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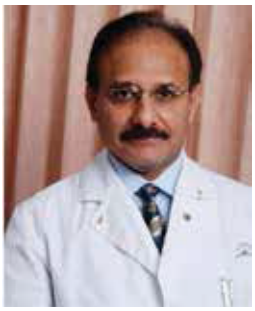

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Incorporating Clinical Genetics in Routine Patient Care

"One general law, leading to the advancement of all organic beings, namely, multiply, vary, let the strongest live." Charles Darwin, The Origin of Species 1859 (1)

The discovery of the double helical deoxyribonucleic acid (DNA) structure by Watson, Crick & Wilson, for which they received the Nobel Prize for Physiology/ Medicine in 1962, heralded the start of unravelling the mysteries of the human genome. The genome of an organism is responsible for encoding of all information necessary for its existence and propagation of life. All living organisms on earth can trace their origin to 3.8billion years ago, when our universal ancestor resided in water (2). Subsequent evolutionary changes led to diversification of the phylogenetic tree with the emergence of new and distinct species. It is due to having common ancestry than humans share 96% and 40% of the genetic material with chimpanzees and bananas respectively (3). Human species are 99.9% identical, with the least diversity observed among monozygotic twins.

In order to decode the human genome, the National Institutes of Health undertook the Human Genome Project (HGP) and mapped out the entire nucleotide sequence consisting of 3 Billion base pairs contained in 23 chromosome in the nucleus and mitochondria in the cytoplasm. Of these, only 1% of the human genome encodes for proteins, with the other 99% not yet fully understood. The humans genome encodes for approximately 20,000 proteins, which averages 1,000 proteins per chromosome. The HGP formed the basis of understanding human genetics and its role in physiological and disease states. Subsequent advances in medical and population genetics have led to the discovery of genetic variants and their relationship to physiologic and disease states (4). Initial HGPs had little representation of Africans residing in Africa and there are ongoing efforts to decipher the genome of the African.

With the subsequent advancement of genetics, medical genetics has evolved from a purely lab based discipline to an established subspecialty in internal medicine, paediatrics, pathology and feto-maternal medicine. Medical genetics has immense potential for altering medical diagnostics for patients and the at risk relatives, treatments options and reproductive choices.This has been most evident in oncology where genetic testing is used in tailoring patient treatment as per somatic genetic mutations identified.

With the emergent good molecular laboratory infrastructure, and current ongoing works in medical and population genetics in Kenya, there exist a tremendous unmet need for routine genetic counselling and testing in everyday clinical practice. With the ever decreasing costs, genetic test requisition may become as common place as a haemogram.

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Original paper

Clinical Profiles and Outcomes of End-Stage Kidney Disease in Adult Patients Treated with Haemodialysis at The Kenyatta National Hospital during Out-of-Pocket Payment and National Health Insurance Reimbursement for Haemodialysis Services

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Abstract

Background: The demand for haemodialysis has grown briskly especially in low- and middle- income countries. Sadly, availability of kidney replacement therapy in developing countries is scarce and may be unavailable in very-low-resource regions. As a result, a compelling number of patients have finite access to Kidney Replacement Therapy (KRT) resulting in premature deaths. In July 2015, the National Hospital Insurance Fund (NHIF) launched a renal dialysis package which caters for haemodialysis two sessions per week.

Objective: To describe and compare selected clinical profiles and clinical outcomes amongst ESKD patients treated with HD in Kenyatta National Hospital (KNH) between June 2013 to June 2015 and July 2015 to May 2018 i.e., during the out-of-pocket payment period (pre-NHIF) and the national health insurance reimbursement period (post-NHIF).

Methods: This was an ambispective observational study among End Stage Kidney Disease (ESKD) patients treated with haemodialysis (HD) in KNH between June 2013 to June 2015 and July 2015 to May 2018. The medical records of the 338 randomly selected patients were retrieved from the health records and information department in KNH. Data on the patients' sociodemographic characteristics, clinical profiles and outcomes was collected and analysed.

Results: Comparing the two groups (pre- and post-NHIF), the mean age at HD initiation did not differ significantly (46.76 vs 46.96 years). Males outnumbered females in both groups, at 64% and 60% respectively. Diabetes and hypertension remained the most common documented causes of ESKD in both groups. Following the introduction of NHIF reimbursement, there was a significant rise in HD sessions (1.94 ± 0.7 vs 2.12 ± 0.4, p value 0.04), however, the HD vintage decreased (36.3 vs 30.5 months). Our mortality rate was high at 85% (pre-NHIF) and 76% (post-NHIF).

Conclusion: The mortality rate was quite high during both time periods; hence the emphasis should be on prevention, early detection, and treatment of diabetes and hypertension as well as making kidney transplantation accessible and affordable to all. Hopefully, these will have a positive impact on the mortality rate of ESKD patients.

Key words: Out-of-pocket payment, NHIF reimbursement, KNH, End Stage Kidney Disease patients, Haemodialysis

Introduction

Chronic Kidney Disease (CKD) is becoming a common disease in the general population and a major public health problem world over (1). There is a rising incidence and prevalence of CKD globally which poses an important challenge to many health systems. It is an important contributor to morbidity and mortality among the Non-Communicable Diseases (NCD). Patients with CKD have a higher mortality rate in comparison to the general population (2).

According to the Global Burden of Disease Study in 2017, the global prevalence of CKD was 9.1% across 195 countries, this translated to 697.5 million cases globally. Chronic kidney disease resulted in 1.2 million deaths in 2017 and it was ranked as the 12th leading cause of death worldwide. In a systematic review assessing the burden of CKD in Africa, the prevalence of CKD was found to range from 2% to 14% in sub-Saharan Africa (3).

Kidney Replacement Therapy (KRT) broadly encompasses dialytic modalities and kidney transplantation. Dialytic modalities include haemodialysis (HD) and Peritoneal Dialysis (PD). In the last two decenniums, great advances in treatment of CKD have emerged. Dialysis treatment ameliorates

most of the clinical manifestations of End Stage Kidney Disease (ESKD); this helps improve the survival of haemodialysis patients. The population of patients in need of KRT is growing rapidly particularly in Low- and Middle- Income Countries (LMIC). Currently, there are about two million people on KRT worldwide. This represents only 10% of the people who need it. The demand for HD has grown tremendously in the recent years and it has become an important issue in healthcare. Unfortunately, the availability of KRT in developing countries is scarce and may be unavailable in very-low-resource regions. As a result, a sizeable number of patients lack access to KRT and large numbers of people die due to kidney failure annually, often without any form of supportive care (4).

Health is a basic human right as enshrined in the 2010 Kenya constitution. However, health care cost limits the attainment of this constitutional right. This therefore is bound to select for those who have resources to afford the care. National Health Insurance Fund (NHIF) is the primary health insurance provider in Kenya; its mandate is to enable all Kenyans to access quality and affordable health care services. The NHIF has evolved over the years and in July 2015, NHIF launched a renal dialysis package which caters for two haemodialysis sessions per week. Before July 2015, patients used to meet all the costs by themselves. The influence of national insurance reimbursement for haemodialysis services has not been studied.

Significance of the study

Chronic Kidney Disease (CKD) has a major impact on global health given the associated significant morbidity and mortality. The outlay of HD care is high and are prone to rise. The effect of national health insurance reimbursement on HD remains largely unknown. A few sets of data suggest that decreased reimbursement may increase morbidity and mortality directly or indirectly.

It is plausible to think that national insurance reimbursement for the HD services is likely to result in improved access to this care. It is not clear whether the patients' demographics and clinical profiles have changed. The outcomes of patients on HD during the out-of-pocket payment of HD services costs and during the national health insurance reimbursement in our setting has not been studied.

Objectives

To describe and compare selected clinical profiles i.e., age at initiation of haemodialysis, sex, cause of ESKD and haemodialysis vintage of ESKD patients treated with HD in KNH between June 2013 to June 2015 and July 2015 to May 2018.

To document and compare selected clinical outcomes i.e., alive on HD, alive having transplanted, deceased while on HD, deceased after kidney transplantation, of ESKD patients treated with HD in KNH between June 2013 to June 2015 and July 2015 to May 2018.

Materials and methods

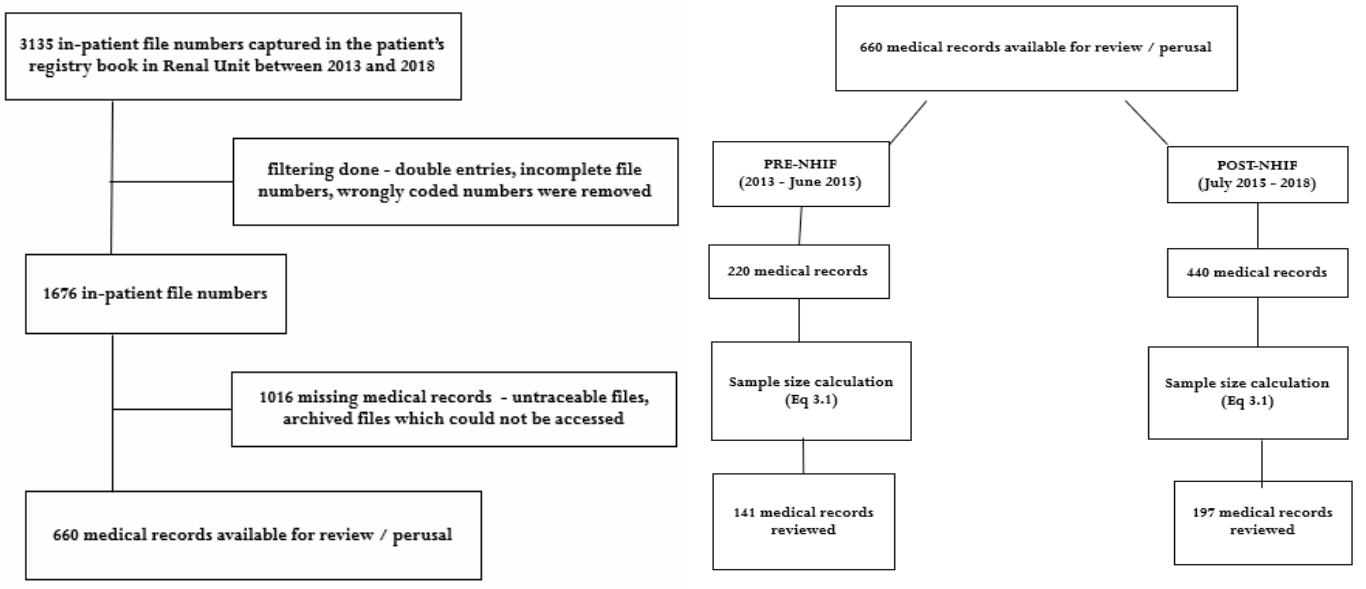
This was an ambispective observational study among ESKD patients on HD in KNH between June 2013 to June 2015 and July 2015 to May 2018. A total of 3135 patient records were captured in the patient's registry book in Renal Unit between 2013 and 2018. Filtering was done and out of the remaining 1676 files, only 660 medical records were available for review. The sample size was calculated and random sampling done, 141 medical records in the pre-NHIF group and 197 in the post-NHIF group were reviewed. The data collected was transferred to an SPSS data sheet and analysis done using SPSS. The equation below was used to calculate sample size, with a confidence interval of 95% and a margin of error of 5%.

Sample size calculation (Equation):

$$Sample\ size = \frac{\frac{z^2 \times p(1-p)}{e^2}}{1 + \left(\frac{z^2 \times p(1-p)}{e^2 N}\right)}$$

where N = population size; e = margin of error;
z = z score; p = sample proportion.

Figure 1: Recruitment process



Study variables: Dependent variables - clinical outcome (dead or alive, on haemodialysis or transplanted)

Independent variables - age, sex, documented cause of ESKD, haemodialysis vintage

Data analysis: Descriptive statistics were used to summarize the data. For continuous variables, means (SD) or medians (IQR) were reported. For categorical variables, frequencies and proportions were reported in tables.

Ethical considerations: The study was undertaken after approval by the DoCMT, UoN and the KNH/UoN ERC, Research Approval number P325/05/2021. Authority to use the medical records was sought from the in-charge of Health Information and Records Department.

Results

A total of 338 files, 141 in the pre-NHIF group and 197 in the post-NHIF group were reviewed.

The mean age at onset of HD did not differ significantly between the two groups during the study interval, with a reported mean age of 46.76 years in the pre-NHIF group and 46.96 years in the post-NHIF group. Males constituted a larger proportion of study participants in both groups, accounting for 64% (pre-NHIF) and 60% (post-NHIF). As shown in Table 1, majority of the study participants in both groups were married.

Table 2 summarises the documented causes of ESKD. Hypertension, diabetes, chronic glomerulonephritis and obstructive uropathy were the leading causes of ESKD in both groups. Overall, the number of cases for the various causes of ESKD increased over the

Table 1: Demographics

Characteristic	Pre-NHIF (N = 141)	Post-NHIF (N = 197)	All (N = 338)	P- value
Age at HD initiation (year) Mean ± SD	46.76 ± 15.55	46.96 ± 15.54	46.88 ± 15.52	0.91
Sex				
Male n (%)	90 (63.8)	119 (60.4)	209 (61.8)	0.52
Female n (%)	51 (36.2)	78 (39.6)	129 (38.2)	
Marital status				
Married n (%)	112 (79.4)	152 (77.2)	264 (78.1)	0.82
Separated n (%)	2 (1.4)	1 (0.5)	3 (0.9)	
Single n (%)	24 (17.0)	38 (19.3)	62 (18.3)	
Widowed n (%)	3 (2.1)	6 (3.0)	9 (2.7)	

Table 2: Clinical characteristics

Characteristic	Pre-NHIF (N = 141)	Post-NHIF (N = 197)	All (N = 338)	P-value
Causes of ESKD				
DM n (%)	43 (30.5)	76 (38.6)	119 (35.2)	0.12
HTN n (%)	78 (55.3)	120 (60.9)	198 (58.6)	0.31
GN n (%)	53 (37.6)	47 (23.9)	100 (29.6)	0.08
OU n (%)	13 (9.2)	19 (9.6)	32 (9.5)	0.90
ADPKD n (%)	3 (2.1)	6 (3.0)	9 (2.7)	0.53
CAN n (%)	2 (1.4)	1 (0.5)	3 (0.9)	0.42
Preg-related n (%)	3 (2.1)	8 (4.1)	11 (3.3)	0.30
RVD n (%)	7 (5.0)	16 (8.1)	23 (6.8)	0.40

years. Diabetes and hypertension saw the greatest percentage increases, at 8% and 6%, respectively.

During the study, the number of hepatitis B positive patients increased from 5 to 13. Similarly, the number of HIV-positive patients increased from 7 to 16. None of our patients were found to have hepatitis C. However, none of these increases in the number of cases were found to be statistically significant as depicted in Table 3.

Looking at the number of haemodialysis sessions per week, patients in the pre-NHIF group had a lower mean (1.94 ± 0.6 months) compared to patients in the post-NHIF (2.12 ± 0.35). This was also found to be statistically significant (p value 0.04). The average HD

Table 3: Clinical characteristics

Characteristic	Pre-NHIF (N = 141)	Post-NHIF (N = 197)	All (N = 338)	P- value
HBsAg status				
Negative n (%)	136 (96.5)	184 (93.4)	320 (94.7)	0.20
Positive n (%)	5 (3.5)	13 (6.6)	18 (5.3)	
HIV status				
Negative n (%)	134 (95.0)	181 (91.9)	315 (93.2)	0.40
Positive n (%)	7 (5.0)	16 (8.1)	23 (6.8)	
HCV status				
Negative n (%)	141 (100)	197 (100)	338 (100)	0.28

vintage in our study was 32.9 months overall, but we noted a decrease in HD vintage after introduction of NHIF (36.3 vs 30.5 months) as shown in Table 4.

The mortality rate for ESKD patients receiving haemodialysis was 79.6%. Of the 67 patients who survived, 42 were on HD, 9 had a functioning kidney graft, and 16 had recovered kidney function. As summarised in Table 4, 269 (79.6 %) patients died while

Table 4: Clinical characteristics

Characteristic	Pre-NHIF (N = 141)	Post-NHIF (N = 197)	All (N = 338)	P-value
HD sessions				
Mean ± SD	1.94 ± 0.663	2.12 ± 0.358	2.05 ± 0.515	0.04
HD vintage (month)				
Mean ± SD	36.28 ± 34.09	30.48 ± 18.99	32.90 ± 26.47	0.07

Table 5: Clinical outcomes

Characteristic	Pre-NHIF (N = 141)	Post-NHIF (N = 197)	All (N = 338)	p value
Outcomes				
Alive n (%)	20 (14.2)	47 (23.9)	67 (19.8)	0.47
Dead n (%)	121 (85.8)	150 (76.1)	271 (80.2)	
Alive on HD n (%)	9 (6.4)	33 (16.8)	42 (12.4)	0.12
Alive on KTx n (%)	6 (4.3)	3 (1.5)	9 (2.7)	0.13
Deceased on HD n (%)	120 (85.1)	149 (75.6)	269 (79.6)	0.10
Deceased after KTx n (%)	1 (0.7)	1 (0.5)	2 (0.6)	0.76
Alive not on HD or KTx n (%)	5 (3.5)	11 (5.6)	16 (4.7)	0.50

on dialysis, and only two (0.6%) died with a functioning graft. Our mortality rate was high at 80% with more deaths being reported in the pre-NHIF group (85%) but the mortality rate remained high in the post-NHIF group at 76%. Patients on haemodialysis continued to die at a higher rate than patients who had undergone kidney transplantation in both groups.

Discussion

The ever-increasing prevalence of ESKD places a huge burden on healthcare systems, as well as patients and caregivers. This presents a significant challenge in the delivery and management of ESKD services, particularly in resource-constrained settings. Unfortunately, CKD is still under-appreciated, and early diagnosis is frequently missed due to the nature of its nonspecific symptoms. The clinical profiles and clinical outcomes of 338 patients on maintenance haemodialysis at KNH were examined in this study.

When compared to reports from developed countries where ESKD affects the elderly, 60 years and above, the participants in this study were relatively young (5). However, our findings are consistent with many reports from developing countries (6-8). According to a systematic review of studies conducted in Sub-Saharan Africa, the mean age ranged from 35.6 years (SD 13.2) to 58.2 years (SD 15.0) (9).

The mean age at HD initiation did not differ between the two groups (pre-NHIF and post-NHIF), indicating that even with NHIF reimbursement, there was no increase in the number of elderly patients on haemodialysis. Similarly, no difference in gender was found between the two groups. Males outnumbered females in both groups, this is consistent with studies from most other countries (5,10). Male gender is a known risk factor for CKD, hence male predominance among the ESKD population is a worldwide phenomenon (11).

In our study, the leading causes of ESKD were hypertension, diabetes, glomerulonephritis, and obstructive uropathy. Glomerulonephritis and HIV infection decreased with age, whereas diabetes alone or in combination with hypertension increased. This aetiologic profile is consistent with previous African studies (6, 8, 12-14). Diabetes and high blood pressure remained the most common documented causes of ESKD in both groups. Overall, the number of cases for the various documented causes of ESKD was noted to have increased in the post-NHIF group. However, none of these increases in number of cases were found to be statistically significant. It is well known that blacks are more likely to develop hypertension and glomerulonephritis, which may explain the aetiologic pattern of ESKD in our study. Sedentary lifestyles, obesity, and an ageing population may also contribute to the increase in the number of cases reported in this study. In addition, low levels of awareness, detection, treatment, and control of blood pressure and blood sugar are also possible contributing factors, like what has been found in other studies (15-17).

A third of the participants in our study had chronic glomerulonephritis, there was no statistically significant difference between the two groups. In a Nigerian retrospective study, 34.5% of the study population had CGN (18). In our study, CGN was presumed based on either a history of documented glomerular disease or the presence of a glomerular syndrome (proteinuria and/or haematuria, hypertension in the absence of identifiable secondary causes). Only about 6% of patients had a confirmatory kidney biopsy report, indicating a scarcity of facilities capable of performing kidney biopsies and histology at reasonable rates.

ESKD caused by HIV nephropathy was common among young people and women, mirroring the demographics of HIV infection in Africa (19). Only 6.8% of our study participants were infected with HIV, which is comparable to the 6.6% reported in Cameroon but slightly lower than the 10.4% reported in Tanzania (8,14). We noted a rise in the number of HIV cases in the post-NHIF group, though it was not statistically significant. This trend may be due to improved comprehensive care for patients with retroviral disease, as well as easy access to kidney-friendly regimens when indicated. It was difficult to ascertain how many of our patients had secondary hypertension due to a primary renal disease. Unfortunately, many

of our patients did not undergo a diagnostic kidney biopsy as part of their evaluation mainly due to the cost implications, availability of the service as well as late presentation.

Financial constraints are a well-known reason for developing countries' lack of access to KRT (20,21). Prior to the implementation of NHIF reimbursement in July 2015, nearly one-fourth (25%) of our study participants were on once-weekly haemodialysis. However, since the implementation of NHIF reimbursement, this figure significantly dropped to 1% (p value 0.04, 95%). Unfortunately, none of our patients were on thrice weekly dialysis. Failure to meet the international recommendation of thrice weekly dialysis despite NHIF reimbursement, may have contributed to the poor outcomes observed in this study. This reflects a lack of haemodialysis service sustainability, which has been observed in other countries as well (22,23). Haemodialysis is the most widely used form of kidney replacement therapy in the world (24). Inadequate infrastructure and high out-of-pocket costs limit ESKD patients' access to haemodialysis services. As a result, most patients go undiagnosed, untreated, and die prematurely.

The average duration of haemodialysis in our study was 32 months overall, but we noticed a significant decrease in HD vintage after introduction of NHIF (p value 0.04, 95%). This could partly be due to the fact that frail patients and patients thought to have a poor prognosis were now able to access haemodialysis services through the NHIF system. Furthermore, NHIF does not cover the entire cost of haemodialysis, so patients must pay out of pocket for investigations and medications. This in effect means that some patients are unable to cater for the other demands that come with ESKD as documented by Twahir *et al*(21). Third, NHIF only covers two haemodialysis sessions, which is insufficient for the majority of our ESKD patients, this translates to higher mortality and shorter haemodialysis vintage. According to a Tanzanian retrospective study, patients who were not enrolled in the NHIF scheme had a higher risk of poor outcomes (8). Many patients in Nigeria and Sub-Saharan Africa were unable to pay for the recommended adequate dialysis sessions due to high costs, with only 6.8 % of patients able to afford haemodialysis services beyond 3 months, according to studies from Nigeria and Sub-Saharan Africa (18,23).

The mortality observed in our study was high (80%), this was double what was reported by McLigeyo *et al* in 1985. More deaths were reported in the pre-NHIF group (85%) but the mortality rate remained high in the post-NHIF group (76%). This could be attributed to an increase in the number of critically ill patients being initiated on haemodialysis as well as late presentation resulting in unavoidable deaths. NHIF usually caters for two sessions per week meaning that most patients are on suboptimal treatment. Although we did not investigate the causes of death, most of our patients had diabetes and hypertension, which would invariably increase their cardiovascular risk, resulting in poor outcomes. This is consistent with the findings of a two-year retrospective study conducted in a tertiary hospital in southern Nigeria, where only 27% of patients were still alive at the end of the two years (18). Dialysis duration and number of sessions were strong predictors of survival among dialysis patients in Ghana and Lithuania (25,26). Even in resource-rich environments, the same has been reported (27).

Patients had to travel long distances to access haemodialysis services before county hospitals in Kenya began offering the services in 2015. This had a significant impact on adherence to haemodialysis appointments, resulting in premature dialysis discontinuation and hence poor outcomes (21). A systematic review conducted to investigate the outcomes of dialysis in ESKD in Sub-Saharan Africa discovered that the majority of ESKD patients starting dialysis in Sub-Saharan Africa discontinue treatment and die (9). The mortality rate among haemodialysis patients varies by country, ranging from 6% in Morocco and 10.4% in Tunisia and 12% in Algeria (28).

Other KRT options (peritoneal dialysis and kidney transplantation) are less common due to the high costs and lack of facilities (6). Only 3% of patients in our study went on to receive a kidney transplant. This could be because NHIF does not cater for post-transplant costs (medication, clinic visits, laboratory, and imaging costs), so most patients choose to stay on haemodialysis since it is already covered by NHIF. Given the high mortality rate reported in this study, we should endeavour to better support the kidney transplant program which is clearly associated with better outcomes.

Conclusion

This study demonstrated that the mortality rate was quite high during both time periods; hence the emphasis should be on prevention, early detection, and treatment of diabetes and hypertension as well as making kidney transplantation accessible and affordable to all. Hopefully, these will have a positive impact on the mortality rate of ESKD patients.

Recommendations

1. The causes of death in our haemodialysis patients should be investigated in order to identify any preventable measures that can be implemented to reduce mortality in our HD patients.
2. Timely kidney biopsies aid in more accurate diagnosis, especially in our young patient population.
3. Poor vascular access may have contributed to poor outcomes; therefore, we should advocate for early and planned vascular access in our patients.
4. Investigate the reasons for dialysis discontinuation and the factors that contribute to dialysis discontinuation. As well as the difficulties/ challenges faced by haemodialysis patients, this may aid in improving outcomes.
5. Implement electronic medical records, and create renal registries that include all CKD patients. Using such registries, it will be easier to plan for better care and ensure that patients are not lost to follow up only to reappear when they require urgent dialysis.

Study strength

The study center continues to house the country's largest haemodialysis unit. As a result, the population described in this study is very likely to be representative of the people with ESKD in the country.

Study limitations

1. Because this was a chart review, some data was missing or was poorly documented. Record keeping can be quite poor in the absence of electronic records. As a result, the amount and quality of data extracted may be suboptimal.
2. Many of our study participants did not have a histology report to confirm the cause of ESKD.
3. There was recall bias because some patients and their next of kin were unable to recall all the required details.
4. Because some of the potential participants were not reachable by phone, information on the patients' current clinical status was not easily accessible.

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Review article

Utility of Pathogen Genomics in Clinical Care: A Review

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Abstract

Objectives: The primary objective of this review was to describe the impact of genomic and molecular diagnostic tools in diagnosis of infectious disease in clinical settings and to enumerate existing shortfalls in infectious disease diagnostics in Kenya looking at the scope and implementation of use of newer and robust technologies.

Data source: Data was obtained from peer reviewed publications containing surveys of the most common methods used in infectious disease diagnostics clinically in Kenya. Few data sources appear in regards to implementation of much newer methods of infectious disease diagnostics in tuberculosis patients and mixed pathogen species from cerebral spinal fluid.

Conclusions: Current laboratory techniques can be laborious and expensive when it comes to identifying pathogens responsible for many infectious disorders. Faster methods of diagnosis could expedite the administration of the appropriate treatment, reduce healthcare expenditures, and improve infection control and harnessing preparedness of future pandemics. In a clinical setting, when quick and robust choices regarding patient management are required to be made for the purpose of achieving the best possible results and preventing the spread of infectious disease, precision is very crucial. The technologies that are available today can test for a wide variety of pathogens using a variety of clinical samples, and they can produce results in under an hour while requiring less than a minute of manual intervention. The power of pathogen genomics diagnostic tools presents prospects that would take a more anticipatory approach to accurate clinical diagnosis, prevention and control of outbreaks.

Key words: Pathogen genomics, Molecular diagnostics

Introduction

Within the past ten years, advancements in genetics have led to numerous improvements across the board in healthcare systems all around the world. It is encouraging to see that Kenya, despite having a low GDP per capita, has become one of the pioneers in Eastern and Sub-Saharan Africa, in the spread of the application of genomic technology in molecular diagnostics. In this article, we provide a spectrum of pathogen genetic diagnostic tools that are both presently accessible for use, as well as those that, if implemented, would enhance the quality of healthcare provided to a number of patients at all stages of the medical process, from the laboratory to the bedside. We address their skills in terms of supporting clinicians in obtaining a higher diagnostic yield of attributed infectious agent, as well as some of the limitations they confront, such as cost. Technologies such as Polymerase Chain Reaction (PCR) and next-generation sequencing are able to perform simultaneous and complete detection of a wide variety of infectious pathogens directly from patient samples. Use of this genomic technologies also present a potential in infectious disease surveillance and ability to equip healthcare systems with future pandemic preparedness. Even though genomic tests for infectious diseases hold an amazing amount of potential in changing public health in Kenya, it is still unclear whether we will be able to surmount the substantial obstacles that stand in the way of molecular diagnostics becoming applicable on a more widespread scale.

Infectious disease genomics

To enhance healthcare outcomes and provide timely patient intervention, the area of molecular genomics has been considered a multidisciplinary one that sees an interplay of genomic techniques, data analytics,

and clinical history (1). The current fight against the Covid-19 pandemic has made it necessary to use genomic technologies like whole genome sequencing and PCR to monitor the spread and evolution of the SARS-CoV-2 virus in Kenya. Understanding and controlling infectious diseases at the patient and population level has benefited greatly from this genomic approach with significantly improved knowledge of the pathogen and the host population.

One of the most innovative new scientific breakthroughs to emerge and completely alter the field of molecular biology is Polymerase Chain Reaction (PCR). This procedure needs a template molecule, which can be either DNA or RNA, a DNA polymerase enzyme, a primer, which is a brief, precise sequence of nucleotides that aids in the beginning of the DNA copying process, and a chain of nucleotides (which comprises the four bases A, T, C, and G)(2). These components are combined in a tube and put in a device known as a thermocycler, which allows repeated cycles of DNA amplification to happen in three steps: denaturation, which causes the double helix strand of DNA to separate; annealing, which occurs when the temperature is lowered to enable the specific primers to bind to the target DNA if their sequences are complementary; and extension, which occurs when the temperature is raised again to extend the primers through the target DNA (3). The procedure produces billions of clones of a particular DNA fragment, giving biologists the chance to discover and recognize gene sequences as well as visually gauge its size.

With changes to the conventional PCR technology throughout the years, significant advancements have been made; in this case, DNA amplification is monitored while it is taking place. Real-Time PCR is a technique whose primary goal is to quantify and differentiate nucleic acids in a sample (4). Quenchers and reporters are two types of specialized fluorescently labeled oligonucleotides that are used in this procedure. These oligonucleotides give signals during amplification and provide data output that is depicted in graphical format (4). Fluorescent signals are measured at each PCR cycle and a cycle threshold value is determined and this value is inversely proportional to the viral or bacterial copy number in a specimen (1).

Within the clinical context and HIV burden, the Kenyan Government through the National AIDS and STIs Control Program (NASCOP) has been able to partner with UNAIDS seeking to achieve the goal of ending HIV by 2030 (5). In order to accomplish this goal, they have collaborated with a variety of partners to deliver point-of-care tests that monitor patient outcomes and progress while on receiving antiretroviral medication. In order to provide information on the levels of viremia in HIV-1 positive individuals, the viral load assay has been developed for use by local healthcare providers (6). Real-Time Polymerase Chain Reaction (rPCR) is used in the current technologies that are involved. The HIV-1 virus is extracted from blood plasma using this technology, and quantification is performed. Not only has this system been utilized in the delivery of point-of-care services to HIV/AIDS patients, but it has also been utilized in the fight against Covid-19 in recent years.

In March 2020, at the beginning of the pandemic, the World Health Organization (WHO) provided interim guidance on laboratory testing for coronavirus disease in suspected human cases. These techniques included serological testing, viral sequencing, and screening by real time reverse transcriptase-PCR (rRT-PCR). In addition, the WHO also recommended that all suspected human cases be tested (7). Because of this, it was possible to implement the use of this technology at a variety of testing facilities across Kenya. As a consequence, the government was able to arrive at well-informed decisions concerning the tracking of contacts and the management of transmission inside the country.

An expanding number of potentially dangerous variants of the SARS-CoV-2 virus, which were caused by mutations in the virus itself, led to the development of new insights into methods of surveillance and tracking based on molecular sequencing. This idea was initially conceived in the early 1970s in an effort to determine the sequences in DNA via primed synthesis with DNA polymerase. This was the first time this concept had been presented. Then, in the early 1990s, automated fluorescent sequencing equipment was developed, which made a significant contribution to mammalian genomics research as well as the famous Human Genome Project. The Human Genome Project's research effort was aimed at deciphering the chemical make-up of the entire human genome. Automated fluorescent sequencing equipment played a significant role in both of these endeavors (8).

As a result of the high prevalence of HIV-1 disease in Kenya, additional points of care besides the measurement of viral load have been established. These points of care monitor drug susceptibility in order to determine whether or not a patient with HIV has a form of the virus that is resistant to antiretroviral treatment. The testing is carried out to provide clinicians with assistance in the selection of active medications to use when altering their ART regimens. Therefore, Sanger sequencing has been utilized in order to pinpoint with accuracy locations within the pol region, which is a gene within the HIV virus that codes for proteins that are ART medication targets (9). Using this approach provides more accuracy in determining resistance and provides detailed and comprehensive reports from the Stanford HIV Database regarding drug regimens that the patient has developed resistance to over the PCR viral load assay which determines the levels of viremia.

In just a few short decades, the scientific profession has become increasingly dependent on computers in regard to medical informatics, medical imaging, telemedicine, and medical research. In addition, advancements in computing capacity led to the creation of Next-Generation Sequencing Technology, which brought together improved sensitivity, higher capacity, shorter turnaround time, and the ability to sequence hundreds of genes simultaneously (10). The scope has been relatively novel in Kenya, with various stakeholders developing comprehensive workshops that have highlighted the importance of access to Next Generation Sequencing and bioinformatics in a few research laboratories. These research laboratories include the Kenya Medical Research Institute (KEMRI), the International Livestock Research Institute (ILRI), and the Centre for Molecular Biosciences and Genomics (CMB). These research laboratories have been involved in the surveillance of variants and emerging variants of concern in Kenya (11). However, the use of this platform has only been described in infectious disease research and species identification in plant pathology strategies.

Tuberculous molecular diagnostics

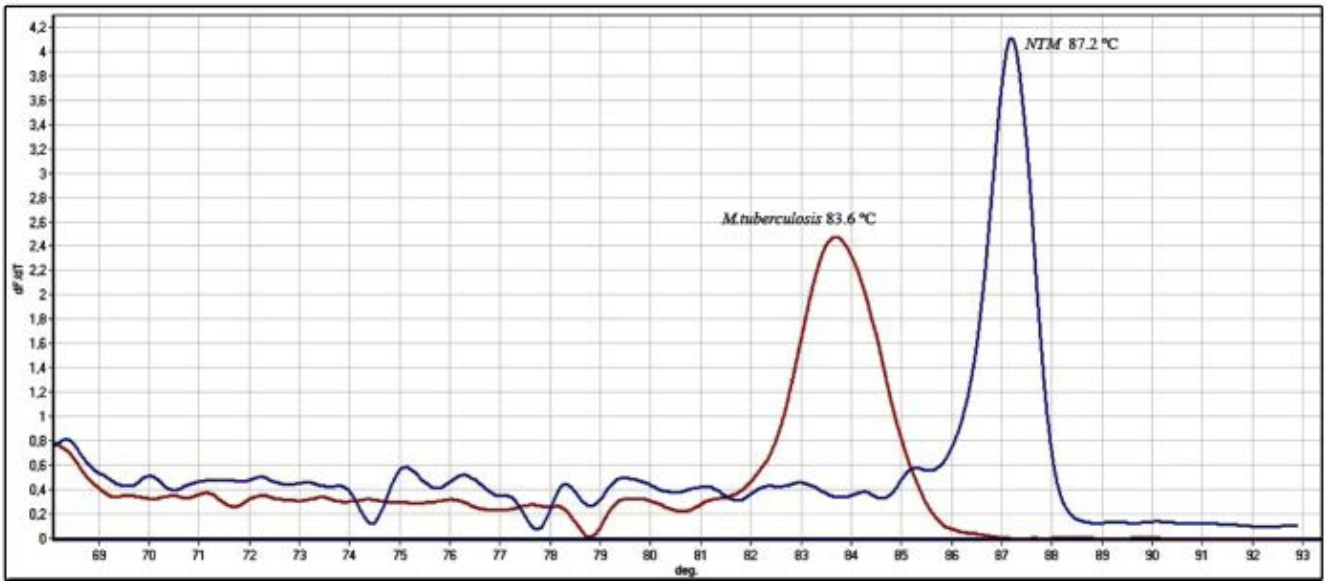
The World Health Organization has identified Kenya as one of the 30 states with the highest rate of tuberculosis (TB), and the Kenyan Ministry of Health has made it an extremely high priority to locate people who are afflicted with TB disease and provide them with the most effective treatment possible (12). Non-molecular TB diagnostic have been extensively used due to low costs and require direct visualization of acid-fast bacilli making it the most common method of diagnostics globallyheBACTEC™ mycobacterial growth indicator tube (MGIT™) platform from BD (USA) is a culture method also being used in Kenya and takes up to four weeks to generate a test result and although there remains a large turnaround time, the method is highly sensitive and can be used for phenotypic determination of drug resistance.

Molecular TB diagnostics offer the advantage of higher sensitivity, faster turnaround time of 3 days and relatively low cost. There has been the development of Nucleic Acid Amplification based diagnostics that are accurate in diagnostic testing and employ PCR techniques to amplify a specified region of genomic DNA; nevertheless, in the context of tuberculosis diagnostics, it has a number of problems, including but not limited to specimen type such as sputum, which produces a low number of pathogens, and difficulty in lysing the cell wall to liberate nucleic acids. Since it takes months to diagnose TB using culture-based procedures (which are the gold standard for TB diagnostics), the use of these nucleic acid amplification techniques to identify and diagnose TB is more efficient and accurate. It is still quite evident that culture-based methods cannot be discarded entirely; however, it is recommended that clinicians and laboratory personnel collaborate in order to conflate the use of nucleic acid amplification techniques in conjunction with liquid culture-based methods in order to improve the accuracy.

Non Tuberculous Mycobacteria (NTM) is currently an increasing opportunistic infection within the Kenyan population and is phenotypically indistinguishable from tuberculosis (TB), which remains a challenge in poor nations where several clinical and phenotypic aspects of NTM species are comparable to those of MTB (13). Because of this, non-tuberculous mycobacterium displays comparable traits such as morphology, and as a result, they can often be confused for MTB when it comes to methods such as microscopy and liquid culture.

Specialized techniques such as Sanger sequencing and multiplex real-time PCR-High Resolution Melting (PCR-HRM) techniques can rapidly identify non-tuberculous mycobacteria with high throughput to aid in the therapy of patients despite their limited sensitivity and lengthy turnaround time (14). The benefits of obtaining precise results with a short response time exceed the aspect of cost implications, owing the fact that the service is exorbitant.

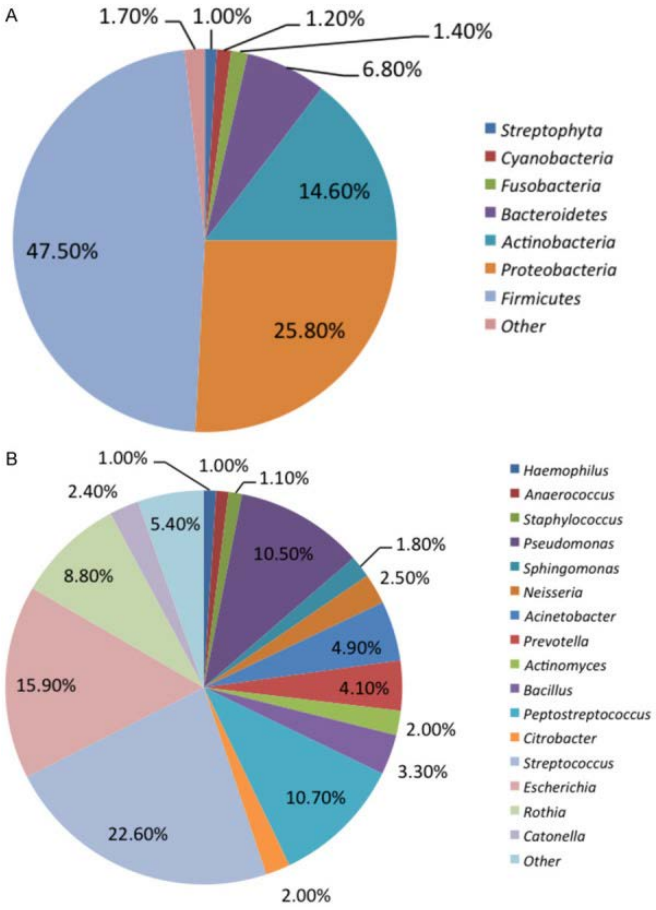
Figure 1: Standardization of melting temperatures in multiplex real-time PCR-HRM showing differences in nontuberculous mycobacteria and mycobacteria tuberculosis in two patient samples (14).



Utility of molecular diagnostics in isolating pathogens in cerebrospinal fluid

The bacteria *Streptococcus pneumoniae, Neisseria meningitidis,* and *Haemophilus influenzae* are the most prevalent in the development of endemic illnesses such as meningococcal meningitis. In most cases, the diagnosis of bacterial meningitis is made based mostly on the results of a positive cerebrospinal fluid (CSF) culture or a positive CSF latex agglutination test (15). The majority of the diagnostic labs in Kenya are equipped to carry out tests such as the Bacterial Antigen Testing (BAT) of cerebrospinal fluid (CSF) by latex agglutination test with a turnaround time for this test estimated to be two hours and the typical cost is approximately four thousand Kenyan shillings (US$35).One of the shortcomings of the culture-based approaches however is the presence of many different types of culture media as well as the possibility of a high sample size and contamination. With this in mind, a recently published study by Men *et al* (15) where routine clinical laboratory diagnostics was performed through the use of microscopy and culture-based procedures on thirty-one patients, showed that thirty patients (97%) exhibited negative culture results. In order to circumvent false positives, genomic DNA was isolated, and subsequent next-generation sequencing as well as 16S ribosomal DNA analysis were carried out.

Figure 2: Distribution of predominant microflora in 31 CSF samples (15)



According to the results obtained by Men *et al* (15), it is abundantly clear that the majority of the bacteria were not identifiable through the use of standard culture-based approaches, which end up producing false negative cultures. Therefore, sequencing approaches have shown that they are capable of identifying bacterial species from culture-negative samples, which is a capability that current clinical detection methods lack with benefits of sequencing approaches perform with high accuracy and in a relatively short amount of time of three days. This context is also applicable to many other areas such as vaginal, respiratory and wound specimens.

Current laboratory techniques can be laborious and expensive when it comes to identifying pathogens responsible for many infectious disorders. Faster methods of diagnosis could expedite the administration of the appropriate treatment, reduce healthcare expenditures, and improve infection control and harnessing preparedness of future pandemics. In a clinical setting, when quick and robust choices regarding patient management are required to be made for the purpose of achieving the best possible results and preventing the spread of infectious disease, precision is very crucial. The technologies that are available today can test for a wide variety of pathogens using a variety of clinical samples, and they can produce results in under an hour while requiring less than a minute of manual intervention.

Conclusions

Current laboratory techniques can be laborious and expensive when it comes to identifying pathogens responsible for many infectious disorders. Faster methods of diagnosis could expedite the administration of the appropriate treatment, reduce healthcare expenditures, and improve infection control and harnessing preparedness of future pandemics. In a clinical setting, when quick and robust choices regarding patient management are required to be made for the purpose of achieving the best possible results and preventing the spread of infectious disease, precision is very crucial. The technologies that are available today can test for a wide variety of pathogens using a variety of clinical samples, and they can produce results in under an hour while requiring less than a minute of manual intervention. The power of pathogen genomics diagnostic tools presents prospects that would take a more anticipatory approach to accurate clinical diagnosis, prevention and control of outbreaks.

Recommendation

We recommend that clinical specialists and laboratory scientists begin to wade deeper into the subject of the utility of pathogen genomics for clinical intervention and possible implementation.

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Approach to a Patient with Suspected Genetic Disorder: Case Report

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Abstract

A middle aged male known to have polycystic kidneys on ultrasound presented with features suggestive of end stage renal disease. Family history revealed presence of similar phenotype in multiple family members suggesting a genetic cause. The pedigree also determined the mode of inheritance and phenotypic expression of the disorder. Genetic testing is warranted in this family in order to anticipate and mitigate complications of the disorder. Genetic testing, though costly and not readily available locally, is an increasingly necessary armamentarium for the management and control of disorders with a genetic cause.

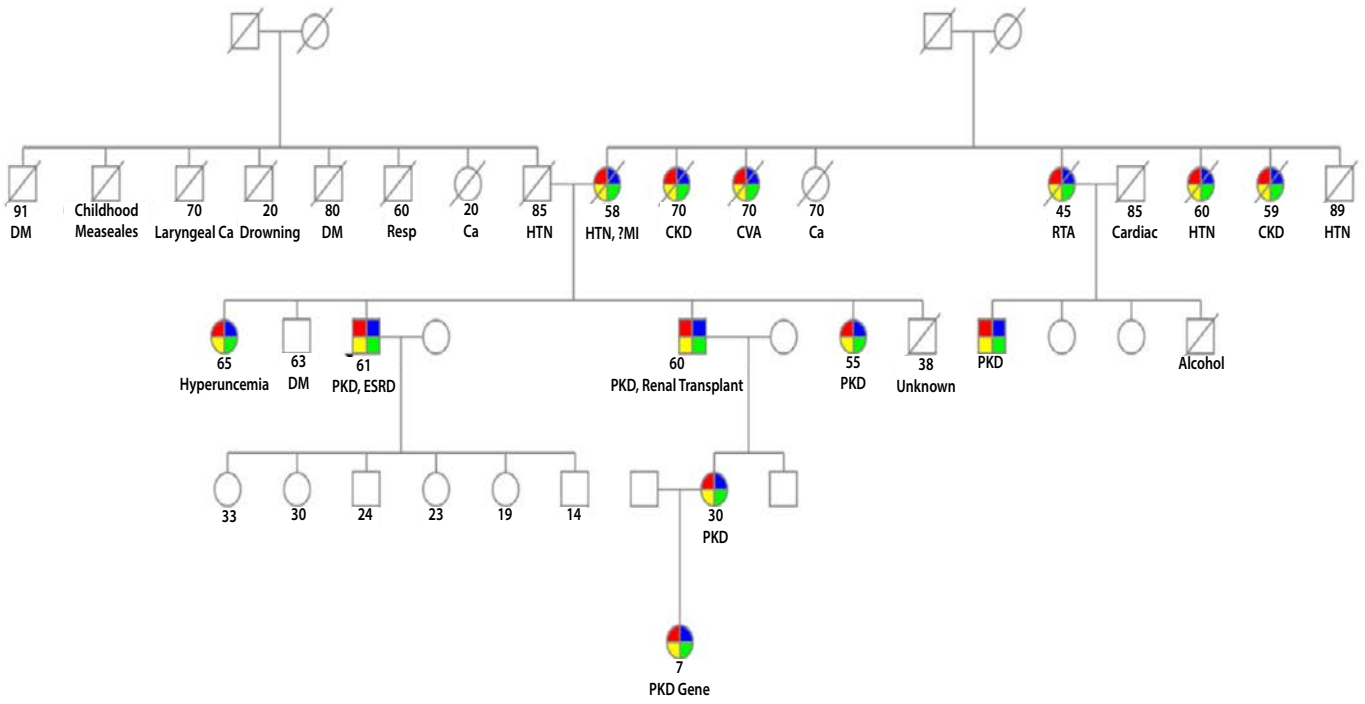
Key words: Genetic disease, Pedigree, Phenotype, Genotype

Introduction

Autosomal polycystic kidney disease is an inherited genetic disorder that manifests with cystic kidneys, pancreas liver and cerebral aneurysms. It is a highly prevalent disorder affecting 1 in 10,000 in the general population (1) and is not an uncommon disorder in the physician's practice. We highlight this case to demonstrate a systematic approach of evaluating genetic disorders and approach to genetic testing.

Case report

We present a case of a 62-year-old male who presented to our inpatient ward with signs and symptoms of End Stage Renal Disease (ESRD). Of note, five years prior, he had been found to have enlarged, polycystic kidneys on ultrasonography. His maternal lineage family history was remarkable for multiple cases of ESRD as shown in the pedigree below.



By convention, a pedigree has the following characteristics:

- Proband is the family member who brings the condition to the attention of the healthcare system member and is denoted with an arrow
- Female is denoted by a circle, male by a square
- Spousal relations are joined by a horizontal line, with the male appearing on the left of the female and their offspring as vertical offshoots
- Consanguineous relations are joined by two parallel horizontal lines
- Those with the disorder are shaded partially or wholly
- Deceased are crossed out
- Each generation is drawn along the same horizontal plane

A good pedigree aims for at least three generations where feasible. In our patient, the pedigree spans five generations and captures 38 relatives to the proband, with 24 relations from the maternal side. In evaluating the proband's paternal and maternal lineage, it is evident that the maternal lineage has the disease of concern as demonstrated in the presence of kidney disease, stroke and hypertension. In trying to decipher the mode of inheritance, the following criteria is used:

- Does it skip generations?
  - o Yes- Recessive or dominant with variable penetrance
  - o No- Dominant
- Does is affect one sex
  - o Yes- Sex-linked
  - o No- Autosomal
- Does inheritance come from maternal lineage to all her offsprings
  - o Yes- Mitochondrial
- Does inheritance come paternal lineage to only the sons- Y-linked

In our patient, the pedigree demonstrates inheritance through this maternal lineage, affecting both males and females and does not skip generations. This is in keeping with an Autosomal Dominant Disorder (ADD). This coupled with his clinical manifestation is highly suggestive of Autosomal Dominant Polycystic Kidney Disease (ADPKD). Being an autosomal dominant disorder, each individual has a 50% chance of inheriting the disorder. On the maternal lineage 13 out of 25 (52%) individuals have the gene of concern. Each affected individual having an affected parent suggests that the disorder is fully penetrant, meaning each person carrying the mutated gene manifests the phenotypic disease.

In deciphering of a pedigree, certain hypothesis may be prudent; if an offspring has a condition but their parent doesn't manifest it may mean that the condition is recessive; dominant with incomplete penetrance or a *denovo* mutation in the offspring.

In the pedigree above in the second generation, the female who died from an RTA with no phenotypic manifestation of the disorder, is denoted as having the defective gene as she passed it on to her offspring. She may not have manifested the phenotype as she died at 45 years of age whilst the age of presenting with the symptoms is in the sixth and seventh decade of life.

Regarding the phenotypic characteristics of the disorder, the following conclusions are reasonable from the pedigree;

(i) 2nd generation- phenotype results in death by the 7th and 8th decade
(ii) 3rd generation- develop end stage renal disease in the 6th and 7th decade
(iii) 4th generation- has not manifested the phenotype yet as they are still young
(iv) ADPKD1 is more likely than ADPKD2 due to the earlier onset of ESRD (54 years vs 73 years in ADPKD2)
(v) The disease expressed itself in different phenotypes (renal cysts; strokes suggesting aneurysms)
(vi) Advanced in genetic testing had led to the identification of asymptomatic persons in the 5th generation
(vii) Homogeneity in the cause of death on proband's maternal (affected) side compared to his paternal unaffected side which has a heterogeneous cause of death
(viii) In addition to screening for polycystic kidneys, there is need for surveillance for aneurysms as this seems to have been the cause of death in some of the affected persons

Genetic testing

Human Genome Project (HGP) which mapped out nucleic acid sequence in healthy persons drawn from a diverse racial and geographic populations forms the template from which normal genetic makeup is determined. Off-shoots from the HGP have been population genetics studies to determine normal variants amongst specific racial and ethnic groups under-represented in the initial HGP. Variants from the expected normal sequence are classified on a 5 point spectrum depending on whether they are identified to cause disease or not; (i) Pathogenic (ii) Likely pathogenic (iii) Variant of undetermined significant (iv) Likely benign (v) Benign. Location of pathogenic variants in gene sequences has resulted in establishment of databases for different disease entities and gene panels. A gene panel is a predetermined set of genotyping that are carried out for specific disease entities.

There are gene mutations for both autosomal dominant and autosomal recessive forms of PKD. However, given the family pedigree above, this rules

out ARPKD. Therefore, gene testing will be limited to only those mutations that are known to be autosomal dominant in nature. In ADPKD, there are two mutations; PKD1 located on chromosome 16p13.3 (short arm of chromosome 16, at locus 13.3) and PKD2 located on 4q21 (long arm of chromosome 4, locus 21). Gene panel for ADPKD would entail localization of these genes on the patient's genome at the exact locus on the chromosomes (2).

Although genotyping is not necessary to make a clinical diagnosis of ADPKD, it may be warranted in order to cascade gene testing to family members at risk. The proband's grand-niece had already had the pathogenic gene mapped out; this information if available can be used to guide of the gene testing of all the family members. If unavailable, the proband would be screened for both ADPKD1 and ADPKD2 genes. Once the exact gene mutation is established, cascading of testing to his descendants and family members at risk would entail screening for only the identified mutated gene thus ensuring cost effectiveness. Gene testing, though costly, has the potential to be cost effective as only those with the mutated gene will require follow-up for complications of ADPKD. It also has the potential of alleviating worry in those without the gene mutation and their offspring (3).

Conclusion

ADPKD, a genetic disorder commonly encountered in clinical practice requires a genetic approach in order to mop up at risk family members for screening and retarding progression to chronic kidney disease. With the lowering cost of genetic testing, and increasing number of genetic therapies, management of genetic disorders will become a mainstay of medical practice in the next decade (4,5).

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Do Conferences Contribute to Continuing Medical Education —Or is it Time for a Change in Approach?

Based on a paper presented to the Kenya Association of Physicians Annual Conference, 2014

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Two apparently conflicting pieces of evidence exist about physicians' Continuing Medical Education (CME). Physicians report spending, on average (and among other activities), many hours per year in CME activities, ostensibly geared toward improving their performance and/or optimizing the outcomes of their patients. In addition, producing and accrediting formal, planned CME events and activities are large enterprises intended to bring physicians up-to-date with rapidly expanding medical information. Patterned after undergraduate medical education consisting of lectures, audio visual presentations, and printed materials, CME activities appear underpinned by a belief that gains in knowledge lead physicians to improve how they practice and thus improve patient outcomes. Despite this belief and the level of participation in and resources dedicated to CME, many studies have demonstrated a lack of effect on physicians' performance of current practice guidelines or sizable gaps between potential and real performance. In addition, a relatively weak effect of formal, planned CME on physician performance has been demonstrated in some studies.

Despite seemingly endless rounds of conferences, symposia, round-table discussions, and panel debates over the years, Continuing Medical Education now is not greatly different from what it was 40 years ago. There is simply a greater quantity of the same familiar things.

In light of the foregoing, one may be justified to ask: Why Continuing Medical Education? Three generalizations keep recurring in the literature. We say, first, that it is the personal responsibility of professionals to engage in never-ending refinement of their professional competence; second, that the body of biomedical knowledge is changing so rapidly that each of us must struggle constantly simply to keep up with an increasingly narrow field since it is hopeless to try to keep abreast of general medical knowledge; and third, that many deficiencies in health care not only exist but could be corrected by the appropriate continuing education of practitioners—particularly those practitioners who do not take part in regular programs of continuing education.

The diagnosis of deficiencies in the care of patients is surely an indispensable strategy, but far more difficult is the successful translation of even distasteful findings into sound educational practices that have some hope of alleviating the shortcomings which are identified. As professionals, we doctors seem more willing to consider or even to adopt new information or new technology than to change in any fundamental fashion the way we use it ourselves. We are convinced, or so the literature of Continuing Medical Education would make us seem, that it is our failure to apply new knowledge that represents the weakest link in the chain of assuring that the highest quality of medical care is delivered by the greatest number of physicians to the largest number of patients.

While this view may be correct, I am not familiar with any solid data to support it. In fact, the correction of the major health problems in Africa, as in other parts of the world, does not appear to require any substantial body of new knowledge. Rather, it requires that physicians use the knowledge they already have in a different way or more fully exhibit the professional attitudes that have characterized the physician's role as long as there have been physicians. As a more eloquent speaker recently put it, *"If I were asked to compose an epitaph on medical profession throughout the 20th Century, it would read: 'Brilliant in its discoveries, superb in its technological breakthroughs, but woefully inept in its application to those most in need…."*

Since I was a medical student 50 years ago, I have heard and I have read in medical literature covering a far longer period that physicians can be of the greatest service to society if they work at preventing disease rather than treating it. But which gets more academic attention and reward: the replacement of damaged arteries and heart valves or the prevention of smoking and obesity? We have been told again and again that most of those who consult us are the anxious well rather than the curable sick. But which gets more attention in our educational programs—the pharmacologic action of drugs and their side effects or the skill of listening and providing reassurance?

I am afraid that most of us have been seduced by the notion that we have a primary professional

responsibility to keep abreast of current information—even if the information may have little use to many patients, and even if it means diverting attention from other elements of professional competence that may be of far greater importance to those we serve. Having been convinced that "Keeping up" is the goal, we are easily led to the conclusion that the need in Continuing Medical Education is for more instruction. Regrettably a recently completed survey by the World Health Organization on Continuing Medical Education in member nations has shown that the lecture is still the most widely used instructional method by a large margin.

If, indeed, change in behavior is the goal of continuing education, whether it is offered to practitioners or to medical educators, then perhaps most of what we now do must be dismissed in much the same way as Oliver Wendell Holmes, the autocrat of the breakfast table and one-time dean of the Harvard Medical School, once dismissed another component of medicine when he said: "I firmly believe that if the whole materia medica as now used could be sunk to the bottom of the sea, it would be all the better for mankind—and all the worse for the fishes."

It is time for change in our approach to Continuing Medical Education

The ultimate effect of formal CME interventions on the practice of physicians and the health of their patients as in the case of any intervention must be understood in the context of the methods by which the CME is delivered, including but not limited to the nature of the enabling resources available, the environment in which the translated competence is played out, and in the complex intrapersonal, interpersonal, and professional educational variables that affect the physician-learner's immediate goal of a CME activity. The exclusively didactic CME modality has little or no role to play. Knowledge is clearly necessary, but it is not in and of itself sufficient to bring about change in physician behavior and patient outcomes. Didactic interventions should receive less credit than do more effective methods or perhaps they should receive no credit at all. In contrast, variables over which the CME provider has control and appear to have a positive effect are the degree of active learning opportunities, learning delivered in a longitudinal or sequenced manner, and the provision of enabling methods to facilitate implementation in the practice setting.

While numerous questions remain regarding formal CME, including group size, the role of the learning and practice environment, the clinical dimensions of care, the assessment of learner needs, and barriers to change, one question still looms large: *"In the face of longstanding knowledge about adult, self-directed learning and the general disinclination to believe that didactic CME works—now coupled with findings that indicate it does not—why would the medical profession persist in delivering such a product and accrediting its consumption?"* The reasons for the persistence of didactic CME include—but are definitely not limited to—the ease of designing and providing such activities, the substantial pharmaceutical sponsorship that promotes the transfer of information about new medications, and the dependence on traditional undergraduate models of education that are easy-to-mount and revenue generating.

Changing this delivery system carries serious implications for several groups of stakeholders that want to design and deliver effective CME. First, medical licensing boards and others with a genuine interest in assuring the public of physician competence must rethink the value of the CME credit system. Second, medical schools, specialty associations and societies, and other providers of CME must reconsider the value of the credit they provide, as well as the type and duration of learning activities they produce.

Further, organizations intending to ensure the quality of CME must evaluate the services that they provide to a large, complex, and expensive CME enterprise that values the production of single-session, teacher-centered activities over learner achievement. Finally, physicians must reflect on what they perceive as the CME experience itself and weigh the costs and lost learning opportunities of attendance at ineffective didactic sessions against participating in interactive, challenging, and sequenced activities that have enhanced potential for positively affecting their performance and the health of the patients they serve—the most important outcomes of all.

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Reporting Medical News: The Medical Journalist

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Medical news, particularly findings from research studies must be communicated to the public. The trade offs between expediency and ensuring quality and accuracy is critically important.

Medical journalists or journalists who report medical news, are the gate keepers controlling the dissemination of medical information to the public. Many in medical journalism would argue that there should be a substantial difference between the reporting of general news and the reporting of medical news. General news consists of relatively circumscribed events that can be reported according to the traditional checklist of journalists: the famous who, what, where, when and why. In contrast, medical news does not usually happen at an isolated point in time that can be encapsulated by those traditional descriptions. Rather, medical information is part of an ongoing stream of experimentation and data production that typically grows out of past experiments and will undoubtedly change, often very quickly, with future experiments. In contrast to general news, which is based on facts and sources and opinion, medical information is traditionally based on data and probabilities and conclusions. Anecdotal evidence, which is on the lowest rung of the evidentiary ladder in science, is often the basis of general news reporting, indeed, the anecdote the event is often the entire focus of a general news report.

This is not to say that one type of content is better than another simply that they are very different and require different kinds of analysis and presentation. Unlike the reporting of standard news, which requires general journalistic skills and familiarity with the subject matter, good medical-news reporting requires additional and very specific skills in the understanding of biostatistics and epidemiology. Given that most medical news stems from scientific studies, it is virtually impossible to do a good job of analyzing and reporting such information without a basic grounding in knowledge of such matters as the strengths and weakness of descriptive studies and analytical studies, the evaluation of association, and potential cause effect and the critical differences between relative and absolute risk in real-life interpretation of results.

The need for such knowledge leads directly to the controversial and complicated question of whether or not those who report medical news should have special training and or credentials. Many journalists may not agree with me! Meteorologists who report weather are part of the news team. Some local journalists have scientific training background. This gives certain comfort level in knowing the reporter has some scientific background, but one does not have to be a doctor to be a good medical journalist. Doctors are good in a different area of journalism, the medical journals.

The fundamental question in medical journalism is how best to identify, process report legitimate medical information to the public. This calls for professional standards of truth, accuracy and context in every report, free from any personal financial or other conflicts of interest. There is however a more pertinent issue. At the core of media as in medicine, is the principle of self regulation. In such circumstances it is the attitudes of journalists, their editors and program executives that drive standards and in this quest for medical reportage.

Doctors often blame the media for misleading the public about important medical issues. Journalists on their part often argue that doctors contribute to sensational stories about health risk when they prevent the public dissemination of information. Responsible reporting by journalists can illuminate important issues for the general public that might otherwise remain obscured in the scientific arena. In some cases investigative reporters have exposed aspects of medicine that prompted legislative and policy changes in public health care system. Reporters and those in health care industry may never be "pals" but the mass media has an important role to play by engaging public service journalism that uncovers problems in medicine and medical science.

Too often, journalists pursue medical news as if they are reporting on a hostage crisis. Information is delivered rapidly, but little time is taken to provide a context for the story. Instead, the reporting is sensationalized: the journalist overstates a scientific finding and, as a result, the public is misled about the implications of that finding. This sort of reporting has its roots in newsroom pressures to dramatize stories by sounding alarms or touting cures, but scientists and scientific institutions occasionally contribute

to sensationalism. Scientists have understandable desires for publicity. It may help them get funding, is valued by institutions and increases awareness of their research. The efforts of scientists to attract media attention, however, can result in flawed coverage. For example, press releases are issued that are inaccurate or incomplete and press conferences are held even though the data being discussed are preliminary. Scientific organizations invite the media to their presentations without providing explanations of epidemiologic and statistical concepts or access to scientists who can critique a given research effort.

What is medical news? Who defines news? Medical journalists are in competition with literally hundreds of stories everyday, political and economic stories of compelling interest. They often have to overstate, they have to come close to within boundaries of truth to a dramatic compelling statement, as a weak statement will go no place! There are similar competitive pressures on the medical establishment, a world where medical centers, researchers, biotechnology firms, and individual practitioners increasingly use the techniques of the business world, press conferences, press releases, to gain or maintain market share or to increase the chances of receiving funding for research.

The increasing commercialization of medical research by business interests concerned primarily with profits has led to a secretiveness and even cutthroat mentality that prompts blatant attempts to manipulate the media. There are those who use the media for profit. They encourage stories about the faults of their competition. They leak medical stories to the press or in some cases have open press releases to boost their companies stock values This pressure to commercialize has also extended to scientific meetings, which are now becoming more like exercise in public relations organized for the benefit of the media. These meetings, which used to allow the free flow of information between scientists without fear of commercial or media intrusion, are now typically orchestrated to highlight reports that will clearly appeal to the public. The added confusion of financial conflicts on the part of so many presenters at scientific meetings increases the possibility of media manipulation.

Doctors often view the media as conduit or pipeline responsible for transmitting medical information to the public in a way that can be easily understood, they expect to control the flow of information as they do in their own medical journals. They assume that the purpose of medical journalism is to convey a positive image of medical science, yet medical journalists do not see themselves as trumpets of medical science. Growing awareness of the impact of media reporting of medical news is influencing media coverage of medical news. "Be careful about reading medical news, you might die of a misprint or is it of a mistake?"

Health Insurance and the Law in Kenya

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Introduction

Insurance is a contract or policy by which an insurer indemnifies a person (called the insured) against losses from specific contingencies and/or perils. In the case of health or medical insurance, the contract requires the insurer to pay some or all of the insured's healthcare costs in exchange for the payment of a premium. The insured makes an advance payment of the premium to the insurer. In return, the insurer will pay a health service provider some or all the direct expenses incurred when the insured utilizes a health service. Health insurance covers some or all of the costs of consultation, hospitalization, emergency care, and medicine. Its objective is to meet unforeseen costs relating to illness. Typically, premiums are based on the incidence of diseases and utilization of services and are thus related to the insured's risk, irrespective of income.

Health insurance provides a means by which society may share the costs of public health care: those who do not fall sick but participate in insurance schemes contribute towards the expenses of those who fall sick, while they are guaranteed that in times of illness their care will be paid for by a third party.

Health insurance in Kenya has seen many developments in the recent decade, which impact the provision of health care. These developments have included devolution and the categorization of health facilities. Following the promulgation of the Constitution of 2010, Kenya's health system is now organized around two administrative levels. On the one hand, the national level is primarily responsible for policy, regulation, and national referral facilities. On the other hand, the county level is responsible for service delivery. Further, health facilities are categorized into tiers ranging from community to tertiary care.

At present, the main providers of health insurance are the government's National Health Insurance Fund (NHIF), private insurers, and community-based health insurance schemes. These providers offer both inpatient and outpatient services, based on the cover or plan that an insured has selected or is eligible for.

This article examines the regulation of health insurance in Kenya and its implications for healthcare providers. The article is organized as follows. Part II discusses the economics of health insurance. Part III examines how the law regulates the provision of health insurance in Kenya. Part IV concludes by offering some lessons on how health care providers can ensure the provision of health insurance works for them.

The economics of health insurance

Health care is a good that possesses unique characteristics, which need to be considered if the provision of health insurance is to be regulated effectively.

First, health care is a "merit good" in the sense that it is a commodity that society considers everyone should have because it is beneficial, and their ability or willingness to pay for it does not matter (1). This is one of the main reasons why governments frequently finance healthcare.

Second, some forms of health care constitute "public goods" given that one person's consumption does not reduce the amount available for others to consume. The prevention and treatment of communicable diseases are good examples. Consumers cannot be excluded from public goods: if they are made available to anyone, they are available to all. Since people can consume such public goods without having to pay for them, their production will always be less than socially optimal. To ensure socially optimal production of such goods, they must be financed by government or some other non-market alternative.

Third, the provision of health care is characterized by the problem of asymmetric information between the patient and the provider. Thus, for example, patients may be able to describe their symptoms but not know what ails them or what further action to take. In this scenario, visits to doctors may be driven by just as much by a desire for extra information as for curative health-care services. In any case, visits to health care providers often occur when patients are feeling sick and vulnerable, and will thus accept any decision that the health care provider takes. Unfortunately, because health care providers have their own needs and preferences, such decisions may not always be in the interests of the patients. For example, the health provider may prescribe unnecessary or expensive

procedures or drugs. This explains why governments often seeks to regulate the conduct of health care providers to deal with the problem of asymmetric information.

Fourth, the demand for health care is derived. People do not demand health care for the sake of it, but because they desire improved health status; health care is a means to achieving this end. Thus, much demand for health care cannot be planned in advance but is contingent upon deterioration in health status. Moreover, while health care costs may be very high, most people are risk averse and do not want to incur large costs at unforeseeable points in the future. For these reasons, insurance or risk sharing for health care becomes important. Under insurance or risk-sharing schemes, individuals or households pay a premium in advance – which may or may not be related to their actuarial risk of illness – in return for free or subsidized health-care coverage if they fall ill."

But insurance creates a "moral hazard" problem. Since insurance is a contract by which someone other than the patient agrees to pay for his or her health care, the insured has an incentive to indulge in health risks that otherwise would have been avoided or consuming more health care than otherwise. When that happens, the cost of insurance is likely to rise in order to accommodate the increased demand. Further, insurers will be reluctant to insure high-risk individuals unless they can charge them premiums that reflect their high chance of becoming ill. Alternatively, insurers may seek to deter high-risk individuals from registering with them. In these circumstances, governmental intervention may be required to ensure optimal consumption of health care and coverage for high-risk individuals.

The market for health care, therefore, has unique characteristics, which justify varying degrees of public financing and provision, and governmental regulation of private provision. To recap, there are three distinct economic justifications for government intervention in the health care market: to ensure the optimal production of public goods, to subsidize poor consumers, and to correct or offset failures in the market for health insurance. The first two justifications explain why many governments often finance and manage health care systems. Indeed, governments often establish social security systems to manage health care and finance risk pooling in the social security systems using formal sector payroll taxes.

But what failures can arise in the market for health insurance? As we have noted, the moral hazard problem tends to be common in health insurance, as consumers use too much care thereby escalating its costs. Second, insurers are often reluctant to cover high-risk individuals, such as chronic patients, with the result that a significant segment of the population may not be covered. Third, unregulated health insurance may lead to excessive medicalization as health care providers seek to maximize their profits. And in developing countries such as Kenya, the population coverage is limited because of their large informal sectors and urban bias. The resolution of these efficiency and equity problems requires governmental regulation. In addition, policymakers have introduced community-based health insurance schemes, which target self-employed populations.

Regulating health insurance in Kenya

The National Hospital Insurance Fund (NHIF) covers the majority (or 88%) of Kenya's insured population (2). The rest are covered by private health insurance (9%), employer-based medical schemes (3%) and community-based health insurance (<1%) (2).

The NHIF provides contribution-based health insurance services to formal and informal sector workers. It is compulsory for the former but voluntary for the latter. Thus, the NHIF is financed principally through premium contributions from its 5 million registered members. It also receives some funding from the government. It contracts both public and private health care facilities to provide services, consisting of a benefits package, to registered members.

The NHIF's benefits package embraces preventive and curative care comprising consultation, laboratory investigations, drug administration and dispensation, dental healthcare services, radiological examinations, nursing and midwifery services, surgical services, radiotherapy, and physiotherapy (3). Further, subscribers are entitled to specialist care in hospitals for hospitalization (or in-patient care) when needed and referral to specialists where necessary. In-patient benefits are linked to the category of a hospital, hence access to essential surgical services – for example – following a road traffic accident – may be constrained (4).

The NHIF contracts hospitals through a four-step process: application for accreditation, inspection, gazettement and contracting (5). A facility that has applied for accreditation is inspected for the availability of infrastructure, facilities, equipment, staff, and services such as ambulances. Where the inspection recommends accreditation, the NHIF board of directors gazettes the health facility (6). A contract is then signed between the NHIF and the health facility, specifying the category of the health facility, payment mechanisms and rates, and other terms of engagement (6). The accreditation process also serves as a basis for quality assurance. During the initial inspection, the NHIF establishes standards of care and contracted facilities are thereafter regularly inspected for compliance with those standards. The NHIF has established a benefits and quality assurance management committee and an organizational department to handle this task.

The NHIF pays contracted health service providers using capitation, case-based payments and fee-for-service for specific services such as renal dialysis and radiology services. It uses capitation to pay for outpatient services and fee-for-service for both outpatient and inpatient services. The NHIF is supposed to negotiate the payment rates with the service provider (7). In practice, it pays a fixed annual rate per enrollee. Thus, it pays KES 1200 (US$10) per year for an enrollee under its general scheme and KES 1500 (US$13) under its civil servants' scheme (8). Private providers receive KES 2850 (US$25) per year (8). A challenge with capitation is that it often compels service providers to compromise on the quality of services when the number of visits from enrollees increases (8). So that capitation may lead to the under-provision of health services. In addition, capitation works better for public health service providers since they "receive line-item budgets, medical supplies, drugs, equipment and staff salaries from county governments" (8). However, it might lead to losses for private health services providers as they must procure drugs, medical equipment and pay salaries. These costs, therefore, need to be factored in when calculating the cost of health services.

Above all, health providers should be involved in the establishment of capitation rates. Unfortunately, the experiences of health care providers are not always considered when designing provider payment methods such as capitation and fee-for-service (9). For example, public health providers have "complained of receiving lower capitation rates per enrollee as compared with private and faith-based providers and that the rates were not set in consultation with them" (9).

The NHIF uses capitation mainly to pay for outpatient health services. Under this arrangement, the enrollee selects and registers at a healthcare provider where he or she will receive services. The provider then receives capitation payments for that enrollee on a quarterly basis to provide a pre-determined set of outpatient services, as specified in the benefits package. Where a service is not available in the health facility, it is required to outsource the service at no cost to the patient. Further, the NHIF pays fee-for-service reimbursements after claims are submitted in accordance with the contracts signed with the providers.

While the NHIF's provider payment methods are predictable and providers, therefore, know in advance how much to expect, they impose complex reporting requirements on the providers. The NHIF requires providers to complete claims forms, upload them onto an online system, and present paper copies to its offices for verification and approval (9). Claims are rejected where the details on the online system do not tally with those on paper copies. Providers are thus confronted with double reporting that they consider unnecessary (9). In addition, providers are required to promptly notify the NHIF through the online system that enrollees have sought care from their facilities, otherwise they risk not being reimbursed (9). The NHIF, therefore, needs to simplify its claims and reporting processes.

The Insurance Act regulates the provision of private health insurance. It regulates health insurance as a class of general insurance. It defines medical insurance as "the insurance business of paying for medical expenses, including the business of covering disability or long-term nursing or custodial care needs". The Insurance Act sought to separate the businesses of medical insurance and health care provision, to avoid conflicts of interest (10).

However, while the Act regulates the conduct of medical insurance providers, it does not regulate health management organizations. The Act defines a Medical Insurance Provider (MIP) as an "intermediary other than a broker, concerned with the placing of medical insurance business with an insurer, for, or in expectation of, payment by way of a commission, fee or other remuneration". On the other hand, a Health Management Organization (HMO) is an entity that delivers health maintenance and treatment services for a group of enrolled persons who pay pre-negotiated fixed payments. However, while HMOs provide medical insurance to the extent that they offer health packages that include pre-funding mechanisms, the Insurance Act does not apply to them. Instead, the Ministry of Health regulates HMOs with respect to the medical services they provide. The result is that, unlike MIPs, HMOs are not obligated to adhere to policyholder protection mechanisms such as prudential standards with respect to capital requirements, creating an uneven playing field (11).

Unlike public health insurance under the NHIF, the Insurance Act does not prescribe a minimum or core benefit package (2). Requiring core benefits restrains insurers from designing packages to attract only low-risk individuals. However, most health insurance policies tend to have limited coverage of pre-existing conditions, contract exclusions and waiting periods. The goal is to discourage adverse selection and keep premiums affordable. Unfortunately, this approach leads to a situation in which most people will not be able to purchase insurance for high cost diseases such as cancer, "which are often the very conditions for which insurance is most needed" (12). A need, therefore, arises to "set boundaries on what can be excluded and for what period" (12). This will require the creation of standardized packages.

Health insurance providers also seek to discourage excessive use of health care through mechanisms such as deductibles, co-payments, co-insurance and payment ceilings (12). However, these measures may be counter-productive as they "may disproportionately

reduce service utilization among the poor and discourage people from seeking preventive services that would avoid the subsequent need for costly curative care" (12). In addition, insurance is only effective if it covers a substantial share of health service costs. A need, therefore, arises to strike a balance between providing effective financial protection and assuring affordable premiums.

Health insurance providers also use various mechanisms to manage the utilization of services, including the use of formularies with generics or negative lists of medicines excluded from reimbursement (13). The formularies list covered medicines and are updated on a regular basis, typically annually. Medicines are covered on the basis of factors such as meeting regulatory standards of quality and safety, cost-effectiveness, and availability. In some cases, the maximum reimbursement for covered medicines is capped, and their quantities may also be limited.

Monitoring medicines utilization and costs is another mechanism for managing the utilization of services. Thus, health insurance programs usually collect demographic, pharmacy, procedures, outpatient and hospitalization data. However, health care providers do not always provide quality data and hospitals use different coding methods to capture procedures (11). A standard coding method should therefore be instated if the quality of data is to improve.

In private health insurance schemes, there are two main modes of paying service providers, namely credit facilities and fee-for-service. In the former scenario, enrollees receive benefits-in-kind. And in the latter scenario, enrollees pay service providers upfront on a fee-for-service basis and claim reimbursement by submitting claims. Health insurance providers often require service providers to meet performance indicators, such as quality (9). For example, the insurance providers will not pay for complications arising from procedures such as surgeries especially when the costs have escalated. In such scenarios, the service provider is required to absorb the higher costs (9).

A common challenge with private health insurance schemes is the absence of uniform treatment protocols, which can lead to excess testing and increased claims (11). Implementing standard treatment pathways could also help to improve cost management (11).

There is also Community-Based Health Insurance (CBHI), which also contracts public and private health service facilities to provide services to members. CBHIs fall into two categories: (i) those that are formal and offer benefits to members based on a fixed annual fee; and (ii) those that are informal agreements between community members to support each other's medical needs as they arise. Both are not regulated by law.

Another key player in the health insurance industry are the Third Party Administrators (TPAs), which are organizations that accept and process health insurance claims from health service providers such as doctors, hospitals, and pharmacies. TPAs are also not regulated by law.

Lessons for healthcare providers

The health insurance industry places health service providers such as physicians in a difficult position. On the one hand, the physician is a gatekeeper for the insurance provider to the extent that the insurance contract places an obligation on the physician to control the costs of health care. Thus, the contract may require the physician to seek fewer tests and referrals. On the other hand, the physician has a professional obligation to ensure that his or her patients receive adequate health care. Physicians must therefore balance these two roles that may conflict.

Accordingly, healthcare providers need to ensure that they sign suitable contracts with insurance providers if they are to balance these roles. Key lessons for health providers include the following:

Poorly drafted contracts may place healthcare providers at great financial risk, especially when they assume the risk of providing health care. They should therefore ensure that their contracts with the health insurance providers are carefully drafted and fair, including setting reasonable reimbursement timelines, describing covered services, and setting fee schedules, and formal processes for resolving disputes relating to matters such as billing.

Negotiating fair contracts demands that health providers know their data. They should therefore endeavor to know how they perform in standard quality metrics, patient satisfaction measures, and referring physician satisfaction measures.

Health care providers should ensure they participate in the design of health insurance policies (including the development or review of capitation rates), particularly through their associations.

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