruited high-income participants at a tertiary urban private hospital unlike our participants who were mainly rural farmers. The SIGNAL study done at MTRH that looked at 150 participants with atrial fibrillation found that those that had NVAF were more likely to have co-morbid hypertension. Diabetes was not a common co-morbidity in their study. The participants with NVAF were 30 years older than those with VAF (68 vs 38 years, $P < .001$) (20).

CVD risk factor in our population was equally high with hypertension being most prevalent at 44.3%. This compares with what was noted in the Kenya STEPS survey that found the overall prevalence of hypertension to be 24% with the highest being among those aged 60 – 69 years at 53% (5). The Kenya STEPS survey found that 27.8% of Kenyans were either obese or overweight. The Tanzania STEPS survey also

found a similar prevalence of 26%. These findings are comparable to our study where we found that 25.6% of our study population was either obese or overweight. Globally, CVD affects 32.2% of all persons with T2DM and is one of the drivers of mortality in diabetes mellitus accounting for half of all deaths (12). The prevalence of diabetes in our study was high at 15.48%. The national prevalence of diabetes as at 2010 was estimated to be 3.3% though it has been said that it is likely an underestimation as it is based on regional projections and about 60% of persons with diabetes present to health facilities with non-specific symptoms at the point of diagnosis (19). The prevalence of diabetes in the Kenya STEPS survey was found to be 3.1% in the general population but this figure rose to 7% in those aged 60 – 69 years. This contrast could be due to the fact that our population was of hospital patients as opposed to the STEPS survey ones that were community dwellers. In spite of the high cardiovascular risk profile among our participants, only 2 (0.5%) had pathological Q waves on their electrocardiograms. A study by Godsk (22) found that even small Q waves and in particular large Q waves were associated with high risk of ischaemic heart disease and mortality in a low risk population. This was a surprise finding in view of the high CVD burden seen in our population but it is a known fact that Coronary Artery Disease (CAD) is uncommon in black Africans.

## Limitations of the study

Our study was limited by the fact that the cardiovascular abnormalities were not mutually exclusive as one participant may have had more than one cardiovascular disease or risk profile. Also, the fact that the electrocardiograms were done on spot, some paroxysmal rhythm abnormalities may have been missed.

## Conclusion and recommendation

There was a high prevalence of CVD and associated risk factors in elderly patients admitted at MTRH. We recommend routine and opportunistic screening and management of cardiovascular disease and risk factors in all admitted elderly patients. Future longitudinal studies in this population should also seek to evaluate cardiovascular outcomes like strokes, acute coronary events and cardiovascular death.

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Original Paper

# Thyroid Dysfunction among Patients with Type 2 Diabetes Mellitus at Moi Teaching and Referral Hospital, Eldoret, Kenya

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## Abstract

**Background:** Thyroid dysfunction is more prevalent among patients with diabetes (10-24%) compared to the general population (2-7%). Coexistence of thyroid disorders among patients with diabetes results in impaired lipid metabolism, endothelial dysfunction and impaired glycemic control. These risk factors have been implicated in worsening of cardiovascular disease which is the leading cause of death in diabetes. Early recognition and treatment of thyroid dysfunction in diabetes is important for mitigation of associated cardiac complications. Whereas diabetes is common in our region, little is known about the prevalence of thyroid dysfunction among patients with diabetes.

**Objectives:** To determine the prevalence and clinical correlates for thyroid dysfunction among patients with Type 2 Diabetes Mellitus (T2DM) in Moi Teaching and Referral Hospital (MTRH).

**Design:** This was a cross-sectional study.

**Methods:** The study was conducted at the diabetes outpatient clinic in MTRH between February and April 2018. The study population included 2500 ambulatory patients aged 35 years and above at the time of diagnosis with T2DM. A total of 368 participants were enrolled by systematic random sampling. Structured interviewer administered questionnaires were utilized to collect socio-demographic, clinical and laboratory data. Third generation immunoassays were used for measurement of Thyroid Stimulating Hormone (TSH), glycated haemoglobin (HbA1c) and Low Density Lipoprotein-cholesterol (LDL-C). Descriptive statistics such as the median and interquartile ranges were used to summarize continuous variables. Frequencies and percentages were used to summarize categorical variables. Association between thyroid dysfunction and categorical independent variables was assessed using Pearson's Chi Square test. Fisher's exact test was reported whenever the Chi Square assumptions were violated. Multiple logistic regression was used to determine the effect of independent variables on thyroid function.

**Results:** The median age of the participants was 59.2 years, females constituted 230 (62.5%) of the study population. Prevalence of thyroid dysfunction among patients was 9.2% (95% CI: 6.4, 12.7) representing 34 participants. Subclinical hypothyroidism was the most frequent dysfunction at 22 (7%). Socio-demographic (age, gender) and clinical characteristics (duration of Type 2 DM, insulin use, hypertension, body mass index and LDL-C) studied indicated no association with thyroid dysfunction. Likewise there was no significant correlation between thyroid dysfunction (TSH, freeT4) and glycemic control (HbA1c).

**Conclusion**: The prevalence of thyroid dysfunction among patients with T2DM was 9.2%. There was no significant correlation found between thyroid dysfunction and the studied clinical correlates.

**Key words:** Thyroid dysfuction, Type 2 diabetes mellitus, HbA1c, TSH

## Introduction

Thyroid disease is the second most common endocrine disorder in the general population after diabetes mellitus worldwide. Hypothyroidism is commoner and overall prevalence of these disorders in the adult population increases with age (1). It has been postulated that thyroid disease and diabetes mellitus have a common genetic background (2). Current genetic evidence is almost exclusively restricted to autoimmune causes with a strong association between Type 1 DM and autoimmune thyroid disease. Thyroid antibody positivity has been found in up to 50% of Type 1 DM patients (3).

Despite an almost similar frequency of thyroid disease in T2DM, genetic links have not been well characterized with only a few studies suggesting a direct genetic basis for thyroid disease in T2DM. Indirect links between thyroid disease and diabetes mellitus are better described with emphasis on effects of the thyroid hormone on glucose and lipid metabolism (4).

Thyroid dysfunction affects glycemic control and also compounds the complications through its effects on the cardiovascular system (CVD) (5). These risk factors have been implicated in worsening of prevalent CVD that is the leading cause of death among patients with diabetes (6). In addition, there is demonstrated evidence of increased risk of nephropathy and retinopathy in patients with T2DM and concomitant hypothyroidism thus favoring routine screening for the latter. In a setting where T2DM has remained a challenge as witnessed in Sub-Saharan Africa (SSA), early recognition and treatment of thyroid dysfunction is important not only for good glycemic control but also for possible reversal of associated cardiac dysfunction (7-9). We therefore set out to describe the prevalence and clinical correlates of thyroid dysfunction among ambulatory patients with T2DM at MTRH to add to the pre-existing body of knowledge on this important public health problem in our region.

## Materials and methods

This was a cross-sectional study conducted at Moi Teaching and Referral Hospital (MTRH) Diabetes Outpatient Clinics (DOPC) between February and April 2018.

The study population included ambulatory patients aged 35 years and above at the time of diagnosis with T2DM. Patients with documented or reported history of conditions known to interfere with HbA1c assay such as anaemia (Hb<10g/dl), recent blood transfusion (3 months), haemodialysis, erythropoietin therapy and haemoglobinopathies (sickle cell disease) were excluded. Three sixty eight participants were recruited, a sample size that was calculated based on a study by Ngugi (10) at Kenyatta National Hospital in 2014, and factoring in a 10% margin for missing data. Structured pre-tested questionnaires were utilized to collect socio-demographic, clinical and laboratory data for each consenting patient. Blood pressure (three readings one minute apart with average of the last 2 recorded, using an OMRON automated device), height and weight were measured before participants were taken to the phlebotomy area where blood samples for HbA1c, TSH, fT4 and LDL-C were then taken. All phlebotomy procedures were carried out under sterile conditions. The collected samples were delivered to the MTRH Reference Laboratory and analyzed on the day of collection.

An automated Cobas 411 electrochemilumiscence immunoassay (ECLIA) analyser was used for analysis of TSH and Ft4. An automated Cobas Integra 400 Plus chemistry analyzer was used for analysis of glycated haemoglobin.

Descriptive statistics such as the median and corresponding interquartile range were used to summarize continuous variables. Association between thyroid dysfunction and categorical independent variables were assessed using Pearson's Chi Square Test, Fisher's Exact Test and Wilcoxon Rank Sum Test. Logistic regression model was used to assess the variables associated with thyroid dysfunction. Bivariate logistic regression model was used to calculate the unadjusted Odds Ratios (OR), and the multivariate logistic regression model was used to calculate the adjusted odds ratios. In the multivariate model, the variables that were significantly associated with the thyroid dysfunction in the bivariate analysis were included. These variables included age, gender, duration of diabetes, insulin use, hypertension, BMI, LDL-Cholesterol and HBA1C. None of the variables was dropped. We reported the OR and the corresponding 95% confidence intervals. Relationship between continuous variables (Serum TSH and Serum T4) with HBA1C was assessed using scatter plots. Spearman rank correlation coefficient was calculated to determine the strength and direction of the relationship.

Approval was sort from IREC and permission to conduct the study obtained from MRTH management. Findings were communicated to the attending clinician for follow up and further care. There was no conflict of interest in this study.

## Results

Three sixty eight participants were recruited out of a sample size of 406 that underwent screening. The median age of the participants was 59.2 years, females constituted 230 (62.5%) of the study population.

Majority of the participants were either overweight or obese accounting for 232 (63%). Six (1.6%) participants reported symptoms related to thyroid dysfunction and on physical examination they were found to have signs of thyroid dysfunction mainly an enlarged thyroid gland. Hand tremors, facial puffiness and protruding eyes were the other signs elicited. Nearly half of the patients 162 (42%) had hypertension. The median serum TSH levels were 1.61(IQR 1.08, 2.5) mIU/l, median serum free T4 was 1.24(IQR 1.1, 1.35) ng/dl and the median HbA1c was high at 8.82 (IQR 7, 10.86). The median LDL cholesterol levels were elevated at 2.89 (IQR 2.25, 3.62) mmol/l. Demographics and clinical characteristics data are illustrated in Table 1.

**Table 1:** Participants socio demographic and clinical characteristics

| Variable | Freq/Median | %/ IQR |
|---|---|---|
| Age in years | 59.2 | (52,67) |
| Gender | | |
| Female | 230 | 62.5 |
| Male | 138 | 37.5 |
| Marital status | | |
| Married | 330 | 89.7 |
| Separated | 4 | 1.1 |
| Single | 15 | 4.1 |
| Widowed | 19 | 5.2 |
| Level of education | | |
| None | 49 | 13.3 |
| Primary | 166 | 45.1 |
| Secondary | 118 | 32.1 |
| Tertiary | 35 | 9.5 |
| Duration of diabetes since diagnosis (months) | 60 | (24, 132) |
| Hypertension | 202 | 54.9 |
| Family History of thyroid disease | 15 | 4.1 |
| History of thyroid surgery | 9 | 2.5 |
| History of radioiodine ablation | 1 | 0.3 |
| History of diagnosis of thyroid disease | 6 | 1.6 |
| Hyperthyroidism | 3 | 0.8 |
| Hypothyroidism | 3 | 0.8 |
| Insulin | 196 | 53.2 |
| Oral anti-diabetes agents | 172 | 46.7 |
| ACE Inhibitors /ARB's | 150 | 40.8 |
| Calcium channel blockers | 86 | 23.4 |
| Beta blockers | 19 | 5.2 |
| Diuretics | 83 | 22.5 |
| Amiodarone | 0 | 0 |
| Atorvastatin | 54 | 14.7 |
| Thyroxine | 2 | 0.5 |

The prevalence of thyroid dysfunction was 9.2% (95%CI: 6.4, 12.7). Of the 34 Type 2 DM patients who had thyroid dysfunction, 31 (91.2%) had hypothyroidism while the remaining 3 (8.8%) had hyperthyroidism. Among those with hypothyroidism, 22(71%) had subclinical hypothyroidism.

On bivariate analysis as shown in Table 2 it is notable that despite differences in age, glycemic control, insulin use, hypertension, sex, BMI and LDL cholesterol in the comparison groups, none of these factors were statistically significantly associated with thyroid dysfunction (all P-values >0.05). However history of diagnosis of thyroid disease was found to be associated with thyroid dysfunction with a significant P-value of 0.000.

**Table 2:** Factors associated with thyroid dysfunction bivariate analysis

| | Thyroid dysfunction | | |
|---|---|---|---|
| | Freq (%)/ Median (IQR) | | |
| | No | Yes | P-value |
| Age | 59 (52, 66) | 59.5 (55,69) | 0.406[1] |
| HbA1c | | | |
| Control | 127 (87.0) | 19 (13.0) | 0.046[2] |
| No control | 205 (93.2) | 15 (6.8) | |
| History of diagnosis thyroid disease | | | |
| No | 332 (91.7) | 30 (8.3) | 0.000[3] |
| Yes | 2 (33.3) | 4 (66.7) | |
| Insulin use | | | |
| No | 154 (91.1) | 15 (8.9) | 0.824[2] |
| Yes | 180 (90.5) | 19 (9.5) | |
| Hypertension | | | |
| No | 149 (89.8) | 17 (10.2) | 0.547[2] |
| Yes | 185 (91.6) | 17 (8.4) | |
| Sex | | | |
| Male | 125 (90.6) | 13 (9.4) | 0.926[2] |
| Female | 209 (90.9) | 21 (9.1) | |
| LDL | | | |
| Normal | 135 (91.8) | 12 (8.2) | 0.561[2] |
| Abnormal | 199 (90.0) | 22 (10.0) | |
| BMI | | | |
| Underweight | 11 (91.7) | 1 (8.3) | |
| Normal | 96 (90.6) | 10 (9.4) | 1.000[3] |
| Overweight | 117 (90.7) | 12 (9.3) | |
| Obese | 93(90.3) | 10 (9.7) | |
| Extreme obese | 10 (90.9) | 1 (9.1) | |

[1]Wilcoxon rank sum test,[2]Chi square test, [3]Fishers Exact test

Multiple logistic regression model results as seen in Table 3 showed that participants who had good glycemic control as assessed by HbA1c had a 57% greater chance of having thyroid dysfunction compared to those with poor glycemic control, OR: 0.431 (95% CI: 0.201, 0.920). However, there was no association found between age, sex, duration of diabetes, insulin use, hypertension, BMI, LDL-cholesterol and thyroid dysfunction.

**Table 3:** Multivariate analysis factors associated with thyroid dysfunction

| Variable | Odds ratio | P-value | [95% Conf. | Interval] |
|---|---|---|---|---|
| Age | 1.025 | 0.140 | 0.991 | 1.059 |
| Sex | | | | |
| Male | 1 | | | |
| Female | 1.109 | 0.798 | 0.501 | 2.454 |
| Duration of diabetes (months) | 1.001 | 0.791 | 0.996 | 1.005 |
| Insulin use | | | | |
| No | 1 | | | |
| Yes | 1.307 | 0.487 | 0.617 | 2.774 |
| Hypertension | | | | |
| No | 1 | | | |
| Yes | 0.566 | 0.156 | 0.257 | 1.242 |
| BMI | | | | |
| Normal | 1 | | | |
| Underweight | 1.027 | 0.981 | 0.112 | 9.397 |
| Overweight | 0.924 | 0.865 | 0.372 | 2.296 |
| Obese | 1.014 | 0.977 | 0.389 | 2.644 |
| Extreme obese | 1.145 | 0.904 | 0.125 | 10.496 |
| LDL | | | | |
| Normal | 1 | | | |
| Abnormal | 1.244 | 0.584 | 0.570 | 2.715 |
| HbA1c | | | | |
| Control | 1 | | | |
| No control | 0.431 | 0.030 | 0.201 | 0.920 |

There was an insignificant negative correlation between serum TSH and HbA1c however no correlation was found between free T4 and HbA1c.

## Discussion

This study found a prevalence of thyroid dysfunction of 34 (9.2%) among the 368 patients with T2DM studied. This is slightly lower than the wide range of prevalence of thyroid dysfunction globally which varies between 10– 46 (11). This difference could be explained by the use of different criteria for the diagnosis of thyroid dysfunction; thyroid function test, presence of anti-thyroid peroxidase (anti-TPO), antithyroglobulin antibody (anti-TG), or both (12). In addition, factors such as iodine status in different regions, selenium deficiency and thiocyanate toxicity have been found to be responsible for variations of thyroid disease epidemiology (12). However, further exploration of these factors may be needed to determine if they are responsible for the lower prevalence of thyroid dysfunction among our population in western Kenya.

The prevalence in our study was however comparable to that of a Greek population of 1029 patients with T2DM who were found to have a prevalence of 12.3% (14). The similarities in prevalence could be attributed to similar methodology in regards to the laboratory procedures for HbA1c and thyroid function tests. However, the slight higher prevalence in the Greece study may be attributed to the much older mean age of participants (67 years) compared to 59 years in this study, given that the prevalence of thyroid dysfunction increases with age (15).

The prevalence of 9.2% found in this study was much lower than that reported in a local study done at Kenyatta National Hospital (KNH) which found a prevalence of 61% among 181 patients with Type 2 DM (10). Some factors that may have been responsible for the high prevalence in the KNH study include: differences in the population characteristics with a higher percentage of patients having a previous diagnosis of thyroid dysfunction (10.6%, compared to 1.6% in this study), 22% of patients reported a positive family history of thyroid disease (hence higher risk) compared to 4.1% in this study; Difference in definition of Type 2 DM with the KNH study including all patients above the age of 30 years regardless of the age at diagnosis hence higher likelihood of inclusion of Type 1 DM patients who are at a higher risk of thyroid dysfunction (16); The use of different test methods in the two studies with our study using electrochemiluminescence immunoassay (ECLIA) technology of Elecsys 2010 which has shown advantages in system performance and superiority to other laboratory methods such as ELISA (KNH study) and Immunoradiometric assay (IRMA) for the measurement of serum TSH with higher specificity (17). Subclinical hypothyroidism (elevated TSH> 4.2mIU, normal free T4) was the most frequent dysfunction found at 7% (22 participants) among our study population. Subclinical hypothyroidism is most common among females above the age of 60 years, which comprised majority of our study population. This is consistent with a number of studies (12,14).

Other studies done in Nigeria (18) and India (19) also reported a higher prevalence of subclinical hypothyroidism at 26% and 24.5% respectively. This difference may be attributed to their use of ELISA for measurement of thyroid hormones compared to ELCIA in this study.

In our study we found an insignificant association between thyroid dysfunction and good glycemic control (HbA1c <8%). This is an uncommon finding and although there is a scientific explanation, it could also be a chance finding as demonstrated by the wide confidence interval for the odds ratio. Majority of the participants had hypothyroidism which increases susceptibility to recurrent hypoglycemia which may lower the overall HbA1c level and hence be interpreted as better glycemic control. In the absence of self-blood glucose monitoring data most hypoglycemic episodes may have gone unnoticed. Hypothyroidism is often associated with a relative adrenal insufficiency which further results in blunting of the hypothalamo-pituitary–adrenal response to hypoglycemia.

Hypothyroid patients also have a reduced cortisol response to insulin-induced hypoglycemia further worsening hypoglycemia in these patients (20). Hypoglycemia has been identified as a risk factor for both major cardiovascular events and death (21). The knowledge that hypothyroidism has a significant role in hypoglycemia necessitates consideration of the appropriate dosing of insulin and oral hypoglycemic agents and treatment of hypothyroidism to alleviate further risks of hypoglycemia. Similarly Telwani *et al* (22) found patients with thyroid dysfunction had a higher chance of good glycemic control. Despite Papazafiropoulou *et al* (14) findings no association between glycemic control and thyroid dysfuction, patients who had thyroid dysfunction had a lower mean HbA1c (7.38% vs 7.81%) compared to those without. On the other hand, Uppal *et al* (19) found that poor glycemic control was associated with thyroid dysfunction. However, this is not surprising given the complexity of the interaction between thyroid disorders and diabetes. Insulin resistance seems to be the possible link between T2DM and thyroid dysfunction. Insulin resistance and $\beta$ cell function are inversely correlated with thyroid stimulating hormone which may be explained by the antagonistic effects of insulin on thyroid hormones along with an increase in TSH (23). Hence, patients with poor glycemic control are equally at risk of thyroid dysfunction.

Our study found, age, treatment modality, duration of T2DM and HTN were not associated with thyroid dysfunction. Similarly, Papazafiropoulou *et al* (14) found no association. Perhaps this could be explained by the fact that majority of our patients were on metformin which has counter regulatory effects on the thyroid hormone release and activity. Metformin decreases thyrotropin levels in patients with hypothyroidism and it has also been shown to have anti-proliferative effects on the thyroid gland. However Uppal *et al* (19) and Ogbonna *et al* (15) found longer duration >12 years and >6.5 years respectively of T2DM was associated with TD. Longer duration of DM increases risk of chronic hyperglycemia which impairs the peripheral deiodination of T4 to T3 leading to thyroid dysfunction. Perhaps there was no association in this study since the median duration of T2DM was shorter (5 years). The other factors studied were gender, BMI, LDL-C, which were not associated with thyroid dysfunction. However, Telwani *et al* (22) found an association between female gender and LDL-C and TD. This may be due to differences in methodology. While this was a cross sectional study, Telwani *et al* (22) conducted a case control study with age and sex matched controls.

There was no significant correlation between TSH and fT4 and HbA1c in this study. However the correlation tended towards the negative and this could have resulted from majority of the thyroid dysfunction being subclinical hypothyroidism. This may have increased susceptibility to hypoglycemic episodes as earlier alluded to. However, Uppal *et al* (19) and Imdad *et al* (24) found a positive correlation which is thought to be as a result of the complex interaction between insulin resistance and thyroid hormones as earlier discussed.

**Study limitation**

The duration from diagnosis with T2DM was self-reported and not objectively obtained.

**Conclusion and recommendation**

The prevalence of thyroid dysfunction among patients with Type 2 DM was 9.2%. There was no significant correlation found between thyroid dysfunction and the studied clinical correlates. Further studies should be considered to include a parallel arm evaluating thyroid function tests in the non-diabetes population in addition to evaluating other clinical correlates that may be associated with thyroid dysfunction.

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Original paper

# Diagnosis of Active Pulmonary Tuberculosis using The Xpert MTB/RIF Assay in Smear Negative Tuberculosis Suspects at Kenyatta National Hospital and Mbagathi District Hospital, Kenya

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## Abstract

**Background:** Pulmonary tuberculosis (PTB) is a major global public health problem and currently it is the second leading cause of mortality from a single infectious disease worldwide according to the WHO World TB report 2012. Over the past century, diagnosis of PTB has relied mainly on smear microscopy which has been shown to have a low sensitivity especially in patients co-infected with HIV. Novel diagnostic methods, such as the recently developed Xpert MTB/RIF assay are bound to be essential tools in the global fight against TB.

**Objectives:** This study sought to determine the yield of this novel assay in the microbiological diagnosis of PTB in patients suspected to have PTB but are sputum smear negative.

**Design:** This was a cross sectional descriptive study.

**Setting:** The Kenyatta National Hospital (KNH) and Mbagathi District Hospital (MDH).

**Methods:** Records of prospective patients seen at the TB clinics of both hospitals and the TB wards in MDH were perused. Those patients who met the inclusion criteria were recruited with consent into the study and the study questionnaire was administered. Spot sputum samples from each patient which were of proper quality were tested for active mycobacterium tuberculosis and rifampicin resistance using the Xpert MTB/RIF assay. Data from the study questionnaire and results of the assay were entered and analyzed using SSPS version 17.0 software. Measured outcomes included the proportion of active PTB in smear negative PTB suspects; the prevalence of rifampicin resistance in this group and the association between the Xpert MTB/RIF assay results and patients presenting symptoms.

**Results:** A total of 179 sputum samples were run from 179 eligible participants. The Xpert MTB/RIF assay yield was high at 19% (95%CI 13.5-25.5) with a 0% rifampicin resistance rate. Presence of night sweats on its own, or both night sweats and weight loss were weakly associated with Xpert MTB/RIF assay positivity (OR 10.1; 95%CI 1.3-76.7, p=0.007) and (OR 7.1; 95% CI 2.1-24.3, p<0.001) respectively.

**Conclusion:** The additional yield of the Xpert MTB/RIF assay in patients who were sputum smear negative PTB suspects in our study was 19%. This has important public health implications wherein patients who can transmit TB are not being identified by smear microscopy.

**Key words:** Xpert, TB, Yield, Sputum, Smear negative

## Introduction

Tuberculosis (TB) continues to be one of the major global health problems. The greatest burden is borne by the developing countries which continue to suffer high rates of morbidity and mortality. According to the WHO global TB report 2012, there were nine million new TB cases in 2011, of which 1.4 million deaths were recorded globally. In Kenya, the estimated prevalence of TB in 2011 was 291 per 100,000 populations, in both HIV positive and negative patients (1). The HIV epidemic contributes greatly to the disease burden. Globally at the end of 2011, there were 34 million people living with HIV (PLWHIV). Sixty nine percent of PLWHIV and almost 80% of people living with both HIV and TB are in Africa. The incidence rate worldwide stood at 2.5 million people and there were 1.7 million deaths related to AIDS. Sub-Saharan Africa (SSA) accounted for 70% of all AIDS related deaths witnessed worldwide. In Kenya, the estimated incidence of HIV/TB co-infection in the same period was 113 per 100,000 populations (2).

For over a century, smear microscopy for Acid Fast Bacilli (AFB) has been the initial diagnostic tool. It is simple and its low cost has made it ideal especially in the developing nations and most national TB control programs continue to rely on it despite its low sensitivity (3). Automated liquid culture is the recommended gold standard diagnostic test for tuberculosis. It is highly sensitive and specific. However, it delays time-to-treatment with a range of two to three weeks from sample collection to results.

It is also quite expensive as it requires specialized equipment and a bio-safety level 3 facility (4).

Recently, methods based mostly on nucleic acid amplification for direct organism detection have reduced the diagnostic time while increasing sensitivity (5-7). The Genexpert mycobacterium tuberculosis/rifampicin assay (Xpert MTB/RIF assay) is one of such methods which has recently been developed and approved for TB diagnosis (8, 9).

In this study we sought to determine the yield of this novel assay in the diagnosis of active pulmonary tuberculosis in suspected cases who are sputum smear negative for AFBs, as well as the rate of rifampicin resistance in this group.

## Materials and methods

*Design*: This was a cross sectional descriptive study from two hospitals.

*Setting:* The study was carried out at two proximal hospitals; The Kenyatta National Hospital (KNH) outpatient TB clinic and Mbagathi District Hospital (MDH) TB clinic and medical wards.

The KNH is a teaching and referral hospital situated at the Upper Hill area in Nairobi County, Kenya. It has since its inception offered referral services for all specialties from across the country. It is however not a major center for cases of tuberculosis which tend to be treated at the peripheral facilities. The TB clinic is located within the medical outpatient unit of clinic 17 and runs from Monday to Friday. Records perused at the clinic indicate that on average 12 patients are seen per week, all from the Nairobi area. Only eight of these patients complete sputum microscopy testing of which three are smear negative. We thus envisaged a greatly lower recruitment rate from this facility.

The MDH is a level 4 health facility in Nairobi County. It has served as the TB referral treatment center for Nairobi for the past 58 years. Despite being upgraded to a general medical, surgical and paediatric hospital in 1995, it has continued to be the major TB treatment center for Nairobi and its environs. There are four medical wards at MDH (2 male and 2 female), two of which are specialized wards for suspected PTB cases. Patients found not to have PTB are subsequently transferred to one of the other two wards. The TB clinic is located within the special clinics building and runs between Monday and Friday.

*Recruitment of participants:* Between January and April 2014, medical records of prospective participants with suspected PTB and who were sputum smear negative, were perused. Participants who declined informed consent or who were on treatment for any form of tuberculosis were excluded.

*Participants data, specimen collection, storage and transportation*: Upon obtaining written informed consent from the participants, the principal investigator and his two assistants completed a questionnaire to compile demographic data, symptom screening, past medical history of TB treatment, HIV status and CD4 counts. Standard instructions on proper sputum submission were then given to the participants and each one then provided a spot sputum sample (10). Sputum quality was assessed according to standard guidelines (11) and those which met the criteria were accepted. Poor quality samples were discarded and a repeat sample requested.

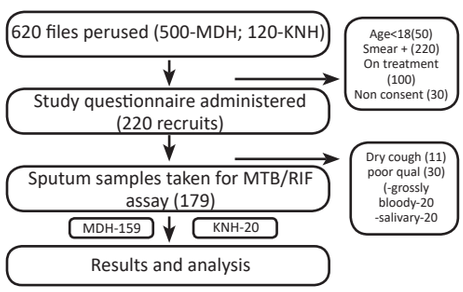
Samples were stored in a cooler box at 4 degrees Celsius and transported to the KNH CCC Xpert MTB/RIF assay laboratory for analysis. Samples which were not tested on the same day were frozen at -30 degrees Celsius and thawed on day of testing.

*Specimen testing by Xpert MTB/RIF assay:* Sputum specimens were prepared and analyzed according to the manufacturer's specifications as follows: Sample reagent was added in 2:1 ratio (v/v) to sample and shaken vigorously 10 - 20 times. Resulting specimen was then left to incubate at room temperature for 15 minutes. Specimen was again shaken at mid-point of incubation. The now liquefied specimen was then transferred into a sterile pipette until above the minimum mark. A pre-labeled Xpert MTB/RIF cartridge was opened and the specimen introduced into the port slowly. The cartridge was then shut and loaded into the Xpert module. The sample ID was loaded into the Genexpert DX system software and automated testing commenced. Results were interpreted by the Genexpert DX system and presented as; MTB detected/ MTB not detected/ invalid. Rifampicin results were presented as: Rifampicin resistance detected/rifampicin resistance not detected. Specimens that attained an invalid reading were re-tested.

## Results

*Participants:* Two hundred and twenty participants who met the case definition and inclusion criteria were enrolled in the study. Forty one were subsequently excluded due to: Dry cough (11 cases); poor quality sputum samples (30 cases). Thus we analyzed 179 samples in this study (Figure 1).

**Figure 1:** Recruitment of participants



The sex distribution of the study population was 52.5% male vs 47.5% female with a mean age of 37.7 years. Ninety five percent of participants had attained a minimum primary level of education (Table 1).

**Table 1:** Socio-demographic characteristics of study population (N=179)

| Variable | Frequency (%) |
|---|---|
| Age in years | |
| Mean (SD) | 37.7 (13.5) |
| Min-Max | 18-83 |
| Sex | |
| Male | 94 (52.5) |
| Female | 85 (47.5) |
| Level of formal education | |
| None | 9 (5.0) |
| Primary | 77 (43.0) |
| Secondary | 71 (39.7) |
| Post-secondary | 22 (12.3) |

The commonest presenting symptom among our study population was weight loss (83.8%). This was closely followed by night sweats (80.4%). A considerable number of participants were shown to have both symptoms of night sweats and weight loss (65.4%) (Table 2).

**Table 2:** Presenting symptoms among study population (N=179)

| Variable | Frequency (%) |
|---|---|
| Night sweats | |
| Yes | 144 (80.4) |
| No | 35 (19.6) |
| Weight loss | |
| Yes | 150 (83.8) |
| No | 29 (16.2) |
| Both symptoms | |
| Yes | 117 (65.4) |
| No | 62 (34.6) |

A vast majority of participants did not report any history of past treatment for any form of tuberculosis (76%) (Table 3).

**Table 3:** Prior PTB treatment (N=179)

| Variable | Frequency (%) |
|---|---|
| Prior treatment | |
| Yes | 43 (24.0) |
| No | 136 (76.0) |

Of the 179 participants, 40 had recorded HIV status positive (22.3%) while 101(56.4%) were HIV negative. A fair number of these participants did not have a recorded HIV status (21.2%). The median CD4 cell count of the 40 HIV positive patients with documented CD4 count, was 152.5cells/microliter (Table 4).

**Table 4:** HIV status of study participants (N=179)

| Variable | Frequency (%) |
|---|---|
| HIV status | |
| Positive | 40 (22.3) |
| Negative | 101 (56.4) |
| Unknown | 38 (21.2) |
| CD4 cells count (n=40) | |
| Available results | 16 (40.0) |
| Median (IQR) | 152.5 (74.0-460.0) |

*The Xpert MTB/RIF assay yield:* The Xpert MTB/RIF assay in this study yielded 34 cases or 19% (95% CI 13.5-25.5) of active PTB out of the 179 suspected cases. Of these 34 cases with MTB detected by the assay, none was found to be rifampicin resistant, giving a 100% rifampicin sensitivity rate in this group (Table 5).

**Table 5:** Xpert MTB/RIF assay and rifampicin resistance result (N=179)

| Variable | Frequency (%) | 95% CI |
|---|---|---|
| MTB detected | | |
| Yes | 34 (19.0) | 13.5-25.5% |
| No | 145 (81.0) | 74.5-86.5% |
| RIF resistance (n-34) | | |
| None | 34 (100.0) | |

*Association between Xpert assay yield, clinical features and HIV status:* The prevalence of HIV in participants in whom MTB was detected by the assay (34 cases) was 29.4% while 50% were HIV negative. A substantial number of participants in this group (26.6%) did not have a documented HIV status result and hence were classified as unknown.

The symptoms of night sweats, weight loss or both, were very prevalent in this Xpert assay positive group at 97.1%, 94.1% and 91.2% respectively. On univariate analysis, the presence of night sweats alone as well as the presence of both night sweats and weight loss were associated with Xpert assay positive yield; p=0.007 (OR 10.1; 95%CI 1.3-76.7) and p<0.001 (OR 7.1; 95%CI 2.1-24.3) respectively. Both variables attained statistical significance (Table 6).

**Table 6:** Associations between Xpert positivity and HIV status and presenting symptoms

| Variable | MTB detected | | OR (95%) | P-value |
|---|---|---|---|---|
| | Yes (n=34) | No (n=145) | | |
| HIV status | | | | |
| Negative | 17 (50.0) | 84 (57.6) | 1.0 | |
| Positive | 10 (29.4) | 30 (20.7) | 1.6 (0.7-4.0) | 0.266 |
| Unknown | 7 (26.6) | 31 (21.4) | 1.1 (0.4-2.9) | 0.825 |
| Median CD4 (IQR) | 119 (88-180) | 177 (67-543) | - | 0.871 |
| Night sweats | | | | |
| Yes | 33 (97.1) | 111 (76.6) | 10.1 (1.3-76.7) | 0.007 |
| No | 1 (2.9) | 34 (23.4) | 1.0 | |
| Weight loss | | | | |
| Yes | 32 (94.1) | 118 (81.4) | 3.7 (0.8-16.2) | 0.070 |
| No | 2 (5.9) | 27 (18.6) | | |
| Both symptoms | | | | |
| Yes | 31 (91.2) | 86 (59.3) | 7.1 (2.1-24.3) | <0.001 |
| No | 3 (8.8) | 59 (40.7) | 1.0 | |

## Discussion

Tuberculosis remains a major global health problem with approximately 9 million new cases in 2011, the majority of which were in the developing nations. The rate of smear negative disease among notified cases in Kenya is relatively high at 32%, as of 2011 (1). A substantial amount of PTB transmission occurs via smear negative cases as shown by Behr *et al* (12) and Tostmann *et al* (13). It is important that active disease is rapidly established in smear negative cases to prevent such transmission and disease spread. This is even more imperative in a setting of high HIV and TB burden like Kenya (2). This study was an opportunity to assess the yield of the Xpert MTB/RIF assay in a high burden setting of both HIV and smear negative PTB.

The yield of the assay in our study was 19%. This is comparable to published data on yields of the assay in nine countries (14) which revealed an overall yield of 16.8% with a rifampicin resistance rate of 13.6%. These comparative results were from a wide geographical distribution which in similarity to our set-up are WHO classified as high burden TB countries (1). Our study employed the use of passive case finding strategy which entails waiting for patients who have developed symptoms to present to the health facilities as opposed to an active case finding strategy whereby healthcare professionals systematically interrogate all high risk groups at every visit to assess for active or latent TB infection. These comparative studies utilized either case finding strategy with some combining both. The sites utilized in all except two countries (Bangladesh, Pakistan) were public referral, district or sub-district facilities similar to this study. Three sites (Kenya, Mozambique, DRC) of the overall nine carried out Xpert assay testing on single smear negative sputum samples without the use of a chest X-ray as a screening test. This was similar to our study. The yields of the Xpert assay in these three sites were: 10.2%, 15.3% and 10.7% respectively. These lower yields could be due to the fact that the study sites in these three countries were district hospitals with none being a major center for TB diagnosis unlike Mbagathi District Hospital in our study. In the other six sites, patients who were smear microscopy negative but had a suggestive chest X-ray were excluded from Xpert assay testing. This resulted in relatively higher yields of the assay as follows: Bangladesh- 21.5%, Cambodia-23.6%, Malawi-11.7%, Moldova-18.2%, Nepal-22.2% and Pakistan-20.9%.

Our sample collection method could have negatively impacted on the yield of the Xpert assay. We utilized a 'spot' sample collection method whereby a sputum sample was requested from participants once they were enrolled into the study. The use of a morning sputum sample has been shown to have a higher sensitivity with the use of the Xpert assay with 88.4% sensitivity versus 84.1% using a spot sample technique (15). The utilization of an early morning sputum sample or both early morning and spot samples would likely have improved the yield of the assay in this study.

The subjective assessment of sputum samples using the rating system of Bartlett (11) could have also negatively influenced the yield of the assay in this study. In a prospective study in South Korea, Yoon *et al* (16) showed that gross appearance of purulent or blood stained sputa was more associated with smear positive yield than mucoid or salivary samples

{OR 2.05,95%CI (1.21-3.47) (16). In similar fashion, Gounder *et al* (17) in an audit of smear examination in Fiji, showed good quality sputa positively correlated with smear positivity for AFBs. The effect of sputum quality, though not yet assessed in the yield of the Xpert MTB/RIF assay is likely to influence it in similar way to smear microscopy. Besides, the Xpert MTB/RIF assay cannot analyze grossly bloody sputum samples. In our study, we excluded 20 samples from analysis due to the grossly blood-stained nature of the samples. We also excluded a further 10 samples which were salivary in appearance despite patients being symptomatic.

The effect of freezing and thawing of the sputa could also have influenced the yield of the assay in this study by altering the nucleic acid stability of the MTB. Moure *et al* (18) in an evaluation study of the assay, tested 125 samples which had been frozen for over 10 years. The sensitivity of the assay was 75.3% with 100% specificity. This sensitivity while being within the range of other evaluation studies was comparatively lower. In our study, we froze 100 samples for later testing.

The quality of laboratory personnel preparing the samples for the assay as well as the calibration of the Xpert MTB/RIF assay console could also negatively impact assay yield. However there are so far no studies to identify inter-laboratory variability in the assay results.

The yield of the assay in this study could be statistically lower than it otherwise would, assuming an estimated sensitivity of 86.7% and specificity of 97.3% in smear negative cases on which this study was based (19), the true estimated yield of the Xpert assay in this study could be 19.6% (95% CI 12.7-26.5%); Positive Predictive Value (PPV) – 88.6%; Estimated Negative Predictive Value (NPV) – 96.7% (20).

The rifampicin resistance rate in this study was 0%. This is not surprising based on the fact that Kenya is currently rated in the World TB report 2012 as a low burden MDRTB country (1). A study by Ogaro *et al* (21) in Nairobi found a 0.81% rifampicin resistance rate among new patients who made up 65% of that study. This same study also found an MDRTB prevalence rate of 0.54%. In our study, 76% of participants were new PTB suspected cases having thus never been treated before for any form of TB. False positive rifampicin resistance results from the Xpert assay have been reported, leaving a substantial reduction in the positive predictive value of the assay for diagnosis of rifampicin resistance in this setting of low MDRTB prevalence (22).

In this study, the group HIV prevalence in those who tested positive for the assay was 29.4%. A high number (26.6%) of assay positive cases had unknown HIV sero-status due to a nationwide shortage of testing kits at the time of this study. Hence the absence of association between the HIV sero-status and assay positivity in this study cannot be forcefully put forward.

In relation to the symptoms of the study participants in association to the Xpert assay result, we found that the presence of night sweats alone was statistically significant p=0.007, along with presence of both symptoms of night sweats and weight loss p<0.001 in the participants who tested positive for the assay confirming active disease. This association is in keeping with the very definition of PTB 'suspects' which incorporates the symptoms of night sweats and weight loss. It is also comparable to findings by Elizabeth *et al* (23) which showed a negative predictive value of both night seats and weight loss of over 99% in the diagnosis of active PTB in suspected cases in a setting of high HIV prevalence. However the wide confidence intervals noted in this analysis did not allow us to draw a definite conclusion from this due to a potentially underpowered sample size of 179. The public health impact of the Xpert MTB/RIF assay in our setup could be quite substantial. An estimated 400,000 lives per year can be saved by making a diagnosis of active PTB using a sputum based assay with a sensitivity of 85% and specificity of 97% (24). The Xpert MTB/RIF assay has achieved these rates and indeed surpassed them in almost all evaluation studies done so far. A rapid turnaround time, though not assessed in this study, will certainly reduce the rate of under treatment of patients with smear negative disease. The Kenya national algorithm for the diagnosis of smear negative suspected PTB advocates for an initial trial of antibiotics and eventual treatment for PTB should symptoms persist. This delay in definitive diagnosis and treatment of active disease in smear negative PTB suspects, will most certainly adversely affect the TB control at national level. The Kenya national genexpert algorithm limits the diagnostic use of the assay to HIV positive, smear negative patients and children. In our study, we found that 50% of patients who were Xpert assay positive were HIV negative. As per this finding, a significant number of patients with smear negative active disease may be otherwise missed without the use of the Xpert assay. The resultant spread of infection will place increased burden on the public health systems.

In conclusion, the additional yield of the Xpert MTB/RIF assay in smear negative PTB suspects is 19% which when taken in the context of a 34% smear negative rate in Kenya, is relatively high. The rate of rifampicin resistance in smear negative PTB suspects is

very low at 0%. Our data suggests that smear negative PTB suspects could greatly benefit from the Xpert assay especially in areas of low culture availability regardless of HIV status. This benefit results from the fact that a high number of smear negative cases will be detected as having active disease by the assay, hence reducing the spread of the disease by avoiding the time delay in treatment which the national algorithm for diagnosis of TB allows for (25).

Our study does have some limitations. The absence of HIV testing in 26.6% of the participants who were positive by Xpert makes it difficult to ascertain the true yield of the assay in HIV positive individuals. Furthermore, the full effect of freezing and thawing on the assay yield has not been exhaustively assessed in literature so far, neither in this study. Finally confirmation of the positive Xpert assay results with culture would have been ideal as the assay is a novel technology. However, this is offset by the fact that several evaluation studies have indeed shown the assay to be highly specific.

Future studies are recommended to assess the yield of the Xpert assay in various populations to enable plotting of the overall prevalence of active PTB in smear negative cases. This will in the long term help in defining the area of maximal utility of the Xpert assay. A recommendation for the expansion of the national Genexpert algorithm to include its use in smear negative HIV negative patients can also be drawn from the findings of this study.

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**Original paper**

# Primary Health Care Integration for Four Chronic Diseases in Western Kenya: The PIC4C Baseline Study Protocol

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## Abstract

**Background**: Chronic diseases are a major cause of morbidity and mortality in Kenya, but thus far, early detection, treatment and control rates for these diseases are very low in most of the Low- and Middle-Income Countries (LMICs). Absence of effective integrated care for these diseases at the primary health care level is one of the factors that appears to affect the treatment, control and prevention of chronic diseases. In this study, we therefore describe a protocol for exploring the barriers and facilitators to the integration of four chronic diseases (diabetes, hypertension, cancer of cervix and cancer of breast) in primary health care services in western Kenya. The project is called Primary Integrated Care for 4 Chronic Diseases (PIC4C).

**Objectives:** To explore perceived barriers and facilitators to the prevention and management of four non-communicable diseases (diabetes, hypertension, cancer of cervix and cancer of breast) at the primary health care level by patients, community members and health care providers in four counties of western Kenya.

**Design:** Four counties in western Kenya will be targeted in a mixed-methods cross-sectional survey.

**Methods:** The study will commence with community mapping with assistance of local chiefs, community health volunteers and public health officers stationed in the four counties. Next, a baseline needs assessment will be conducted to document the risk factors, staffing level, health system infrastructural challenges as well as levels of knowledge, practice and attitude of community members towards these four diseases. Using different sampling techniques, the survey will use community questionnaire, health facility questionnaire, focus group and key informant interview guidelines.

**Conclusions**: The results of this baseline survey will yield information on common risk factors for the four diseases, target community's socio-demographic characteristics, level of knowledge, practice and attitude towards the four diseases, the gaps in health records information system for the four diseases, gaps in drug supply as well as supply of other essential consumables, gaps in health personnel staffing levels and health facility physical infrastructural deficiencies.

**Key words:** Community units, Integrated care, Diabetes, Hypertension, Breast cancer, Cervical cancer, Primary health care, Community-based

## Introduction

The growing threat of Non-Communicable Diseases (NCDs) in Sub-Saharan Africa (SSA) is hard to overstate because NCDs pose a great socio-economic burden (1,2). Health care costs associated with NCDs care are high due to late diagnosis, longevity and complications of these diseases (1,2). In addition, NCDs contribute significantly to mortality and morbidity (1,2). Therefore, NCDs drain household finances, reduce quality of life, lead to loss of breadwinners, thus pushing families into poverty and hindering a nation's development (1,2). In Kenya, according to the World Health Organization (WHO), ten of the top twenty causes of mortality in the country are NCDs. Of these top ten causes of mortality in Kenya, cardiovascular disease, diabetes, cervical and breast cancer feature prominently (1,2).

The Academic Model Providing Access to Healthcare (AMPATH) program is an academic global

health partnership between Moi Teaching and Referral Hospital (MTRH), Moi University College of Health Sciences, and a consortium of North American universities led by Indiana University (3,4). In recognition of the growing Non-Communicable Diseases (NCDs) burden in LMICs (5). AMPATH has established a Chronic Disease Management (CDM) Program in collaboration with the Ministry of Health (MOH) in Kenya (5). The CDM Program has enrolled over 15,000 patients with diabetes, hypertension and different cancers at over 150 health facilities spanning all levels of the health care system in western Kenya (5).

The Primary Integrated Care for four Chronic Diseases (PIC4C) is a Non-Communicable Disease (NCD) pilot project to be implemented by AMPATH in partnership with the Kenyan Ministry of Health division of non-communicable diseases and the four counties of Busia, Siaya, Trans Nzoia and Vihiga. This pilot project is necessitated by the fact that despite the great strides and successes achieved by AMPATH under the chronic disease management program, the services were implemented with a programmatic outlook that failed to include clear needs assessment and rigorous documentation of the processes, challenges and costs (5). This has made scale up of the AMPATH CDM program difficult and necessitated the design of a large pilot utilizing implementation research concepts to generate scale up evidence. In the proposed PIC4C project, AMPATH will adapt its integrated comprehensive primary health care program model for the prevention and control of diabetes, hypertension, breast and cervical cancer in a wider catchment of Trans Nzoia, Busia, Vihiga and Siaya counties of western Kenya. This work will yield evidence of common risk factors, strategies, costs and impact of scaling up an integrated chronic disease care model that would be utilized by the MOH in shaping policy (6).

In this paper, we describe the methods being applied in part one (Baseline Survey) of a four-part study that will be implemented in western Kenya over a three-year period called PIC4C. Part one is the baseline survey, part two will be the implementation stage to fill the gaps identified in baseline, part three will be an evaluation of the implementation approaches and part four will be end line survey. We report on the novel approaches that are being utilized on community entry and collection of baseline information on the four NCD disease conditions in western Kenya. The purpose of this baseline survey is to explore perceived barriers and facilitators to the early detection, prevention and management of the select NCDs (diabetes, hypertension, cancers of the cervix and breast) at the primary health care levels by general community members, patients, community leaders and health care providers in four counties of western Kenya.

**Materials and methods**

*Study aims:* To explore perceived barriers and facilitators to the prevention and management of four non-communicable diseases (diabetes, hypertension, cancer of cervix and cancer of breast) at the primary health care level by patients, community members and health care providers in four counties of western Kenya.

*Primary outcomes to be measured*

(i) Level of community knowledge, attitudes and practice concerning the care and prevention of the four diseases.
(ii) Level of availability of essential diagnostic equipment and drugs for the care of these four diseases.
(iii) Proportion (%) of health care staff cadres available for the care of these diseases.
(iv) Knowledge, attitude and practice of health care providers towards the four diseases.

*Secondary outcomes*

(i) Level of National Hospital Insurance Fund (NHIF) awareness and uptake among patients with the four diseases conditions as well as healthy community members.
(ii) Geospatial information on the distribution of the four disease conditions.
(iii) Prevalence of biological and behavioral risk factors for the four disease conditions.

*Study design and sampling frame:* This baseline survey phase of the PIC4C project will apply a cross-sectional study design. This design allows for timely collection of data in a systematic manner to be able to inform the implementation phase of the project. The baseline survey will have three complimentary components: (i) community survey, (ii) health facility survey and (iii) the qualitative survey (Focus Group Discussions plus key informant interviews. For the community survey, systematic random sampling will be used to get the Community Units (CUs), villages within a CU and then households within a village (Tables 1-5). Once at the selected household, the head of the household or any adult member aged above 18 years available in the house at the time

of the interview will be consented and interviewed using the community questionnaire. For the health facility survey, interviews will be conducted in selected Ministry of Health (MOH) facilities in the four counties. Using the facility questionnaire, the facility in-charges will be consented and interviewed, alongside documentation of available medical records, patient flow systems, presence or absence of patient clinical management algorithms, posters, pamphlets. In addition to the community and health facility interviews, 18 Focus Group Discussions (FGDs) and at least 87 key informant interviews will be conveniently selected and conducted to get detailed information on the barriers and facilitators of care and prevention of the four NCDs under the study.

*Study setting:* The study will be conducted in four counties in western Kenya-Busia, Siaya, Trans-Nzoia and Vihiga.

Trans Nzoia County covers an area of 2,495.6 $km^2$ and has 5 sub-counties namely: Endebes, Cherangany, Saboti, Kwanza and Kiminini (7,8). The county population is estimated at 1,111,686 persons and projected to increase to 1,265,797 by 2022 (7,8).

Busia county has 7 sub- counties; Teso North, Teso South, Matayos, Butula, Bunyala, Samia and Nambale sub- counties. It covers a surface area of 1,694.5 $km^2$ and has an estimated adult population of 953,337 people of whom 52% are above 18 years. The county has high poverty rates at 66.7% (7,9).

Vihiga county covers an area of 563 $Km^2$ and has a population of 590,013 of which 55% are above age 18 years. It is divided into 5 sub-counties namely, Luanda, Emuhaya, Hamisi, Sabatia and Vihiga. Its poverty level is 41.8% (7,10).

Siaya county covers an area of 2496.1 $Km^2$ with a population of 993,183 of which 53% are above 18 years of age. The county is divided into six administrative sub-counties namely; Gem, Ugunja, Ugenya, Alego-Usonga, Bondo and Rarieda (7,11).

*Study population:* This baseline survey will include adults aged above 18 years residing in the four counties. Nevertheless, the target population will be variable for the different components of the baseline survey activities.

*General community survey component:* The target population for this component will be the adult community members aged more than 18 years in the four counties, which also includes certain indigenous, vulnerable and marginalized communities. The sample size for this component is 3,594 adults (Busia 900; Trans-Nzoia 897; Siaya 897and Vihiga 900).

*Health facility survey component:* This component of the survey targets health care staff who have worked in the 87 ear-marked PIC4C health care facilities in the four counties for at least 6 months prior to study commencement. Specifically, the following cadres of staff will be interviewed: the health facility in – charges, pharmacy managers, records managers, medical officers, nurses and clinical officers who manage patients with the four PIC4C disease conditions. General observations to document the patient flows, disease management tools and care services will also be documented at the health facilities.

*Qualitative component:* Eighteen Focus Group Discussions (FGDs) will recruit a total of 144 participants (24 community leaders, 24 health care providers, 24 patients with diabetes, 24 with hypertension, 24 with cancer of the breast and 24 with cancer of the cervix) in the four counties. The participants will have to be between the ages of 18 – 60 years and able to speak English or Kiswahili language. For the FGDs that target patients with cancer of cervix and breast, only females will be recruited while for participants with the other two disease conditions (diabetes and hypertension), there will be mixed gender in the FGDs.

*Participant recruitment procedures:* For each of the three components of the survey (general community survey, health facility survey and FGDs), different recruitment strategies and sampling procedures will be applied to ensure fair selection of participants (Tables 1-5). Convenient and systematic random sampling will be applied for general community survey component while purposive sampling will be utilized for health facility and qualitative components.

*Community survey component recruitment procedures:* The community survey component will utilize a stratified sampling technique. Stratification being done starting with the community link health facility, then to Community Units (CUs) linking to the selected health facility, then villages attached to the CUs, then the households within the villages, then the house hold members. The study shall ensure that there is gender balance during community interviews at the household level. Community units and villages will be selected using the existing locator maps from the county governments. The sampling frame for health facilities will use the national master list of public health facilities in the four counties stratified further into dispensaries (Level 2), health centers (Level 3), sub-county hospitals (Level 4) and county referral hospitals (Level 5). Tables 1-5 show the sampled link health facilities, CUs, villages and households.

**Table 1:** PIC4C link health facilities in the four counties

| County | Sub-county | Number of PIC4C link facilities per sub-county |
|---|---|---|
| Busia | Teso North | 9 |
| Busia | Teso South | 4 |
| Busia | Butula | 4 |
| Busia | Matayos | 8 |
| Busia | Bunyala | 9 |
| Busia | Samia | 3 |
| Busia | Nambale | 3 |
| Trans Nzoia | Endebess | 4 |
| Trans Nzoia | Kwanza | 3 |
| Trans Nzoia | Kiminini | 8 |
| Trans Nzoia | Cherangany | 10 |
| Trans Nzoia | Saboti | 8 |
| Siaya | Alego-Usonga | 3 |
| Siaya | Bondo | 1 |
| Siaya | Rarieda | 1 |
| Siaya | Ugenya | 1 |
| Siaya | Ugunja | 2 |
| Siaya | Gem | 1 |
| Vihiga | Vihiga | 1 |
| Vihiga | Sabatia | 1 |
| Vihiga | Hamisi | 1 |
| Vihiga | Luanda | 1 |
| Vihiga | Emuhaya | 1 |
| | Total | 87 |

*Link facility selection:* In each sub-county the health facilities will be first stratified per the levels of care, i.e. Level 5 – County Referral Hospitals, Level 4 – Sub County Hospitals, Level 3 – Health Centers and Level 2-Dispensaries. Community Units (CUs) linked to each health facility will then be listed.

*Community Unit (CU) selection*: All active community units served by each selected link health facility in all the four counties will be listed against their respective health facilities. According to the Kenya community strategy, a health facility has between 3-6 active community units (13).

*Village selection:* Out of the total community units selected, a list of their respective villages will be made in consultation with the chiefs, village elders and facility link Public Health Officers (PHOs) to verify the exact number of villages per community unit. Once each village has been listed against the community unit, villages from a CU will be systematically selected to make to total of 900 households for Busia county, 897 households for Trans-nzoia county, 897 households for Siaya county and 900 households for Vihiga county.

*Household selection:* A list of all households in each selected village will be prepared by the village elders and given to the study team. The study targets a total of 900 households for Busia county, 897 households for Trans-nzoia county, 897 households for Siaya county and 900 households for Vihiga county (Tables 2-4). Once at the household level, the household head or any other adult member of the family present at the time of the interview will be selected and interviewed.

*Community component - sampling for indigenous peoples, vulnerable and marginalized groups:* The study will ensure that marginalized populations are included in the project by purposively including the CUs which host them. They include the *Sengwer* and *Ogiek* ethnic groups in Trans Nzoia county, plus the *fisher folk* and *island dwellers (Bulwani)* in Busia county. There are no indigenous communities in Siaya and Vihiga counties. In Trans Nzoia county, the *Sengwer* and *Ogiek* people are in Cherangany Sub-county, and the link health facility is Kapsara Sub-county hospital. The relevant CUs are Kabolet1, Kapchemakwer, Kipsoen, and Ex Jarvis. In Busia the *fisherfolk* live in in Bunyala sub-county, and the link health facility is Osieko dispensary. The CU is Osieko and it has 13 villages. Fishermen reside in four of these villages namely: Nakhairira/Obaro (52 households); Bukhuma (17 Households); Busikhoba (9 households); and Ingerekha (23 households).

**Table 2:** Community component: Baseline survey sampling process for Busia county

| Sub-county | Number of health facilities | Community Units | Villages | Number of House Holds (HHs) to sample proportionate to size of village |
|---|---|---|---|---|
| Teso-South | 3 | Amerikwai | High Rock | 82 |
| | | | Road Block | 90 |
| | | Amaase | Aloet | 11 |
| | | | Omuye | 9 |
| | | Odioi | Amairo A | 12 |
| | | | Amairo B | 9 |
| Teso-North | 3 | Adanya | Adanya C | 9 |
| | | | Osasame A | 12 |
| | | Onyunyur | Agonget | 9 |
| | | | Aleles | 7 |
| | | Kokare | Kasogol Kapel | 7 |
| | | | Kokare A | 17 |
| Butula | 3 | Bumala B CU | Akanyo | 9 |
| | | | Isongo B | 13 |
| | | Kingandole CU | Sigomere B | 21 |
| | | | Sieywe | 25 |
| | | Bukati C U | Elusiba | 15 |
| | | | Mukongolo | 11 |
| Bunyala | 3 | Magombe West | Khumalaya “A” | 5 |
| | | | Makunda “A” | 7 |
| | | Osieko CU | Nakharaia | 2 |
| | | | Bukhuma | 2 |
| | | Bulwani | Mukhuwa “A” | 4 |
| | | | Inyanga “A” | 4 |
| Matayos | 3 | Bugengi | Bukalama B | 38 |
| | | | Lwero A | 26 |
| | | Mjini | Burumba B | 200 |
| | | | 48 Estate | 100 |
| | | Lunga | Sikhabwa | 16 |
| | | | Nyaranga | 12 |
| Samia | 3 | Ludacho | Busibi | 6 |
| | | | Mukhwayo | 7 |
| | | Sirekeresi | Ebwani | 12 |
| | | | Sirekeresi A | 9 |
| | | Bujwanga | Mufumu A | 13 |
| | | | Buramonyi | 10 |
| Nambal**e** | 3 | Lwanyange A and B | Nandafumbwa B | 8 |
| | | | Musoma B | 15 |
| | | Mungatsi A and B | Busakadi B | 5 |
| | | | Madende B | 10 |
| | | Musokoto | Logiri | 11 |
| | | | Musokoto | 10 |
| | | Total | | 900 |

**Table 3:** Community component: Baseline survey sampling process for Trans-Nzoia county

| Sub county | Number of health facilities | Community Units | Villages | Number of Households (HHs) to sample proportionate to size of villages |
|---|---|---|---|---|
| Endebes | 3 | | Naminit | 21 |
| | | Lower Kaptega | Kiringet | 14 |
| | | | Suam Boarder | 16 |
| | | | Lukhuna | 26 |
| | | Endebess South | Manyatta | 53 |
| | | | Lungai | 31 |
| | | | Cherumbe | 8 |
| | | TulwopKesis | Kipsibo | 14 |
| | | | Kipsirir | 9 |
| Kwanza | 3 | | Koros Centre | 14 |
| | | Kwanza | Maili saba | 18 |
| | | | Weyeta | 11 |
| | | | Karaus Catholic | 13 |
| | | Karaus | Kesogon Farm | 13 |
| | | | Sokomoko | 14 |
| | | | Mukweya | 10 |
| | | Namanjalala | Maliki | 33 |
| | | | Nabin'genge | 25 |
| Kiminini | 3 | | Ndelema | 27 |
| | | Sabata | Makani | 5 |
| | | | Misemwa | 26 |
| | | | Siuna B | 22 |
| | | Kiungani | Sosio | 8 |
| | | | Mnyama B | 11 |
| | | | Kaptien | 48 |
| | | Toro | Toro B | 25 |
| | | | Kitongoria | 23 |
| Cherangany | 3 | | Kipsoen | 15 |
| | | Kabolet1 | Ex jarvis B | 48 |
| | | | Kapchemakwer | 19 |
| | | | Kimoson | 12 |
| | | Kaplamai | Acre Tano | 37 |
| | | | Munaha | 10 |
| | | | Marura | 25 |
| | | Nairobi | Nairobi Ndogo | 23 |
| | | | Sinyereri | 17 |
| Saboti | 3 | | Sukwo Kween | 10 |
| | | Sukwo | Cheptilil | 35 |
| | | | Lamaywet | 10 |
| | | | Mukuha | 17 |
| | | Gitwamba | Museng | 23 |
| | | | Sigerger | 26 |
| | | | Soweto | 5 |
| | | Shauri Moyo | Site and Service 1 | 19 |
| | | | Pangani | 8 |
| Total | 15 | 15 | 45 | 897 |

**Table 4:** Community component: Baseline survey sampling process for Siaya county

| Sub-county | Number of sampled health facilities per sub-county | Community Units (CUs) | Villages | Number of Households (HHs) to sample proportionate to size of villages |
|---|---|---|---|---|
| Alego-Usonga | 3 | 4 | 8 | 147 |
| Bondo | 1 | 3 | 6 | 150 |
| Rarieda | 1 | 3 | 5 | 150 |
| Ugenya | 1 | 3 | 6 | 150 |
| Ugunja | 2 | 3 | 6 | 150 |
| Gem | 1 | 3 | 6 | 150 |
| Total | 9 | 19 | 38 | 897 |

**Table 5:** Community component: Baseline survey sampling process for Vihiga county

| Sub-county | Number of sampled health facilities per Sub-county | Community Units (CUs) | Villages | Number of Households (HHs) to sample proportionate to size of villages |
|---|---|---|---|---|
| Vihiga | 1 | 3 | 7 | 180 |
| Hamisis | 1 | 3 | 9 | 180 |
| Sabatia | 1 | 3 | 9 | 180 |
| Luanda | 1 | 3 | 9 | 181 |
| Emuhaya | 1 | 3 | 9 | 180 |
| Total | 5 | 15 | 43 | 901 |

*Health facility component recruitment procedures:* PIC4C study intends to engage 87 facilities to participate in the baseline survey and later implement the project in the four counties. A health facility questionnaire will be utilized in order to assess and get baseline data for health facility staffing levels, staff cadres, staff qualifications, NCD care services offered (screening and treatment), level and frequency of availability of equipment and supplies for each of the four NCDs, screening and treatment data from medical records for the four NCDs, availability of essential drugs, knowledge, attitude and practices among the healthcare providers on the four conditions. The study will purposively sample and interview health staffs in all the 87 health facilities. As shown in Table 5, the 40 facilities in Busia, the 33 health facilities in Trans Nzoia, 9 in Siaya and 5 in Vihiga were included to represent all the public county health facilities in the project.

**Table 6:** Health facilities sampled in the PIC4C study

| Health facility level of care | Busia | Trans-Nzoia | Siaya | Vihiga | Total |
|---|---|---|---|---|---|
| Level 2 (Dispensaries) | 22 | 13 | 0 | 0 | |
| Level 3 (Health centers) | 10 | 13 | 1 | 0 | |
| Level 4 (Sub-county hospitals) | 7 | 6 | 7 | 4 | |
| Level 5 (County referral hospitals) | 1 | 1 | 1 | 1 | |
| Total | 40 | 33 | 9 | 5 | 87 |

*The qualitative component recruitment procedures*: Eighteen Focus Group Discussions (FGDs) will recruit a total of 144 participants (24 community leaders, 24 health care providers, 24 patients with diabetes, 24 with hypertension, 24 with cancer of the breast and 24 with cancer of the cervix) in the four counties. The participants will have to be between the ages of 18 – 60 years and able to speak English or Kiswahili language. For the FGDs that target patients with cancer of cervix and breast, only females will be recruited while for participants with the other two disease conditions (diabetes and hypertension), there will be mixed gender FGDs. Recruitment guides have been prepared and will be shared with the RAs.

*Study materials:* Three different types of questionnaires will be used: (i) The community questionnaire, (ii) The health facility questionnaire and (iii) The FGD interview guide. The community questionnaire for the baseline survey (12) will cover

the following domains: demographic information (age, sex, marital status, ethnicity, education, and occupation); work history (salaries and benefits); Medical history (history of chronic diseases and drugs used, hospital attended, family history of chronic disease, and family planning use), social history; tobacco use; alcohol consumption; physical activity (activities as work, travel to and from places, and sedentary behavior); nutrition; and knowledge, attitude and practice on health in general details on including blood pressure, heart rate, height, weight, and waist circumference were also captured (12). The health facility questionnaire (12) will capture health facility data on the following domains: Facility information on the total number of staff per given cadre, screening, referrals and treatment for the four diseases; type of data registers used; health services and messaging available; availability of equipment and supplies (blood pressure machine, glucometer, HBA1c machine, sterilizer, ultrasound machine, cryotherapy equipment, X-ray machine, and autoclave); and provider knowledge, attitude and practices on the four conditions.

The FGD guides were developed based on the Health Belief Model" and focuses on the following domains: perceived severity, perceived benefits, perceived barriers perceived susceptibility, cues to action, and self-efficacy. Additional domains incorporated in the FGD guide include community perception of NCDs, successes and challenges of existing NCD programs, and recommendation for appropriate NCD programs. The FGD guide for patients with any of the four disease conditions will include domains that will explore experiences with NCDs, while the one for health care providers has incorporated sections on experiences with prevention and treatment of NCDs at the primary health care levels. The guides were translated from English to Swahili and back translated.

These questionnaires for the three components of the baseline survey (community questionnaire, health facility questionnaire and the FGD interview guide) were adapted from three sources:

(i) The World Health Organization (WHO) STEPwise approach to chronic disease risk factor surveillance (STEPS) with modification to suite the Kenyan situation (12).
(ii) Previous studies conducted by the AMPATH CDM (3,4).
(iii) FANTA 24 Hour Recall Questionnaire (13)

In addition to the above questionnaires, each Research Assistant (RA) will have to be equipped with the following tools while conducting the community survey:

(i) Hand held electronic device (Tablet) with the REDCAP community plus health facility questionnaire software installed in it.
(ii) Ten backup physical copy forms of the questionnaires in case power ran out from the tablets during the interviews.
(iii) A weighing scale (SECA BRAND).
(iv) An OMRON – Blood Pressure Machine.
(v) Blood glucose testing machine and strips (FREESTYLE – OPTIUM NEO).
(vi) Hand gloves, cotton wool and surgical spirit for taking the blood glucose.
(vii) Two tape measures and masking tape for taking height and waist circumference.

*Training of the research team members:* A team of sixteen Research Assistants (RAs), research coordinator and data entry clerks are being trained on study aims and procedures. Topics to be covered include research ethics, use of FGDs, questionnaires, and REDCAP for data collection. They will also learn about the NHIF (benefits, packages, and the enrollment processes) and take time to review each study tool page by page, in both English and Swahili languages. The health facility questionnaire is a technical questionnaire which require RAs who understood the clinical terminology used. For that reason, two clinical officers will be trained specifically to collect the data for the health facility component.

**Data collection procedures and processes**

*Pretesting the study tools:* This will be done in order to allow for testing of the tools as well as for the research assistants to gain confidence in using the tools (tablets with REDCAP, glucometer, BP machine, weighing scales). A pilot will be conducted in Turbo sub-county and Huruma sub–county in Uasin-Gishu county. These two sub-counties were picked because they are within easy geographic reach and they are similar to the study counties of interest. The team will pretest the tools in these sub-counties as well as test the feasibility of the study. For the pretesting of the community questionnaire, 20 interviews will be conducted in Huruma and 15 in Turbo (20 females and 15 males). Regarding the health facility questionnaire, two facility in charges, two pharmacists, and two records officers will be interviewed in each of the two sub-counties. While still at the health facilities, the trained RAs are also to make observations of the facility screening and treatment processes, data capture and relay plus the available supplies for the treatment of the four chronic diseases. Pretesting of the FGDs will include one FGD to be conducted in Huruma Sub-county and one FGD in Turbo sub-county.

**Data collection process**

*Community survey component:* On the morning of data collection from a selected village, the research assistants will meet with the village elders and sub-chiefs in a predetermined meeting point indicated on the village maps. The starting point (household) will be picked randomly and then the household sampling interval determined by the total number of households in the village divided by the targeted household sample size in that village. At the household level, the research assistants will obtain written consent and then conduct face to face interviews by administering the community questionnaires. The study interviews will follow a sequential process consisting of interviews on socio-demographic information, and then selected major health risk behaviors and then subsequently taking anthropometric measurements including height, weight and waist circumference. Other measurements as included in the questionnaire are random blood sugar, blood pressure and heart rate. Weight measurement will be done in kilograms using a portable weighting scale. Waist circumference measurements in centimeters to be done using a tape across the umbilicus level. Blood pressure and pulse rate will be taken three times using an automated blood pressure measuring instrument (OMRON®). The height measurements will be taken in centimeters as well.

After collecting data in the household, the RAs will synchronize the data on REDCAP app and send the data to the central server. Each RA will then call his/her colleagues to share the sex and age of the interviewed participants so as to ensure a balance between the male and female participants and the age bracket before going to the next household. The data management team at the research headquarters in MTRH will continuously check the synchronized data to check for errors and communicate promptly to the RAs for correction before they move to the next village.

*Health facility survey component.:* The RAs for collecting data on this component will be clinical officers and nursing officers who understand the medical terminologies used in the facility questionnaire. They will interview health care providers and make observations in all the 87 health care facilities that are targeted. One RA will cover the 40 PIC4C health facilities in Busia county and the others to cover the 33 health facilities in Trans Nzoia county, one in Vihiga county and one in Siaya county. Interview schedules will be prepared in advance for the four counties. The study coordinators will make phone calls to book appointments for the surveys in all the 87 health facilities. The trained RAs (clinical officers or nurses) will be required to call and remind the facility in charges of the interviews a day prior to the interview days.

At each health facility, written consent from the facility in-charges to interview them will be obtained. Others to be interviewed will include the heath facility departmental heads; pharmacy and records officers, clinical staff who run the diabetes, hypertension, cancer of the cervix and cancer of the breast clinics. The RAs will at the same time review health records at the facility for screening, referrals and treatment services for the four diseases (diabetes, hypertension, cancer of the cervix, and cancer of the breast). While reviewing the medical records, they will also check the type of registers that are used by the facilities to capture the clinical care data. They will note down if the data registers at the health facilities are MOH registers, partner registers or a facility modified register. This review will cover data from diverse medical records including patient files or booklets, clinic registers, clinic diaries, triage desk registers, data reporting tools, education and awareness materials, and job aids available at the health care facilities. They will then visit the pharmacies to physically verify the availability drugs for diabetes and hypertension plus the two cancers. They will lastly walk through the health facilities to check for posters and teaching materials addressing the four chronic diseases.

*The Focus Group Discussions (FGDs):* A day before the date the FGD is to take place, the participants will be called via mobile phone and reminded of the time and venue of the FGD. The FGD sessions will be conducted in English or Swahili and in a private space (venue), and at a time that is convenient for the majority of the participants. During the sessions, data will be collected using audio recorders plus scribe notes templates. On the morning of interview and prior to the FGD session, all participants will give written consent. The FGD moderator (an RA) will guide the discussions using the FGD question guide as the scribe takes notes and ensure the audio recorders are working. At the end of the FGD, a light snack and tea will be served and participants' transport costs reimbursed.

**Data management and analysis plan**

Data will be captured on REDCAP and downloaded on a central server at the study head office at AMPATH/MTRH, Eldoret. Data will be cleaned and de-identified in preparation for analyses. Questionnaires will be programmed into Research Electronic Data capture (REDCAP) database, which allows for direct data entry, daily cleaning and close oversight. Several lessons are to be learnt from the pilot phase. Piloting of community questionnaire to show whether the offline REDCAP mobile app is faster than the online REDCAP option.

All the hand-held electronic devices (tablets) will be loaded with this app for use in the study. The REDCAP has in-build data quality checks that will be used during the study to prevent incomplete forms/ questionnaires. A standard operating procedure for synchronization of data will also be installed and applied. The study team (RA and data managers) will be able to monitor tablet battery half-life, amount of mobile data bundles per client interviewed or per day, and choose the type of tablet to use for data collection. They will also agree and test the back-up paper forms that may be required during the study. It is estimated that most of the community interviews will take approximately 1 hour per client and the RAs will be able to conduct 6 to 8 questionnaires in a day. Piloting the health facility questionnaire will show which facility registers and records are to be checked.

Each interview session for the facility questionnaire is expected to take about 2 hours and there is need to group and ask all questions relevant to any one department so that the RA would complete data collection with specific participants during one visit. Regarding the FGD, the sessions are expected to last one to two hours.

The team will test and revise the questions to ensure they are clear and non-repetitive in order to stay within one to two-hour sessions. The tools will also be cross-translated because the 'proper Swahili' used may be too technical for the ordinary community members to understand.

*Ethical considerations and approvals:* The study was approved by the Moi University College of Health Sciences/Moi Teaching and Referral Hospital University Institutional Research and Ethics Committee (IREC Number: IREC/2017/163) and National Commission for Science, Technology and Innovation Kenya (Reference number: NACOSTI/P/18/74238/24329). Written informed consent will be sought from all study participants and privacy/confidentiality of participant information assured. All information collected will be kept confidential and all research materials stored safely. Personal identifiers will only appear in the consent forms and will be stored separately. The data will be stored in the REDCAP server and password protected with access only granted to approved data managers and study investigators. All study team and staff will be trained in ethical procedures and measures to protect human subjects. The risk of participation for all the respondents in this study is minimal, being limited mostly to temporary discomfort associated with the finger prick blood collection process. Participants identified as requiring referral for care (such as those with high blood sugar or bood pressure) will be directed to relevant health facilities.

Approvals to enter community will be sought from the county health management teams through the chief officers of health and they will routinely be updated as the study progresses. Prior to kicking off the community entry, the research team will organize community entry meetings in each county with the link facilities picked to be part of the sample. The health facility in-charges, public health officers, chiefs and village elders of the villages sampled will be included in these community entry meetings.

*Plans for dissemination of the study outcome once completed:* The study method will be disseminated to the community via the county health management teams, chiefs' baraza sessions, medical peer reviewed journals, workshops, and scientific conferences among others.

## Discussion

In Kenya, healthcare is structured into six levels: Level 1: household/community, Level 2 and 3 facilities: dispensaries and health centers serving a population of 5000 to 20000. Level 4 facilities: Sub-county hospitals that serve a population of approximately 500,000 to 100,0000 and Level 5 and 6 facilities: county and national referral centers respectively (6,7). Traditionally, as in most countries in Sub-Saharan Africa (SSA), Level 1-3 facilities have focused exclusively on promoting Maternal and Child Health (MCH) activities in addition to prevention and control of communicable diseases. Treatment for NCDs has traditionally only been available in Level 4-6 facilities. As a result, very little effort has been put towards community prevention activities, early detection and treatment, or improved continuity of care for NCDs; yet these elements are fundamental to successfully addressing the threat of NCDs. Additionally, given the growing numbers of patients with NCDs, limiting their care to Level 4 and above health facilities has caused unnecessary congestion and delay in detection, and increases in costs of seeking care among patients with NCDs as patients have to traverse long distances looking for a Level 4, 5, or 6 health facility to get care (6,7).

Over the years, AMPATH has adopted and uses system-wide approaches to NCD care, ranging from task redistribution (task-shifting/sharing), use of mobile -health platform, electronic decision support and ensuring a reliable supply of medicines plus other essential medical commodities for NCD care (3-5). This approach has created a unique, but yet to be tested opportunities to address the rising burden of NCDs within the AMPATH catchment. Using lessons learnt from these interventions, the primary health care system within the AMPATH catchment has also

been re-designed to not only cater for Maternal-Child-Health (MCH) and infectious diseases but also incorporate NCDs into its care programs. This integration is expected to promote both efficiency of health care delivery and increase cost- effectiveness of interventions (1,2). Therefore, a good paradigm of an integrated primary healthcare model for chronic non-communicable diseases in primary care settings is the AMPATH model in western Kenya.

Despite all these efforts, integration of NCDs into primary healthcare is still suboptimal in western Kenya. Furthermore, in many developing countries, Kenya included, NCD care and prevention do not seem to be highly rated among other priorities in the Ministries of Health (1,2). Another important component of NCD care in primary health setting that has been ignored is demand creation. Before demand is created for NCD services in any community, one needs to carry out a need's assessment looking for barriers and facilitators for the uptake of the services. There is therefore need for baseline data on available risk factors for NCDs, data on community knowledge, attitudes, and practice for NCDs, data on health system capacity to tackle NCDs. It is within this AMPATH-MOH clinical infrastructure and community background setting that we anticipate that the planned PIC4C pilot project will inform scale up of integrated NCD care at the primary health care level in western Kenya.

## Conclusions

The results of this baseline survey will yield information on common risk factors for the four diseases, target community's socio-demographic characteristics, level of knowledge, practice and attitude towards the four diseases, the gaps in health records information system for the four diseases, gaps in drug supply as well as supply of other essential consumables, gaps in health personnel staffing levels and health facility physical infrastructural deficiencies.


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***Competing interests:*** The authors declare that they have no competing interests.

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**Commentary**

# Undergraduate Medical Education at Cross Roads

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There is a growing concern that all is not well with undergraduate medical education. Indeed, representatives of 67 countries at the World conference on medical education in 1988 were in little doubt that medical education is in a poor state (1). Furthermore, one medical dean has referred to a crisis in undergraduate education, and some of the shortcomings of medical education have been referred to as scandals (2). I believe that the responsibility for this unhappy state of affairs resides within the medical schools (3). Although a squeeze on resources has not helped, it has not been the critical factor. I do not believe that improvements in student selection procedures would have a major impact. There is no denying, however, the striking difference between the bright, interesting 18 year olds seen at interviews and the weary, disillusioned, unquestioning absorbers of information seen during the clinical years.

The most influential factors in this change must be medical schools. Undergraduate teaching is uneven in quality, variable in commitment, and lacking in coordinated objectives. The main problem is that medical schools are attracting some of the most able young people in the country and simply boring them to death (3). The consequence is that the students are the losers. And if medical students are losing out today, patients will lose out tomorrow.

I think that patients are already losing out. Indeed, a large proportion of graduates have a poor grasp of clinical logic, are uncertain in their choice of diagnostic tests, make poor decisions in prescribing, have limited communication skills, and have a poor grasp of ethical principles (2). Even more alarming, studies have shown that a significant minority of senior medical students and house officers are deficient in the basic clinical skills of taking a history and making a physical examination. If matters are to be rectified we need a fundamental rethink of the role of medical schools in producing the doctors of tomorrow.

**Perceived importance of teaching**

Unfortunately, some medical schools are less than fully committed to teaching (3). A major difficulty, therefore, is that students' education is controlled by those whose principal interests lie in areas such as patient care or research rather than in teaching. Medical schools need to be reminded that they are the only institutions with the responsibility of preparing medical students to become doctors, it is a task they must take more seriously. Even those who are committed to teaching are professors who spend more time away from teaching their own students. In Europe the Professors engage in research for pharmaceutical companies and go on lecturing trips all over the world. They also spend more time attending conferences and workshops organized by pharmaceutical companies fully sponsored. In Africa Professors spend time on patient care as they are paid for the same (4).

**The notion of "entitlement" (Haki yetu)**

Even if it were possible to eradicate all the short comings of the medical curriculum and medical teachers it would still be necessary to overcome the problem of "entitlement," with which a growing minority of medical students is becoming afflicted (5). "Entitlement" has been described as "a sense of being entitled to attention, caretaking, love, successful income without having to give anything in return. The first is that they believe that it is a student's right to acquire knowledge with minimal exertion- for example, they may demand to be given just the facts or told which pages to read so that they don't read too much. The second is that they think that learning problems are due to inadequacies in anything and anyone other than their own shortcomings – for example, it is their teacher's fault, the fault of the course. The third, and perhaps most distressing, characteristic of "entitlement" is the aggressive response to any feelings of discomfort- for example, if a cherished view is challenged or a limited capacity for critical thinking is exposed the student's response too often is to cause a hostile and disrespectful confrontation rather than reflection and participation in a reasoned interchange of views.

**Hospital versus community based teaching**

Traditionally, the teaching hospital has been the dominant teaching and learning environment for basic medical education. No one would dispute that the teaching hospital has had and still has much to offer student doctors. A hospital is probably the best environment for introducing students to inductive history taking and comprehensive physical examination. Students can be given multiple

opportunities especially in the wards, to memorize the range of questions which patients may need to be asked and to develop skills in eliciting abnormal physical signs (later, hopefully, they will become more selective in both history taking and physical examination). They can also learn how to recognize and manage serious and acute medical conditions, and management will often entail using high technology equipment.

On the other hand, the longstanding imbalance between hospital based and community based teaching and learning has some negative consequences (6). For example, students have been exposed to highly selected patient populations with the rarest and most serious diseases or at best atypical examples or presentations of the commoner ones. This creates a misleading picture of the real nature and extent of society's medical and health problems.

Hospital based teaching has also tended to concentrate on biological factors. Students are faced with "the notion of the body as a machine, of disease as a consequence of breakdown of the machine, and the doctor's task as repairer of the machine,"(7). This is a very restricted view because much scientifically credible evidence transcends the biomedical model, casting doubts on the adequacy of the model to explain a wide variety of phenomena associated with health and disease. Students need to be exposed more to models of care and to teaching which appropriately integrate the physical, social, and psychological aspects of clinical practice.

The traditional drawbacks of hospital as the predominant base for undergraduate teaching have been compounded by recent changes in the pattern of health care provision. Increased through put of patients combined with shorter patient stays and super specialization have all adversely affected the ability of hospitals to provide a suitable context for basic medical education. It is therefore becoming increasingly difficult for students to acquire and develop certain skills within the modern teaching hospital (7). For example, as most patients now reach the wards, and to a lesser extent the outpatient departments, with their condition having already been diagnosed by their general practitioner or through a routine work up, students are denied sufficient practice in diagnostic reasoning. Furthermore, there has been a shift of emphasis towards more primary and community care. Indeed, many observers believe that the modern general practitioner is increasingly occupying the clinical role traditionally occupied by the hospital general physician (7). All these factors argue for much greater emphasis on community based teaching.

**Training the doctors of tomorrow**

The problem in medical education is that the doctors of tomorrow are trained by Professors of today using tools of yesterday (8). Training tomorrows doctors demonstrates the challenges facing medical education. Artificial Intelligence (AI) is a growing phenomenon, and will soon facilitate wide-scale changes in many professions, including medical education. In order for medical educators to be properly prepared for AI in relation to learnig and teaching, and the extent to which it will impact on medical education (9).

Medical education must evolve because future physicians will encouter patients in quite different health care contexts from the present. Ubiquitou and digitalized health care systems allow both physicians and patients to access biomedical information from a surplus of options. Artificial intelligence will reduce the effort required by physicians to interpret digital data and improve their ability to establisha diagnosis and prognosis. Therefore, the non-analytical, humanistic aspect of medicine will come to be more emphasized because it is hard to replace it with technology. Moreover, advanced medical technology leads to physicians encountering a growing number of elderly people and latent patients with chronic conditions and comorbidities due to their prolonged life span.

**Medical education and training in Sub-Saharan Africa**

By reviewing literature on Africa's epidemiologic and demographic transitions, we establish the need for increasing the output of well-trained doctors in order to match the continent's complex current and future healthcare needs. Challenges that bedevil African medical education are outdated curricula. Limited educational infrastructure and chronic resource constraints are presented and discussed. Furthermore, increased students enrollments, a trend observed at many schools, coupled with chronic faculty shortages have inadvertently presented specific barriers against the success of small-group active-learning strategies such as "Problem-Based and Case-Based learning".

Sub-Saharan Africa suffers a disproportionate share of the world's burden of disease while having some of the world's greatest health care workforce shortages. Doctors are an important component of any high functioning health care system. However, efforts to strengthen the doctor workforce in the region have been limited by a small number of medical schools with limited enrollments, international migration of graduates, poor geographic distribution of doctors, and insufficient data on medical schools. Over the last 30 years, several changes have been introduced in medical education including the introduction of new contextualized approaches to instruction (e.g.

Problem-Based Learning [PBL]), the use of multimedia to enhance self-directed leaning, the use of an integrated curriculum to address basic and clinical sciences, and the introduction of new formative and summative assessment tools that match with the curriculum changes.

Trainers of Africa's future doctors have recognized the need for medical schools to adopt active-learning strategies in order to nurture holistic development of the doctor. However, medical education in Africa remains largely stuck with traditional pedagogies that emphasize the 'hard skills' such as knowledge and clinical acumen while doing little to develop 'soft skills' such as effective communication, teamwork, critical thinking or life-long learning skills.

What is fundamental for medical students to learn in the 21st Century? Many medical educators understandably focus on the explosion of new medical knowledge and technology that will be essential for medical students to master in the 21st Century. These include advances in molecular medicine, genomics, a plethora of new pharmacological approaches, among other stunning discoveries in medicine. Moreover, there will be a continued need to ensure that medical students acquire the highest level of professional ethics leadership skills, empathy, and counication and patient-centered counseling skills. All of these have been a core focus of medical educators over the past decade and will continue to be a priority. In thinkings about the 21st Century, there are several key additional areas of content knowledge and skills that will be essential for future physicians that to date have not received sufficient attention in medical skill curricula (10).

The medical students whom we teach today become the doctors of tomorrow, carrying our values, skills and our hopes for the profession into the future (11). Therefore, it is no exaggeration to say that medical education represents the future of medicine (7). Medical education must adapt to different health care contexts, including digitalized health care systems and a digital generation of students. The pursuit of future medical education is about strengthening the humanistic approach to patients and other professional teams to ensure patient safety. Early clinical experience and longitudinal integration are very helpful in promoting effective and lifelong learning. Community-based programs enable students to broaden their perspectives on society and develop respect for diverse patients (12). Future physicians will be able to use high technology for individualized learning, social interaction, and access to vast resource. It is a hyper-connected world.

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**Obituary**

# Medical Fraternity Tribute to Dr. Martin Luther Oduori

**Aluoch JA**

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***Dr. Martin Luther Oduori***
*MBChB, DCH, FRCP (Edin)*

April 2017 heralded the end of an epic journey of heroism and achievement of an illustrious member of the medical profession. A brilliant, unassuming and humble man, who gave his life to God, family and the medical profession, specialized and excelled in the Paediatrics and Child health, who gave his entire life to serving mankind in both the public and private sector. The medical fraternity would like to join others in expressing our deepest condolences to Martin's family. The medical fraternity feels the tremendous loss of such a great and esteemed colleague, our prayers and thoughts are with the family at this hour as we come to grips with this loss.

As a long serving member of Kenya Medical Association (KMA) he made his mark as one of the longest serving Chief Editor of the *East African Medical Journal* (EAMJ) a position he held for over 8 years, from 1979 to 1987. Dr. Oduori combined this position with other key KMA engagements, serving as the Chairman of the standing committee of the EAMJ in addition to being its Chief Editor and also as the Convener and Chairman of the standing committee on standards and ethics. He also served as a member of KMA Trustee and was often prominent by his quietness at KMA elections.

Following his rotation as an intern in Kenyatta National Hospital (KNH), then known as King George Hospital in 1962, having graduated from Makerere University Medical School and post graduate training in the United Kingdom first in England in Paediatrics at Great Olmond Street Hospital attaining a Diploma in Child Health in 1966, he them proceeded to Edinburg Q1 Glasgow in 1967 where he attained an MRCP. Dr. ML Oduori was in the group of the first paediatricians.

In KNH he was promoted as hospital administrator, an assignment he carried with devotion, dedication and excellence. Martin was later transferred to the Ministry of Health in Afya house, where he served as the first head of Primary Health Care for several years before retiring from civil service to the private sector. However before he left the civil service he was appointed to serve the Nairobi City Commission, where I had the opportunity to work with him as a fellow commissioner.

He was always active in many medical associations, a prominent member of the then APECA, when there was no paediatric association, the small doctors were still growing up under the care of adults.

On behalf of professional colleagues and peers in the practice of medicine, I am today privileged to say something in honour of my fallen colleague, Dr. Oduori. The late enjoyed an illustrious career spanning over 50 years. This is particularly of relevant to me as I had the opportunity to have had a long interview with him towards the end of last year about my book, just before he fell sick.

Dr. Oduori was a thorough, going professional whose attention and presence in a medical case was most assuring. In his long and illustrious career, I can say without fear of contradiction that we have all lost a dear friend and colleague and an inspiration to many young doctors. Dr. Oduori's passion, professionalism and leadership skills were recognized far and wide, and not just by personal acquaintances. As one of the pioneers of medical practice in Kenya, he garnered a lot of accolades and held several important positions pivotal to the development and practice of medicine in Kenya.

Dr. Oduori was one of the pioneers of the Department of Paediatrics and Child Health at the Kenyatta National Hospital in the country together with others such as the late Prof. Normano Bwibo, who forged a strong link between the practice of medicine at the KNH and the teaching and research at the University of Nairobi. The founding staff of the Department of Paediatrics and Child Health came from Mc Gill University Canada, they were six namely: Prof. Allan Ross as the Chairman of the Department and Prof. Donald Hillman and his wife Prof. Elizabeth Hillman, Prof. Donald Clogg, Prof. Collin Forbes and Prof. Leaky. By June 1972, Professor Allan Ross, the Chairman, had six months to go before his return to Canada. He soon relinquished the position of Chairmanship of the Department to Prof. Nimrod O. Bwibo.

The Medical School worked closely with the Kenyatta National Hospital Paediatric Consultants under the leadership of Dr. Martin Luther Oduori, who was then the Government Chief Paediatrician

and head of the Kenyatta National Hospital team. The other members of his staff were Dr. Kimemia and Dr. Peter Muiva.

Thus, even as we mourn the loss of such an illustrious son of Kenya and servant of the people, let us also boldly celebrate his lifetime achievements. For a life meaningfully lived is worth celebrating. Dr. Oduori may have transitioned to distant shores, but his indelible mark upon us yet endures, and his achievements cannot be undone by even the cruel hand of fate.

I am challenged to think what shall be said about us when our time comes; whether our achievements will shine as brightly, and whether our services will be missed as much as I know that Dr. Oduori's will.

## Rest in Peace, great doctor.

**Do** ***not stand at my grave and weep,***
***I am not there, I*** **do** ***not sleep.***
***I am a thousand winds that blow.***
***I am the diamond glint on snow.***
***I am the sunlight on ripened grain.***
***I*** **am** ***the gentle autumn rain.***
***When you wake in the morning hush,***
**I am** ***the swift, uplifting rush***
***Of quiet birds in circling flight.***
***I am the soft starlight at night.***
**Do** ***not stand at my*** **grave** ***and weep.***
***I am not there, I*** **do** ***not sleep.***
***(Do not stand at my grave and cry.***
***I am not there, I did not die!)***

**Obituary**

# The Late Prof. Mohammed Abdalla Said

**Warshow MM**

Aga Khan University Hospital Nairobi, PO Box 32070 – 00100, Nairobi, Kenya

**Prof. Mohammed S. Abdullah**
*MBChB, MMed, FCP(ECSA)*

We are here to mourn a great family man, a brother, a friend, and a pioneer.

We first met in 1953 when during the colonial times, we joined the Arab primary School in Mombasa. The school was later renamed as The Serani School at independence.

Even at this early stage Mohamed's personality and authoritative skills earned him status as a prefect. His academic prowess and oratory abilities were also evident as exemplified by the fact that examination rankings rated him amongst the top five in his class.

In 1960 having passed the KCPE exam we progressed to what is now known as the Khamis Secondary School. His academic performance continued to blossom and so did his status having been made a prefect and later a head boy despite his relatively small physical stature at that time. Being a prefect and me being a non-conformist meant that we were often on the opposite side of the law which he vehemently enforced with gusto.

As a good sprinter he was a member of the athletic team. See picture below taken when Khamis Secondary School won the annual Coast interschool football championship (which was rather often), Shimo La Tewa Secondary School being our most worthy challengers.

In 1963. after passing the Cambridge "O levels examination". We moved to the Allidina Visram High School in Mombasa, our first CO-ED experience. This was a rather short but intensive period in our lives when academic requirements had suddenly accelerated with socializing taking a back seat. High school exams came swiftly and having passed well we were offered the privilege of proceeding to the stellar Makerere University in Uganda to study medicine as government sponsored candidates.

At Makerere we were housed in adjacent halls (New Hall and North Court) spending many hours socializing in between academic commitments. It was here that I appreciated his tremendous sense of humour and his unforgettable and infectious laughter. Mohamed had a lovable character and I instantly forgave him for the times he marched me to the headmaster's office for disciplining in the secondary school.

On completion of our medical training and internship we were both accepted as the first MMed batch in Kenya and at that time bonded by the Ministry of Health to serve out our bursary financial assistance.

His inclination to nephrology started very early and I remember that in our first year, he approached the "Chinese team" who incidentally came with the donation of the first dialyses machines in Kenya, then located at the Kenyatta National Hospital. I remember an amusing moment when after a tedious exchange in English and a predominantly Chinese response with a sprinkle of English, he enquired "Do you have a manual for these machines". The response was immediate, defensive but rather hilarious. "Sorry, no manual everything automatic"!

As we progressed towards the second part of the MMed course, he embarked on his thesis which was a study of albuminuria. At a time when there was no ultrasound or CT scanning, he was already doing renal biopsies. Needles being in short supply I remember requesting a fabricator friend to make a replica in steel so that it can be repeatedly sterilized and even re-sharpened. I can safely mention this now as the "statute of limitation" for a patency breach is long expired!

During our M Med years, we both got married and with Allah's blessings expanded our families and our children spent hours playing together. Literally most of our leisure time were spent with Dr. Mohamed's family, "a memory I will always cherish".

Just prior to our MMed finals we were offered The Canadian International Development Agency

scholarship, nephrology for mohammed, and cardiology for me. The offer was only valid if we transferred from the MOH to the University of Nairobi. Having no post- graduate qualifications at that time this was a major hurdle. At the insistence of the Canadian faculty (then seconded to Kenya) a solution came in the form of the creation of an "assistant lecturer's" post. This did not come on a plate as we had to endure an advertised competitive interview with better qualified contestants which with Allah's grace we managed to upstage!

After our sub-specialty training, we worked in our respective units as lecturers in the Department of Medicine. Those were happy years and we both enjoyed the academia and particularly our teaching duties interacting with all the budding doctors.

In 1979, I moved into private practice at the Nairobi Hospital and Dr. Mohammed later moved to the Aga Khan University Hospital. Although geographically near to each other it proved to be a world apart! Our interactions were reduced to very occasional and mainly professional exchanges. During this time, he acquired many distinguished accolades and to mention a few, Chair of the Department of Medicine at the Aga Khan University Hospital, KEMRI, and a prominent member of the Kenya Renal Association. At the Aga Khan University Hospital, he rose to the status of a professor in the Department of Medicine. He was also amongst the first indigenous members of the Kenya Medical Association (KMA).

I will always remember Mohammed for all the great, memorable, and happy times we shared for so many years. I mourn him as a brother, a friend and proudly as a pioneer of medicine in our country. It is only appropriate that I end with a prayer.

" ارحمهـ و اسكنهـ في الجنة الفردوسنا و أنا اليهـ راجعون اللهـم"

"May Allah have mercy on him and offer him the highest paradise for we come from ALLAH and to him do we return".

# Instructions to authors

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Note that references should be numbered in order of appearance (Vancouver style) and strictly only those cited in the text should appear in the reference list.

All manuscripts should be submitted to the Editor-in-Chief, Prof. Omondi Oyoo, email: jokapkenya@gmail.com