JOURNAL OF KENYA ASSOCIATION OF PHYSICIANS

March 2018 Vol. 1 No. 1

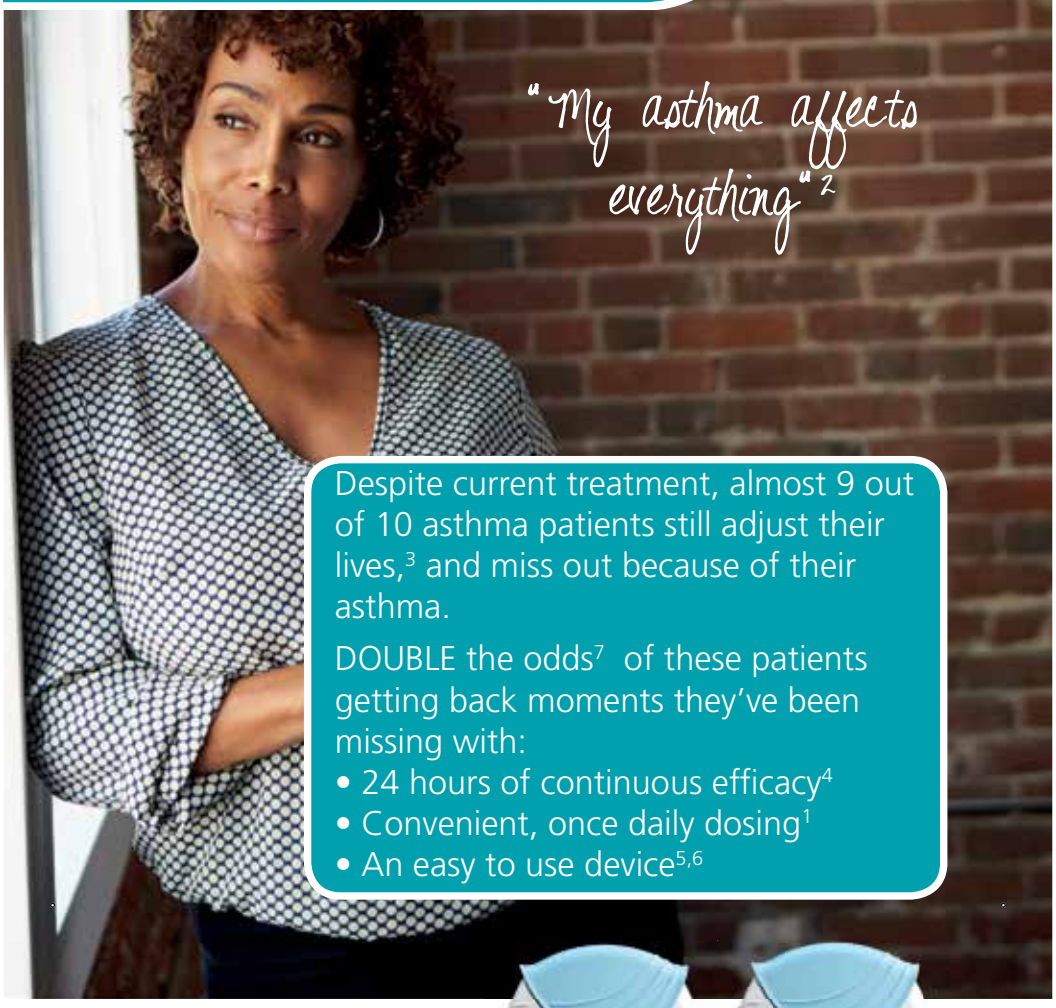
CONTENTS

No.	Paper title
1.	**Chairman's message** Karim YS
	Editor's note
2.	**Welcoming a Kenyan asset: Journal of the Kenya Association of Physicians** Oyoo GO
	Editorial
3.	**Journal of Kenya Association of Physicians** Aluoch JA
	Original papers
5.	**Diagnostic accuracy of focused cardiac ultrasound for common cardiac conditions in a Kenyan hospital** Barasa FA, Bloomfield GS, DeLong A, Kimaiyo S, Koech MM, Binanay C, Foster M, Velazquez EJ
14.	**Prevalence of hypertension and prehypertension: Retrospective review of patients attending a clinic in Nairobi, Kenya** Gikonyo D, Nguchu H, Nduiga D, Irungu S, Morara O, Weru B, Nyaga J, Luvayo D, Mudhune S, Ponoth P, Gikonyo A
18.	**Dysglycaemia among kidney transplant recipients at a national referral hospital in Kenya** Faraj FA, Kayima J, Otieno CF, Were A, Ngare S
24.	**Prevalence, severity and short term outcomes of patients with community acquired acute kidney injury in the general medical wards at Kenyatta National Hospital** Taiyebali MM, Kayima J, Were AJO, Ogutu E
29.	**Prevalence and factors associated with Helicobacter pylori infection in adults attending medical out patient unit at Aden Abdulle Hospital, Mogadishu, Somalia** Dhiblawe AOH, Ponsiano O, Opio K, Osman D
35.	**The utility of physiochemical and modified physiological approach in metabolic acidosis at a tertiary level hospital in Kenya** Essaji LT, Kayima J, Joshi MD, Otieno CF, Amayo A, Achieng L, Gacii M
40.	**Thyroid function among pregnant women attending antenatal clinic at Kenyatta National Hospital** Mungla P, Ong'ech J, Joshi MD
45.	**East, Central and Southern Africa College of Physicians**
50.	**Instructions to authors**

Published by Kenya Association of Physicians
P.O. Box 48397 Code 00100, Nairobi, Kenya. www.kapkenya.org

Asthma

RELVAR ELLIPTA is an ICS/LABA indicated for the maintenance treatment of asthma (≥ 12 years)[1]



Despite current treatment, almost 9 out of 10 asthma patients still adjust their lives,[3] and miss out because of their asthma.

DOUBLE the odds[7] of these patients getting back moments they've been missing with:

- 24 hours of continuous efficacy[4]
- Convenient, once daily dosing[1]
- An easy to use device[5,6]

For more information visit https://breathe.gsk.com/

ICS = Inhaled corticosteriod
LABA = Long acting beta$_2$-agonist

SIDE EFFECTS: Very common: headaches, nasopharyngitis. Common: pneumonia, upper respiratory tract infection, bronchitis, influenza, candidiasis of mouth and throat, oropharyngeal pain, sinusitis, pharyngitis, abdominal pain, arthralgia, back pain, fractures, pyrexia. Uncommon: extrasystoles. **WARNINGS AND SPECIAL PRECAUTIONS:** Not to be used to treat acute asthma symptoms or an acute exacerbation in COPD. Increasing use of short-acting bronchodilators to relieve symptoms indicates deterioration of control and patients should be reviewed by a medical practitioner. **CONTRA-INDICATIONS:** Patients with severe milk-protein alergy or who have demonstrated hypersensitivity to either fluticasone furoate, vilanterol or any of the excipients.

References: 1. Relvar Ellipta Full Prescribing Information prepared in September 2016 based on GDS Version 08/IPI09 dated 09 June 2016. **2.** GSK data on file HO-15-15502.2016. **3.** Price D, *et al.* Types, frequency and impact of asthma triggers on patients' lives: a quantitative study in five European countires. *J Asthma* 2014;51(2):127-135. **4.** Bernstein DI, *et al.* Fluticasone furoate (FF)/vilanterol (100/25 mcg or 200/25 mcg) or FF (100 mcg) in persistent asthma. *J Asthma.* 2015;52(10):1073-1083. **5.** Svedsater H, *et al.* Ease of use of the Ellipta dry powder inhaler: data from three randomised controlled trails in patients with asthma. *npj Prim Care Resp Med.* 2014;24:14019. **6.** Svedsater H, Dale P, Garrill K, *et al.* Qualitative assessment of attributes and ease of use of the ELLIPTA dry powder inhaler for delivery of maintenance therapy for asthma and COPD. *BMC Pulm Med* 2013;13:72. **7.** D. Leather *et al.* An abstract on effectiveness of Fluticasoe furoate/vilanterol (FF/VI) compared to ususal care (UC) in patients with asthma. The Salford Lung Study (SLS), 2017.

RELVAR ELLIPTA: Fluticasone furoate/vilanterol:
Each pre-dispensed dose contains either 100/25 micrograms or 200/25 micrograms of fluticasone furoate/vilanterol (as trifenatate). Inhalation powder. Each single inhalation of fluticasone furoate/vilanterol provides a delivered dose of 92/22 micrograms of fluticasone furoate/vilanterol or 184/22 micrograms of fluticasone furoate/vilanterol. Inhalation powder. **INDICATIONS: Asthma:** For the maintenance treatment of asthma. **COPD:** For the maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD) including chronic bronchitis and/or emphysema and to reduce exacerbations of COPD in patients with an exacerbation history. **Dosage and Administration:** *RELVAR ELLIPTA* is for inhalation only. *RELVAR ELLIPTA* should be administered once daily either morning or evening but at the same time every day. After inhalation, the patient should rinse their mouth with water without swallowing. **Asthma: Adults and adolescents aged 12 years and over:** One inhalation of *RELVAR ELLIPTA* 100/25 micrograms once daily. Or One inhalation of *RELVAR ELLIPTA* 200/25 micrograms once daily for patients who require a higher dose of steroid or patients inadequately controlled on *RELVAR ELLIPTA* 100/25 micrograms. **COPD:** One inhalation of *RELVAR ELLIPTA* 100/25 micrograms once daily. *RELVAR ELLIPTA* 200/25 micrograms is not indicated for patients with COPD. **Special populations (Asthma and COPD): Elderly:** No dosage adjustment. **Renal impairment:** No dosage adjustment. **Hepatic impairment:** Caution should be exercised as patients with hepatic impairment may be more at risk of systemic adverse reactions associated with corticosteroids. **Contraindications:** Contraindicated in patients with severe milk-protein allergy or who have demonstrated hypersensitivity to either fluticasone furoate, vilanterol or any of the excipients. **Warnings and Precautions:** Not to be used to treat acute asthma symptoms or an acute exacerbation in COPD, for which a short-acting bronchodilator is required. Patients should not stop therapy with *RELVAR ELLIPTA*, in asthma or COPD, without physician supervision. Paradoxical bronchospasm may occur. Treat immediately with a short-acting inhaled bronchodilator. Discontinue immediately. The patient should be assessed and alternative therapy instituted if necessary. *RELVAR ELLIPTA* should be used with caution in patients with severe cardiovascular disease. For patients with moderate to severe hepatic impairment, the 100/25 micrograms dose should be used. Systemic corticosteroid effects such as HPA axis suppression, decrease in bone mineral density, growth retardation in children and adolescents, cataract and glaucoma may occur especially with high doses. Administer with caution in patients with pulmonary tuberculosis or in patients with chronic or untreated infections. An increase in pneumonia has been observed in patients with COPD. Risk factors for pneumonia in patients with COPD receiving *RELVAR ELLIPTA* include current smoken, patients with a history of prior pneumonia, patients with a body mass index <25 kg/m^2 and patients with a (forced expiratory volume) FEV$_1$ <50% predicted. These factors should be considered when relvar is prescribed and treatment should be re-evaluated if pneumonia occurs. **Interactions:** Beta-adrenergic blockers may weaken or antagonise the effect of beta$_2$-adrenergic agonists. Concurrent use of both non-selective and selective beta-blockers should be avoided. Care is advised when co-administering with strong CYP 3A4 inhibitors (e.g. ketoconazole, ritonavir) as there is potential for an increased systemic exposure. **Pregnancy and Lactation:** Safety not established. **CLINICAL TRIALS: Adverse Reactions: Very common:** Headache, Nasopharyngitis. **Common:** Pneumonia, Upper Respiratory Tract Infection, Bronchitis, Influenza, Candidiasis of mouth and throat, Oropharyngeal pain, Sinusitis, Pharyngitis, Rhinitis, Cough, Dysphonia, Abdominal pain, Arthralgia, Back pain, Fractures, Pyrexia. **Uncommon:** Extrasystole. **POST-MARKETING DATA: Adverse reactions: Common:** Muscle spasms. **Rare:** Hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticarial, Anxiety, Tremor, Palpitations, Tachycardia Paradoxical bronchospasm **Ability to Drive and Use Machines:** No studies. **Management of overdose:** There is no specific treatment for an overdose with *RELVAR ELLIPTA*. If overdose occurs, the patient should be treated supportively with appropriate monitoring as necessary. Cardioselective beta-blockade should only be considered for profound vilanterol overdose effects that are clinically concerning and unresponsive to supportive measures. Cardioselective beta-blocking drugs should be used with caution in patients with a history of bronchospasm.Further management should be as clinically indicated or as recommended by the national poisons centre, where available. **List of Excipients:** Lactose monohydrate (which contains milk protein) (12.5 milligram lactose monohydrate per blister) Magnesium stearate. Storage condition depends on local registration requirements. **Following removal from tray, the product may be stored for a maximum period of:** 6 weeks: below 25˚C or 1 month: below 30˚C Write the date the inhaler should be discarded on the label in the space provided. The date should be added as soon as the inhaler has been removed from the tray. If stored in the refrigerator, allow the inhaler to return to room temperature for at least an hour before use. **GSK is committed to the effective collection and management of human safety information relating to our products and we encourage healthcare professionals to report adverse events to us on +254 20 693 3200/0722 742 998 or email us on ke.safety@gsk.com.** Full Prescribing Information is available on request from GlaxoSmithKline Pharmaceutical Kenya Limited, P.O. Box 78392-00507, 23 Likoni Road, Industrial Area, Nairobi, Kenya. Abbreviated Prescribing Information prepared in September 2017 based on GDS version 09/IPI 10 dated 30 May 2017.

GSK is committed to the effective collection and management of human safety information relating to our products and we encourage healthcare professionals to report adverse events to us on +254 20 693 200 or +254 722 742 998 or ke.safety@gsk.com

Full Prescribing Information is available on request from GlaxoSmithKline Pharmaceutical Kenya Ltd, P.O Box 78392-00507, Likoni Road, Nairobi Kenya

EA/FFT/0004/18 Date of preparation: February 2018

RELVAR ELLIPTA was developed in collaboration with

INNOVIVA

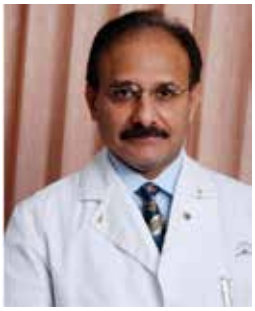
RELVAR ELLIPTA
(fluticasone furoate and vilanterol inhalation powder)
Practical efficacy[4,6]

Editorial Board

Editor-in-Chief

Associate Editors

Members



Duodart
Good times are back

"It's good to be back doing the things I love and looking forward to the future"

Indications[1]:

- Treats and prevents progression of benign prostatic hyperplasia (BPH)
- Reduction in the risk of acute urinary retention (AUR) and surgery in patients with symptoms of BPH

BPH: benign prostatic hyperplasia.

Full Prescribing Information is available on request from GlaxoSmithKline Pharmaceutical Kenya Limited, P.O. Box 78392-00507, 23 Likoni Road, Industrial Area, Nairobi, Kenya

***GSK** is committed to the effective collection and management of human safety information relating to our products and we encourage healthcare professionals to report adverse events to us on* **+254 20 693 3200 or +254 722 742 998 or ke.safety@gsk.com**

Reference:

1. Duodart Prescribing Information based on GDS Version 15/IPI 12 dated 11th April 2016.

DUODART
(dutasteride/tamsulosin HCl) Capsules

EA/DUTT/0022/17a(1)
Date of preparation: February 2018

Chairman's Message

It is with great joy and pride that I write this Chairman's Message to the first edition of our very own Journal of Kenya Association of Physicians. And I fondly hope and fervently pray that this edition is merely the first amongst many that will follow!

Kenya Association of Physicians was inaugurated in 1992. The first Newsletter of the Association was published four years later in1996, with Prof Bill Lore, the Vice-Chairman of KAP also acting as the Editor, and under the Chairmanship of Dr. J. A. Aluoch, with Dr. Were as Hon. Secretary. But for some reason, the KAP Newsletter did not continue for very long. Besides a Newsletter, for many years we have also talked of a peer-reviewed Journal of our own, but little progress was made, that is, until this year! I am very happy to see that at last our dream is being turned into reality! And for this, my heartiest congratulations go to our Chief- Editor, Prof. Omondi Oyoo, and, indeed, to the entire Editorial team! Prof. Oyoo has guided us to this noble goal. Also worthy of particular mention is our KAP Honorary Secretary, Dr. Mohamed Sood, who has persistently harangued and harassed us all into action to produce JOKAP! Well done Dr. Mohamed Sood! And, partnering him has been Mr. David Ng'ethe of Medics Management Services, who has shown us a lot of patience and to whom we owe a debt of gratitude.

You may well ask, do we really need yet another medical Journal when there are already so many excellent journals in the world, many easily accessible on the internet? The answer is an emphatic "Yes!" because, as Kenya grows and with it our medical Services, we as Kenya Association of Physicians also need to grow and have our own independent institutions, including our own journal. Besides, as we expand our capacity to train more physicians, we will have more young physicians who will need to publish in peer-reviewed journals to further their careers, and where our Journal will provide them an avenue to publish their M. Med thesis or other research findings.

I am sure our Journal will grow from strength to strength with the passage of time, and it will mature in its time to take its rightful place amongst the very best medical journals in the world. But how soon we achieve that goal depends entirely on us! We all need to support our editorial team by submitting relevant research papers, be they M. Med thesis, or case presentations, or review articles. For our editorial team cannot produce the Journal if there are no papers to publish! And, equally important, please read the Journal and comment on the articles in the "Letters to the Editor" section!

This is our Journal. Whether it continues to grow and mature or whether it will wither away for lack of interest, depends on all of us!

Wishing you all happy reading!

Karim YS, MBBS (Lon), MRCP (UK), FRCP (Lon), FCP (ECSA)
Chairman, Kenya Association of Physicians - National
Email: yusufkarim351@gmail.com

Welcoming a Kenyan asset: *Journal of the Kenya Association of Physicians*

It is with great pleasure that I allow myself to welcome the *Journal of Kenya Association of Physicians* (JOKAP).

The *JOKAP* joins a highly competitive collection of International journals in existence exclusively devoted to disseminate basic and clinical science developments and observations in the speciality of internal medicine.

In this era of global medicine and internet, availability of the *JOKAP* is a welcome addition. It is hoped that JOKAP will provide a forum where physicians in Kenya will document observations and advancements in internal medicine in this part of Africa. We are as well welcoming submissions from other parts of the world.

Kenya has a population of over 40 million people and with over 400 (physicians) specialist in internal medicine, Kenya should become a rich source of information about development in internal medicine in the continent. The *JOKAP* therefore is a timely addition to the worldwide medical community.

It is my hope that the *JOKAP* will parallel the rapid growth already witnessed in Kenya and that it will become a competitive journal.

The editors, the editorial board and the management of Kenya Association of Physicians should be commended for their efforts in initiating this worthwhile academic enterprise.

The publication of this first edition of the journal of Kenya association of physicians is an indication that though we have a long road to go, we have moved a long way forward.

Oyoo GO, FCP (ESCA TRCP (EDIN), FACR
Editor-in-Chief
Email: geomondi@hotmail.com

Journal of Kenya Association of Physicians

Congratulations to our colleagues at the Kenya Association of Physicians for the birth of a novel idea, the *Journal of Kenya Association of Physicians (JOKAP).*This is a timely move. Starting up a new medical journal from scratch possess tremendous challenges that are not for the faint of heart. JOKAP is fortunate to have an experienced editorial team of talented and creative people. I congratulate you on this initiative and wish you the very best of luck in this new venture.

Right from the onset, it is obvious that this venture is going to pose some financial challenges. To survive; medical journals rely on sponsors, medical societies, universities and in the present environment advertisers, usually pharmaceutical companies. Forming a relationship with the sponsors sometimes can also pose some ethical challenges. It is therefore important that JOKAP remains firmly under the Kenya Association of Physicians as the main sponsor as the relationship with the advertisers is not always easy. Medical journals remain dangerously dependent on pharmaceutical advertisement for financial lifeblood. We as Physicians recognize and appreciate our perennial partnership and friendly relations with the pharmaceutical industry. It is for this reasons that as JOKAP we will delight in the revenue from pharmaceutical competitive advertisement, we should at the same time seek to put restraints on their ultra-persuasiveness and keep it within the bounds of medical propriety and a sense of service to the association in the effort to promote medical education.

Recently several journals have appeared in the Kenya medical scene published by various medical societies and medical colleges. Perhaps it's time to review the role of the many medical journals that have appeared in the scene. The medical journals should serve not only the medical profession but the community at large. They should be great unifier of our past and present medical information and diffuser of new facts, thoughts and medical appliances in the field of medicine. As stated in the JOKAP's instructions to authors; medical journals usually serve best in the dissemination of new research results in medicine and demonstrates the changing ways in which medical knowledge is evolving, Thus journals must play a crucial role in the provision of appropriate medical knowledge and practice. In Kenya, as in many sub-Saharan countries health professionals often argue that all locally conducted research should be published only by local journals. This may not be possible as most of these countries do not have sufficient economic, scientific, technological resources but all the same we should strive to publish most of our research in our local journals. The majority of our local medical researchers prefer to publish their work in overseas journals for obvious prestigious reasons but the disturbing fact is that very few of our medical professionals are capable of writing any medical article leave alone publishing research findings.

The United Nations has embraced the role of journals in enhancing health research in developing countries and its 2004 report focused on sustainable solutions requiring the commitment of Governments funding, though academic Institutions progress in achieving their aim has been modest and slow.

Medical journals play a central role in dissemination of research results at the same time, the importance of scientific publication in advancing the carriers of research scientists can influence and help the pace of medical science advancement in developing countries. Enhancing scientific technology capacity in developing countries is truly a necessity and not a luxury. We should therefore launch JOKAP on a serious note with a well-focused vision.

The future of print medical journals may face some challenges, some of these challenges I stated in an article I wrote in EAMJ in 1998 commemorating 75 years of *East Africa Medical Journal* existence (2). This article is worth reading as some of my predictions have come true. In particularly, the shift of journal publications to online is part of the changing environment in medical journals. Elaborate websites now offer Web only content, including audio and video, and other once-impossible formats. JOKAP must embrace and manage right from the beginning not just the shifting landscape of production and publishing of medical knowledge but also the broader current of their social, economic and political context. This responsibility cannot be borne by the editors alone. The membership of the Kenya Association of Physicians, whose subscriptions we hope will keep the journal going will of necessity shape the decision of JOKAP editors, sponsors and advertisers. Priorities and prospects of JOKAP in the future will therefore depend on how and how well the membership contribute and use it as soon as it is launched.

Aluoch JA, FRCP
Founder Chairman KAP
Email: aluochj@gmail.com

References

1. International Committee of Medical Journal Editors (ICMJE) Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication. ICMJE; Philadelphia, PA: (Accessed 8 Mar 2011) 2008. Available at http.//www.icmje.org/aboutur.ICMJE. Uniform Requirements for Manuscripts Submitted to Biomedical Journals. ICMJE; Philadelphia,PA(Accessed8Mar2011). Available http:/www. icmje.org/index.htmlethic.
2. Aluoch JA. The past and future of medical journals with special reference to the East Africa medical journal. *East Afr Med J*. 1998; **75**(6 supplement):
3. Aluoch JA. How to write a medical article. *The Nairobi Hosp Med J.* 2010; **1**(1):

Original paper

Diagnostic accuracy of focused cardiac ultrasound for common cardiac conditions in a Kenyan hospital

Barasa FA[1,6], Bloomfield GS[3,4,5], DeLong A[2], Kimaiyo S[1], Koech MM[6], Binanay C[4], Foster M[3], Velazquez EJ[3,4]

[1]Department of Medicine, Moi University, Eldoret, Kenya
[2]School of Public Health, Brown University, Providence, RI USA
[3]Division of Cardiovascular Medicine, Department of Medicine, Duke University, Durham, NC USA
[4]Duke Clinical Research Institute, Duke University, Durham, NC USA
[5]Duke Global Health Institute, Duke University, Durham, NC, USA
[6]Moi Teaching and Referral Hospital, Eldoret, Kenya

***Address for Correspondence*:** Dr Felix A Barasa, Moi Teaching and Referral Hospital, Department of Cardiology, PO Box 3 Code 30100, Eldoret, Kenya. Email: barasaceo12@gmail.com

Abstract

Background: Access to standard echocardiography in sub-Saharan Africa is limited and portable technology may increase access to this diagnostic imaging. Utility of such technology at bedside (focused cardiac ultrasound- FoCUS) by less well-trained medical cadres such as Registered Clinical Officers (RCOs) is unknown in Kenya.

Objective: To test the hypothesis that RCOs using FoCUS will significantly improve diagnoses of common cardiac disorders compared to their Physical Examination (PE) skills. These included: Rheumatic Heart Disease (RHD), Left Ventricular Hypertrophy (LVH), Dilated Cardiomyopathy (DCM), Isolated Right Heart Failure (IRHF) and pericardial effusion.

Design and methods: This was a prospective study carried out by RCOs on consecutive adult patients referred for a clinical echocardiogram at Moi Teaching and Referral Hospital. The RCOs were trained for 8 hours in FoCUS using a hand-held device. They performed a history, PE and FoCUS on each recruited patient who also underwent a Standard Echocardiogram (SE) that was over-read by cardiologists. Correct diagnosis of the 5 conditions by each of the 2 diagnostic modalities using over-reads as gold standard was considered the primary outcome.

***Results and conclusion*:** Twelve RCOs studied 211 patients whose median age was 51 years and 136 (64%) were female. Sixty-eight percent of over-read data had at least one of the five conditions: 26 had RHD, 15 had IRHF, 13 had DCM, 12 had LVH, 4 had pericardial effusions and 2 participants had more than one diagnosis. FoCUS had significantly higher sensitivity than PE for RHD (73% vs 38%) and IRHF (60% vs 0%); and higher sensitivity for the remaining disorders that did not reach statistical significance. PE had significantly higher specificity than FoCUS with regard to RHD only. This strategy of equipping RCOs with training to perform FoCUS has the potential to improve cardiac care in resource limited settings.

Key words: Focused cardiac ultrasound, Sub-Saharan Africa, Heart failure, Registered Clinical Officers

Introduction

Echocardiography is the most commonly used imaging modality worldwide for the diagnosis and management of patients with cardiac diseases (1,2). Standard Echocardiography (SE) requires extensive training in image acquisition and interpretation. SE is commonly performed by cardiologists or credentialed sonographer technicians. Until recently, platform technology coupled to these training requirements has limited access to diagnostic echocardiography to specialized laboratories within established hospitals or clinics. The emerging availability of Focused Cardiac Ultrasound (FoCUS) using hand held devices has promised to expand the access to diagnostic imaging beyond established clinical settings to the point of care and has resulted in guidelines related to nomenclature, standards, training, technique and integration into clinical practice (3,4). Studies support the ability of hand-held echocardiography to provide accurate and clinically meaningful information compared to Physical Examination (PE) alone in intensive care units, at the bedside, and in the community (5-9).

Among Low and Middle Income Countries (LMICs), FoCUS may be particularly valuable to enhance access to diagnostic imaging. Several studies from sub-Saharan Africa (SSA) suggest that portable FoCUS is applicable to the diagnosis of several cardiac disorders such as Rheumatic Heart Disease (RHD) which is common in the region (10-13). Most of this research using FOCUS to detect cardiac disease in developing countries has also demonstrated its ability to detect valvular and non-valvular heart disease.

Physician availability and expertise in echocardiography is limited in SSA which renders SE

inaccessible to the majority of patients in need (14). Most health care delivered in SSA is done by Registered Clinical Officers (RCOs) who outnumber physicians by 10:1 (14). In Kenya, RCOs undergo a three-year training program in clinical medicine after high school in accredited medical training colleges and then a one-year internship before deployment and are responsible for health care delivery in the majority of the public hospitals (14,15). They do not receive any specialized training in internal medicine nor cardiology, and their cardiovascular diagnostic abilities are limited which decreases appropriate treatment and/or referral. Our objective, therefore, was to assess the extent to which training the RCOs in FoCUS would improve their ability to diagnose common cardiac conditions. We hypothesized that, after an 8-hour training period, the RCOs equipped with a FoCUS device would improve their diagnostic ability for commonly encountered cardiac conditions compared to PE alone and, thus, allow for more appropriate referral for follow-up care with a SE or cardiac specialist.

Materials and methods

This study evaluated the diagnostic accuracy of FoCUS, PE and SE for five common cardiac conditions encountered in rural SSA: RHD, Isolated Right Heart Failure (IRHF), DCM, LVH and pericardial effusion (16-20). The RCOs were recruited if they were registered by the Kenyan national accreditation board and had at least 1 year experience working in the outpatient or emergency departments of the Moi Teaching and Referral Hospital (MTRH) in Eldoret, Kenya. MTRH is a 750-bed hospital with a catchment area of 16.4 million (21). We recruited consecutive in and out-patients with suspected cardiac disease referred by their primary physicians for routine SE. Exclusion criteria were age under 18 years and known pregnancy. All patients provided informed consent. The study was approved by the Institutional Review Boards of Moi, Duke and Brown Universities. The study was supported in part by a grant from NHLBI of the National Institutes of Health of USA but (the sponsor) had no role in analysis of the data, interpretation nor decision to submit the manuscript.

The RCOs were trained for an 8-hour period by two of the authors (FAB, MF) across 5 sessions. The training incorporated a didactic review of the clinical, diagnostic and physical examination manifestations of the 5 study conditions followed by another didactic session on utilization of the hand-held echocardiography technology (VScan, General Electric Healthcare, Milwaukee, WI) and concluded with a mentored, hands-on practical session with alive model.

Study procedure: After patient recruitment, the RCO took a medical history and performed PE, and then indicated on a case report form whether or not the patient had a diagnosis supporting any one of the 5 cardiac disorders under study. Subsequently, he/she did a FoCUS study and filled out a new report form indicating the new diagnosis. Following the FoCUS exams, patients underwent SE exams done by a qualified sonographer blinded to the RCO's PE and FoCUS results. This SE was performed on a CX-50 machine (Philips Healthcare, Bothell, WA) following the standard image acquisition of the laboratory (2 Dimensional with Doppler) and digitally archived. The sonographer's credentials at the time of the study included a basic diploma in clinical medicine, one year specialized training in echocardiography and an additional 5 years of experience in clinical and research echocardiography. The referring physicians and patients received the results of SE as per the MTRH standard. Archived images were independently over-read by cardiologists and sonographers blinded to the diagnoses from the PE, FoCUS and SE results (GSB, FAB, MF) at Duke University.

Outcome measures: Correct diagnosis of the 5 cardiac conditions by each of the 3 diagnostic modalities (PE, FoCUS, SE) was calculated using the over-reads as the gold standard diagnosis and was considered the primary outcome of the study. A modified version from The World Heart Federation guidelines was used for the diagnosis of RHD while those from American Society of Echocardiography were used for the other 4 conditions (22,23) (Table 1). The presence of any degree of RHD, IRHF or DCM qualified as meeting positive criteria for inclusion. On the other hand, pericardial effusion and LVH were included as major abnormalities in the analysis only if moderate or severe.

Statistics: The sample size was determined so as to achieve adequate power to detect improvements in the sensitivities of the FoCUS compared to PE. Since each RCOs' outcomes were likely correlated, sample size calculations were based on methods for McNemar's test with clustered data (24). It was assumed that the PE would detect any major cardiac abnormality in 50% of patients with disease, that FoCUS would improve sensitivity by 25 percentage points, and that at least 12 RCOs would participate in the study. Sample sizes were calculated with a two-sided alpha type-1 error rate of 5%, power of 80%, Intra-class Correlation Coefficients (ICC) of 0.1 to 0.2, with 5% to 10% of diseased patients classified as diseased by PE and misclassified as not diseased by FoCUS. Based on prior experience, it was anticipated that 70% of enrolled patients would have

abnormal echocardiograms due to the presence of the 5 disorders under study. A minimum sample size of 114 patients was calculated to test the hypothesis that the FoCUS would improve the overall sensitivity as detailed. However, this was adjusted to 210 patients to achieve sufficient statistical power to test the secondary hypothesis that FoCUS would improve the sensitivity of an RCO's diagnosis of RHD. For this calculation, RHD was assumed to constitute 30% of the major abnormalities encountered.

Outcome analysis: Using the over-read of the echocardiogram as the reference gold standard, test diagnostics, sensitivity, specificity, NPV and PPV were calculated for FoCUS, PE and SE. All 4 diagnostic measures were estimated empirically from the data and exact binomial 95% confidence intervals were produced.

With 3 testable modalities, it was possible to make three comparisons with the data (i.e. FoCUS versus PE, SE versus FoCUS, and SE versus PE). However, the comparison of primary interest was between FoCUS and PE and therefore compared using the Odds Ratio (OR). Linear models for clustered binary outcomes were used to incorporate the complex correlation structure in the data, due to clustering at both the patient level (FoCUS and PE performed on each patient) and RCO level. The models were fit using Generalized Estimating Equations (GEE), and Odds Ratios (OR) were estimated along with their 95% confidence intervals using robust standard errors.

Due to low diagnosis rates for some of the diseases, there were cases when the empirical sensitivity or specificity was 0% or 100% and the linear models could not be fit and ORs could not be estimated. In these cases, only p-values using McNemar's exact test are presented. In addition, PPV's could not be compared for some diseases because there were very few (or no) participants with positive tests on some modalities. For an analogous reason, NPV of FoCUS and PE could not be compared with SE due to the 100% NPV.

Results

Study population: Between February 25th and October 1st, 2013, 12 RCOs (2 male, mean age 32 years, median 6 years of experience [IQR 4-8]) recruited 211 out of 260 consecutively screened patients. Among the 49 patients screened but not enrolled, 11 refused consent, 16 were pregnant and 22 were below 18 years (Figure 1). Patient median age was 51 years and 64% were female. Cardinal symptoms at referral for echocardiogram included easy fatigability (74%), palpitations (65%), orthopnea (65%) and exertional dyspnea (59%). Cardiovascular risk factors included history of alcohol use (26%), smoking (11%), diabetes mellitus (5%) and elevated blood pressure (46%). Two-thirds of the recruited patients were outpatients (Table 1).

Table 1: Modified WHF/ ASE criteria for diagnosis of RHD, DCM, LVH, IRHF and pericardial disease

Disease entity	Key echocardiographic characteristics
Rheumatic heart disease	· Significant valve leaflet thickening associated with regurgitation or stenosis · Chordal thickening with restriction of leaflet mobility · Coaptation defect
Pericardial effusion	· Echo free space surrounding the heart/ within the pericardial sac
Isolated right heart failure	· Right ventricular hypertrophy or dilatation · Associated tricuspid regurgitation and dilated, non-collapsing inferior vena cava · Absence of valve disease
Left ventricular hypertrophy	· Abnormally thickened left ventricular walls on both parasternal long and short axis · Associated known hypertension or high blood pressures
Dilated cardiomyopathy	· Left ventricular dilatation associated with poor contractility. · Associated global chamber dilatation. · Absence of valve disease, known congenital heart disease or hypertension.

Test diagnostics: Echocardiogram over-read diagnoses were available for 208 of 211 enrolled participants (99%, Figure 1). Sixty-eight (33%) met criteria for at least 1 of the 5 study conditions. Prevalence rates were 12% (95% CI 8, 18%) for RHD, 7% (95% CI 4, 12%) for IRHF, 6% (95% CI 3, 10%) for DCM, 2% (CI 1, 5%) for pericardial effusion, and 6% (CI 3, 10%) for LVH (Table 2). Two participants were diagnosed with two disorders: one with RHD and pericardial effusion and one with IRHF and LVH. The prevalence of these major abnormalities (33%) was lower than that initially assumed for the sample size calculation (70%).

Prevalence, sensitivity, specificity, and PPV and NPV for all diseases are shown in Table 3. All modalities demonstrated the highest sensitivity for RHD. SE diagnosed 100%, FoCUS 73%, and PE 38% of RHD cases. While specificity was high for both SE and PE (98%), RHD was over-diagnosed by FoCUS resulting in an estimated prevalence of 23% and adversely affecting FoCUS specificity (85%, 95% CI 79, and 90%). A similar pattern was seen for DCM with sensitivity by SE of 77% (95% CI 46, 95%), 46% (19, 75%) for FoCUS, and 23% (CI 5, 54%) for PE. Specificity remained highest for SE (99%, 95% CI 97, 100%) and PE (98%, 95% CI 96, 100%), with FoCUS yielding a specificity of 94% (CI 89-97%). All cases of IRHF, pericardial effusion and LVH were missed by PE, while FoCUS was able to correctly diagnose some cases but with an expected reduced specificity relative to SE. NPVs for FoCUS were all ≥96%, demonstrating that those with negative results on FoCUS had a high probability of not having the specified disease. However, PPVs were comparatively low, ≤50% for all diseases, indicating high false positive rates.

Table 2: Baseline characteristics of patients stratified by gender *

Characteristic	Total N=211	Male N=75	Female N=136	P value
Median age (range)	51 (18, 102)	51.5(18,84)	51 (18, 102)	0.674
History of alcohol use	54/208, 26%	30/73, 41%	24/135, 18%	<0.001
History of smoking	22/207, 11%	13/73, 18%	9/134, 7%	0.018
Blood pressure level				0.881
<90/<50 mmHg	5/199, 3%	1/70, 1%	4/129, 3%	
90-140/50-89 mmHg	103/199, 52%	37/70, 53%	66/129, 51%	
>140/90 mmHg	91/199, 46%	32/70, 46%	59/129, 46%	
Diabetes	10/211, 5%	4/75, 5%	6/136, 4%	0.746
NYHA Class				0.256
1	88/208, 42%	33/73, 45%	55/135, 41%	
2	59/208, 28%	17/73, 23%	42/135, 31%	
3	42/208, 20%	13/73, 18%	29/135, 21%	
4	19/208, 9%	10/73, 14%	9/135, 7%	

* quantitative values (age) are presented as median (range), categorical values as n/N (%). P-values are presented from Fisher exact tests for categorical variables and Wilcoxon Rank Sum test for quantitative variables.

Table 3: Summary of test characteristics for the gold standard and three other modalities*

		Gold Standard	SE	FoCUS	PE
RHD					
	Prevalence	12% (8, 18)	14% (10, 20)	23% (17, 29)	7% (4, 11)
	Sensitivity		100% (81, 100)	73% (52, 88)	38% (20, 59)
	Specificity		98% (94, 99)	85% (79, 90)	98% (94, 99)
	Positive Predictive Value		87% (69, 96)	40% (26, 56)	71% (42, 92)
	Negative Predictive Value		100% (97, 100)	96% (91, 98)	92% (87, 95)
IRHF					
	Prevalence	7% (4, 12)	8% (4, 12)	9% (5, 13)	1% (0, 4)
	Sensitivity		93% (68, 100)	60% (32, 84)	0% (0, 30)
	Specificity		99% (96, 100)	95% (91, 98)	98% (96, 100)
	Positive Predictive Value		88% (62, 98)	50% (26, 74)	0% (0, 81)
	Negative Predictive Value		99% (97, 100)	97% (93, 99)	93% (88, 96)
DCM					
	Prevalence	6% (3, 10)	5% (3, 9)	9% (5, 13)	3% (1, 6)
	Sensitivity		77% (46, 95)	46% (19, 75)	23% (5, 54)
	Specificity		99% (97, 100)	94% (89, 97)	98% (96, 100)
	Positive Predictive Value		91% (59, 100)	33% (13, 59)	50% (12, 88)
	Negative Predictive Value		98% (96, 100)	96% (93, 99)	95% (91, 98)
Pericardial effusion					
	Prevalence	2% (1, 5)	1% (0, 4)	3% (1, 7)	0% (0, 3)
	Sensitivity		75% (19, 99)	25% (1, 81)	0% (0, 72)
	Specificity		100% (97, 100)	97% (94, 99)	100% (97, 100)
	Positive Predictive Value		100% (19, 100)	14% (0, 58)	-
	Negative Predictive Value		100% (97, 100)	99% (96, 100)	98% (95, 99)
LVH					
	Prevalence	6% (3, 10)	3% (1, 6)	9% (5, 13)	3% (1, 7)
	Sensitivity		33% (10, 65)	33% (10, 65)	0% (0, 36)
	Specificity		99% (96, 100)	93% (88, 96)	96% (93, 99)
	Positive Predictive Value		67% (22, 96)	22% (6, 48)	0% (0, 53)
	Negative Predictive Value		96% (92, 98)	96% (92, 98)	94% (90, 97)

*Summaries are presented as percentage (95% exact binomial confidence interval).
SE Standard echocardiogram; PE, physical examination; FoCUS Focused cardiac ultrasound; RHD Rheumatic heart disease; IRHF Isolated right heart failure; DCM Dilated cardiomyopathy; LVH Left ventricular hypertrophy

Table 4 shows the comparison of test characteristics between modalities. Compared to PE, FoCUS had higher sensitivity for all diagnoses and statistically significantly higher sensitivity for RHD (OR 4.37 [95% CI1.7, 11.1], p=0.002) and IRHF (p=0.004). The OR for IRHF was not calculable (infinite) due to the 0% sensitivity on PE and the p-value was calculated using McNemar's test. Sensitivity of FoCUS compared to PE for DCM was higher (OR 3.85 [95% CI 0.7, 21.3], p=ns) but the estimate of the odds was imprecise with wide confidence intervals. With only 4 cases of pericardial effusion, sensitivities could not be compared.

Table 4: Odds ratio (95% CIs)[a] describing pairwise comparisons SE, FoCUS and PE

		SE vs FoCUS	SE vs PE	FoCUS vs PE
		OR (95% CI)	OR (95% CI)	OR (95% CI)
RHD				
	Sensitivity	P<0.05	p<0.001	4.37 (1.72, 11.11)**
	Specificity	7.96 (3.18, 19.9)***	1.02 (0.5, 2.09)	0.13 (0.05, 0.3)***
	Positive Predictive Value	9.58[b] (3.62, 25.34)***	2.13 (1.4, 3.25)***	0.22 (0.08, 0.61)**
	Negative Predictive Value	-	-	1.98 (1.11, 3.55)*
IRHF				
	Sensitivity	7.79 (0.83, 73.49)	p<0.001	P<0.01
	Specificity	4.64 (1.07, 20.01) p<0.05	1.51 (0.24, 9.62) p=ns	0.33 (0.09, 1.16) p=ns
	Positive Predictive Value	5.03 (1.59, 15.9)**	-	-
	Negative Predictive Value	6.24 (0.68, 57.37)	15.09 (2.43, 93.66)**	2.43 (1.26, 4.7)**
DCM				
	Sensitivity	3.46 (0.52, 23.02)	12.4 (1.98, 77.79)**	3.85 (0.7, 21.27)
	Specificity	12.39 (1.78, 86.06)*	2.91 (0.34, 24.82)	0.25 (0.08, 0.73)*
	Positive Predictive Value	16.43 (2.34, 115.56)**	8.54 (1.07, 68.4)*	0.88 (0.16, 4.79)
	Negative Predictive Value	2.46 (0.71, 8.52)	3.35 (1.32, 8.52)*	1.35 (0.78, 2.37)
Pericardial effusion				
	Sensitivity	p=ns	p=ns	p=ns
	Specificity	P<0.05	p=ns	P<0.05
	Positive Predictive Value	-	-	-
	Negative Predictive Value	3.1 (0.63, 15.37)	4.01 (0.73, 22.02)	1.29 (0.74, 2.25)
LVH				
	Sensitivity	1.0 (0.13, 7.57)	p=ns	p=ns
	Specificity	6.99 (1.45, 33.78)*	3.42 (1.11, 10.58)*	0.53 (0.15, 1.89)
	Positive Predictive Value	7.00[b] (1.04, 47.12)*	-	-
	Negative Predictive Value	1.07 (0.61, 1.88)	1.53 (1.05, 2.23)*	1.44 (0.98, 2.13)

[a]As described in the methods section, there are several cases for which the OR was not defined because the estimates were empirically 0% or 100%. For sensitivity and specificity, the p-value from McNemar's test is presented. For NPV and PPV, the "-" mean no value is available.

[b] the model was fit with independent correlation structure because the more complex model did not converge.

P<0.05, ** P<0.01, ***p<0.001, ns = not statistically significant (p>0.05).

FoCUS diagnosed more conditions than did PE which resulted in lower specificities for all conditions compared to PE. The specificities for FoCUS were significantly lower for RHD (OR 0.13 [95% CI 0.05, 0.3], p<0.001), DCM (OR 0.25 [95% CI 0.08, 0.73], p=0.011), and pericardial effusion (p=0.031) compared to PE. There was also a trend toward lower specificity for IRHF (OR 0.33 [95% CI 0.09, 1.2], p=0.084) and major LVH (OR 0.53 [95% CI0.15, 1.89], p=0.327).

Discussion

Common cardiac diseases encountered in SSA can be diagnosed with relative accuracy by RCOs trained in the use of FoCUS. In this prospective study, we demonstrated that these NPCs performing a FoCUS exam, improved their ability to diagnose RHD, LVH, DCM, IRHF and pericardial effusion with improved sensitivity and acceptable specificity beyond those of the PE alone. This was achieved after a short training period of 8 hours. The study also showed that traditional diagnostic skills of history and PE as practiced in this setting missed many cardiac diseases. This suggests a great opportunity to improve cardiac diagnostic capabilities with only a modest expenditure in training time and cost in a setting where the vast majority of patients lack access to specialist care.

Excellent overall improvement in sensitivity was noted by use of FoCUS compared to PE diagnosis. For instance, in diagnosis of RHD, a common condition in Kenya and the rest of SSA, the sensitivity improved from 38% to 73% by use of FoCUS compared to PE alone. Similarly, improvements in sensitivity were achieved for diagnosing IRHF and LVH. An unexpected finding was that specificity diminished by a modest amount when FoCUS was used in conjunction with PE especially for RHD. The decrease in specificity may have been due to the RCOs' short training period on FoCUS and a relative lack of experience on differentiating organic from functional valve disease on echocardiography. Results from a study in Uganda validating the use of hand-held echocardiography in screening for RHD in a paediatric population showed almost similar results, achieving a sensitivity of 90% but higher specificities of 92% (25). Our results also compare well with those from other studies examining other health personnel. Hellman *et al(26)* showed that internal medicine residents quickly acquired competence in assessment of pericardial effusion, LV size, LV function and mitral and aortic valve function after only 1 hour of training. Their results compared closely to those of SE and their rate of learning the skill was fast (26). In a similar study, an 8-hour focused training program allowed non-cardiologist ICU residents to efficiently perform FoCUS to identify gross cardiac changes and pleural effusions. The residents adequately identified the presence of LV systolic dysfunction, right ventricular dilatation, pericardial effusion and the single case of cardiac tamponade diagnosed in that study (27).

The results of the SE performed in Kenya corresponded well with the expert over-read in an accredited echocardiography laboratory. However, the relatively low sensitivity observed, specifically with DCM and pericardial effusion, calls for improvement in local capacity for expert echocardiography to ensure that the practical "gold standard" (SE in Kenya) does not miss important pathology. Building a model where the echocardiographer's report is confirmed by a cardiologist/physician as done in most academic echocardiography laboratories in High Income Countries (HICs) will significantly improve this diagnostic service. In Kenya, as representative for most LMICs where there is limited cardiovascular expertise locally available, this calls for training more cardiologists skilled in the provision of expert cardiovascular diagnostic services. Until 2014, there was one (paediatric) cardiologist serving the entire Western Kenya population. Due to recent efforts supported by grants the clinical, educational and research capacity is growing to meet population needs in Kenya and in other LMICs (28).

The findings of this study have the potential to task share specialized cardiac care between physicians/cardiologists and NPCs. The strategy of task shifting specialized care from physicians to less specialized health professionals has long been recognized as appropriate response to the management of other chronic diseases. The World Health Organization (WHO) recognizes that task shifting can rapidly expand the number of health service providers by offering better use of available human resources without compromising quality thereby strengthening the overall health systems (29-31). Such initiatives have worked well in the management of HIV/AIDs using the "Treat, Train, Retain" plan (32). In a review of the use of NPCs in SSA, Mallen *et al* (14) emphasizes the role of these types of health care cadres in provision of both general medical and specialized services.

One limitation of our study is that some of the patients studied had established cardiac diagnoses and were undergoing follow-up repeat echocardiograms which may have biased the RCOs towards making the known diagnosis. Secondly, our results may not be generalized to other healthcare workers who do not have a background in clinical medicine.

Conclusions

Use of FoCUS as compared to PE by RCOs improved the diagnosis of RHD, LVH, IRHF, DCM and pericardial effusion at a national referral hospital in western Kenya. A strategy of training and equipping RCOs with FoCUS may have the potential to improve cardiac care for the region.

Acknowledgements

The authors wish to thank NHLBI for funding this project and MTRH for allowing the study to be conducted with its

patients and employees. AKD was also funded in part by the Lifespan/Tufts/Brown Center for AIDS Research (NIH P30AI042853). We would like to acknowledge Ms. Seanna Horan for her assistance in manuscript preparation.

References

1. Nihoyannopoulos P. Why is a new journal dedicated to echocardiography required? *Echo Res Pract.* 2014; Sep **1**(1):1E1-E3.
2. Nihoyannopoulos P. Perspective, echocardiography in 2009: the future of clinical diagnosis. *Future Cardiology.* **6**(1):37-49. doi 10.2217/fca.09.60.
3. Via G, Hussain A, Wells M, *et al*. International evidence-based recommendations for focused cardiac ultrasound. *J Am Soc Echocardiogr.* 2014; **27**(7):683. e1-683.e33. doi: 10.1016/j.echo.2014.05.001.
4. Seward JB, Douglas PS, Erbel R, *et al*. Hand-carried cardiac ultrasound (HCU) device: recommendations regarding new technology. A report from the Echocardiography Task Force on New Technology of the Nomenclature and Standards Committee of the American Society of echocardiography. *J Am Soc Echocardiogr.* 2002; **15**(4):369-73.
5. Vignan P, Dugard A, Abraham J, *et al*. Focused training for goal-oriented hand-held echocardiography performed by non-cardiologist residents in the intensive care unit. *Intensive Care Med.* 2007; **33**(10):1795-9. Epub 2007 June 16.
6. Luo H, Chen M, Trento A, Miyamoto T, *et al*. Usefulness of hand-carried cardiac ultrasound device for bedside examination of pericardial effusion in patients after cardiac surgery. *Am J Cardiol.* 2004; **94**(3): 406-7.
7. Kimura BJ, Amundson SA, Willis CL, Gilpin EA, DeMaria AN. Usefulness of a hand-held ultrasound device for bedside examination of left ventricular function. *Am J Cardiol*. 2002; **90**(9):1038-9.
8. Senior R, Galasko G, McMurray JV, Mayet J. Screening for left ventricular dysfunction in the community: role of hand-held echocardiography and brain natriuretic peptides. *Heart.* 2003; **89** (Suppl 3):iii24-8.
9. Royce CF, Seah JL, Donelan L, Royce AG. Point of care ultrasound for basic hemodynamic assessment: novice compared to expert operator. *Anesthesia*. 2006; **61**(9):849-55.
10. Moran A, Forouzanfar M, Sampson U, Chugh S, Feigin V, Mensah G. Progress in cardiovascular diseases. 2013 Nov-Dec; **56**(3):234-9. doi: 10.1016/j.pcad.2013.09.019. Epub 2013 Sep 28.
11. Beaton A, Okello E, Lwabi P, Mondo C, McCarter R, Sable C. Echocardiography screening of rheumatic heart disease in Ugandan children. *Circulation*. 2012; **125**(25):3127-32. doi: 1161/CIRCULATIONAHA.112.092312. Epub 2012 May 24.
12. Carapetis JR, Paar J, Cherian T. Standardization of epidemiologic protocols for surveillance of post-streptococcal sequelae: acute rheumatic fever, rheumatic heart disease and acute poststreptococcalg lomerulonephritis. Department of Health and Human Services, National Institutes of Health (online) (2006).
13. Kwan GF, Bukhman AK, Miller AC, *et al*. A simplified echocardiographic strategy for heart failure diagnosis and management within an integrated noncommunicable disease clinic at district hospital level for sub-Saharan Africa. *JACC Heart Fail.* 2013; **1**(3):230-6. doi:1016/j.jchf.2013.03.006. Epub 2013 Jun 3.
14. Mullan F, Frehywot S. Non-physician clinicians in 47 sub-Saharan African countries. *Lancet*. 2007; **370**(9605):2158–63.
15. Laws of Kenya, Chapter 260, Clinical Officers (Training, Registration and Licensing) Act, Revised Edition 2012 [1990]. Published by the National Council for Law Reporting with the Authority of the Attorney-General. Available at www.kenyalaw.org.
16. Bloomfield GS, Barasa FA, Doll JA, Velazquez EJ. Heart failure in sub-Saharan Africa. *Curr Cardiol Rev* . 2013 ; **9**(2);157-73.
17. Oyoo GO, Ogola EN. Clinical and socio demographic aspects of congestive heart failure patients at Kenyatta National Hospital, Nairobi. *East Afr Med J.* 1999 ; **76**(1):23-27.
18. Ntusi NB, Mayosi BM. Epidemiology of heart failure in sub-Saharan Africa. *Expert Rev Cardiovasc Ther.* 2009; **7**(2):169-80. doi: 10.1586/14779072.7.2.169.
19. Opie LH, Mayosi BM. Cardiovascular disease in sub-Saharan Africa. *Circulation*. 2005; **112**(23):3536-40.
20. Damasceno A, Mayosi BM, Sani M, *et al*. The causes, treatment, and outcome of acute heart failure in 1006 Africans from 9 countries. *Arch Intern Med*. 2012 ; **172**(18)1386-94.
21. Moi Teaching and Referral Hospital Web Site, "About Us" section, http://www.mtrh.or.ke/index.php/about-us. Accessed 27 April 2015.
22. Remeny B, Wison N, Steer A, *et al*. World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart disease; evidence based guidelines. *Nature Reviews Cardiol.* 297-309 (May 2012). doi:10.1038/nrcardio.2012.7
23. Lang R, Bierg M, Devereux R, *et al*. Recommendations for chamber quantification: A report of the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with European Society of Echocardiography, a branch of ESC . *J Am Echocardiogr.* 2005; **18**(12)1440-63.
24. Gönen M. Sample size and power for McNemar's test with clustered data. *Stat Med.* 2004; **23**(14):2283-94.
25. Beaton A, Aliku T, Okello E, *et al*. The utility of handheld echocardiography for early diagnosis of rheumatic

heart disease. *J Am SocEchocardiogr.* 2014; **27**(1):42-9. doi: 10.1016/j.echo.2013.09.013. Epub 2013 Oct 30.
26. Hellman DB, Whilig-O'Keefe Q, Shapin EP, *et al*. The rate at which residents learn to use handheld echocardiogram at the bedside. *Am J Med*. 2005; **118**(9):1010-8.
27. Lemola K, Yamada E, Jagasia D, *et al*. A hand-carried personal ultrasound device for rapid evaluation of left ventricular function: use after limited echo training. *Echocardiography*. 2003; **20**(4):309-12.
28. Binanay CA, Akwanalo CO, Aruasa W, *et al.* Building sustainable capacity for cardiovascular care at a public hospital in Western Kenya. *J Amer Coll Cardiol*. 2015; **66**(22):2550-2560. doi:10.1016/j.jacc.2015.09.086.
29. World Health Organization. Taking stock: health worker shortages and the response to AIDS. WHO/HIV/2006.05. Geneva, World Health Organization (2006). Available at http:/www.who.int/hivtoronto2006/takingstockttr.pdf. Accessed 18 January 2014.
30. World Health Organization. The world health report 2006: working together for health. Geneva, World Health Organization (2006). Available at http://apps.who.int/iris/bitstream/10665/43432/1/9241563176_eng.pdf. Accessed 18 January 2014.
31. World Health Organization. Everybody's business: WHO's framework for action for strengthening health systems to improve health outcomes. Geneva, World Health Organization, 2007. Available at http:/www.Who.int/healthsystems/strategy/everybody_business.pdf. Accessed 18 January 2014.
32. World Health Organization. Treat, Train, Retain. The AIDS and health workforce plan. Report on the consultation on AIDS and human resources for health outcomes. Geneva, World Health Organization (2006). Available at http://apps.who.int/iris/bitstream/10665/43558/1/9241594713_eng.pdf. Accessed 18 January 2014.

Original paper

Prevalence of Hypertension and Prehypertension: Retrospective Review of Patients attending a Clinic in Nairobi, Kenya

Gikonyo D, Nguchu H, Nduiga D, Irungu S, Morara O, Weru B, Nyaga J, Luvayo D, Mudhune S, Ponoth P, Gikonyo A

The Karen Hospital, PO Box 74240−, Nairobi, Kenya

Address for correspondence: Dr. Anthony Gikonyo, Karen Hospital, Nairobi, Kenya. Email: anthony.gikonyo@karenhospital.org

Abstract

Background: Hypertension in Kenya is increasing in prevalence. This could be related to changes in dietary factors, lifestyle and obesity. This increase will eventually lead to an increase in cardiovascular mortality.

Objectives: To determine the prevalence of hypertension and prehypertension.

Method: A hospital based retrospective cross-sectional study of 1411 patients who presented to The Karen Hospital from 2008 to 2009.

Results: The results confirm an increase in the number of people with hypertension and a greater number of people at risk of hypertension.

Conclusion: Local data is required to improve surveillance, management and prevention of cardiovascular diseases.

Keywords: Hypertension, Pre-hypertension, Cardiovascular disease, Obesity, Africa

Introduction

At the beginning of this century, high blood pressure was virtually non-existent among the indigenous Kenyans (1). This was echoed as recently as 1972 in a commentary by Kahugu (2) where he discussed the rarity of hypertension. However, though considered rare, HC Trowel noted a progression from normotension to hypertension in Kenyans and Ugandans between 1928-1978, a precursor to the high prevalence we now encounter in our day to day practice.

By 1997 cardiovascular diseases in medical in-patients at Kenyatta National Hospital were common and especially so with hypertension which played an important role in the aetiology of congestive heart failure and cerebrovascular accidents (3). Hypertension was the leading observed risk factor for stroke (4). Common risk factors included hypertension (35%) for patients presenting with acute myocardial infarction from 2000 to 2009 at Kenyatta National Hospital (5) the prevalence of hypertension was high (65.4%) in patients with documented coronary artery disease group (6). Associated co-morbidities of patients with atrial fibrillation included hypertension (68%) (2). Hypertensive kidney disease carried a high morbidity of 22% (7). Majority of patients with diabetes had hypertension 60% (8) and approximately 50% of patients with diabetes were hypertensive (9).

Some of the changes in blood pressure associated with urbanization could be mediated by changes in dietary electrolytes (10). This is due to our high salt, cholesterol and sugar diet. In rural populations with a low salt intake, there was little or no upward slope of blood pressure with age; hypertension was present in only 5% of the sample population (11). Consumption of sodium salt, obesity, and physical inactivity play an important aetiologic role in the genesis of primary hypertension (12). These findings confirm previous reports that in populations with a low salt intake, there is little or no hypertension or rise of blood pressure with age (11). Systolic BP showed no significant rise with age until after 54 years in a rural community with low salt intake (10).

Hypertension prevalence was found to be 6.4%. There was no difference in the occurrence of hypertension between the urban and rural populations in Kitui district in a comparative study performed in 1991 (13). Hypertension showed no consistent socioeconomic pattern from evidence from three cross-sectional surveys in the Seychelles between 1989 and 2004 (14). It was the most frequently observed risk factor for cardiovascular disease in both urban and rural communities in sub Saharan Africa in a cross-sectional survey in 2009 to 2011 (12).

Age-adjusted prevalence of hypertension was measured at 32.6% from a survey in Old Town Mombasa published in 2011 (15). There was a high prevalence of hypertension, 50.1% from a population based survey in Nakuru between 2007 and 2008 (16).

Cardiovascular disease is the leading cause of adult mortality in low-income countries but data on the prevalence of cardiovascular risk factors such as hypertension are scarce, especially in sub-Saharan Africa. We expect our study to have an impact on the care of patients with prehypertension and hypertension by increasing awareness of prevalence, and associated risk factors in Kenya.

Materials and methods

A hospital based retrospective cross sectional survey that utilized consecutive clinical medical reports of patients at

The Karen Hospital outpatient clinic between January 2008 to December 2009. These patients presented for a wellness check up. The sample size was 1411 patient reports. Data was analyzed using SPSS. The patients were reviewed by a cardiologist.

Approval was granted by the Hospital Ethics Committee, the summarized medical reports were used and data inputted by research assistants. All the medical reports that satisfied the inclusion criteria were entered into the data base.

The study population was described by summarizing the categorical data into proportions and continuous data into means and medians. The prevalence of hypertension and prehypertension was presented as proportions. The student's T - test and the Mann-Whitney U test were used to compare the means and medians respectively. Chi-squared test was used to analyze the associations between the cardiovascular risk factors and other categorical factors. Odds ratio was used to show the likelihood of associations between variables. All statistical tests were performed at 5% level of significance and a 95% confidence interval was applied to the numerical variables that were normally distributed.

Results

One thousand four hundred and eleven patients participated in the study, of which 85.5% were above 65 years. Male participants were 56% while female where 44%. Majority of patients, 72% had BMI above 25. Only 13% had a family history of hypertension and 4% were currently smoking. Thirty three percent of patients were hypertensive and 38% were prehypertensive. The data showed that patients with hypertension took an average of 3 medications, majority 27% were using an angiotensin receptor blocker, 32% had blood pressure that was not controlled and 30% were hypertensive but not on medication (Table 1).

Table 1: Frequency and percentages of different blood pressure categories

	Frequency	(%)
Normal	347	24.59
Prehypertension	540	38.27
Stage 1 hypertension	302	21.40
Stage 2 hypertension	168	11.91
Missing data	54	3.83
Total	1411	100

Majority of the patients fall in the prehypertension category (38.27%) and the least are in Stage 2 hypertension (11.91%) (Figure 1).

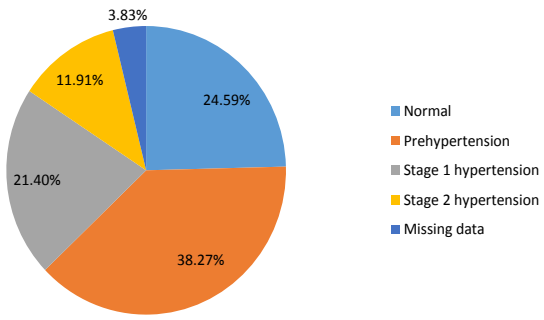


Figure 1: Representation of percentages of different blood pressure categories

A total of 1411 patient records were observed and the results are as follows:

Table 2: Risk factors related to cardiovascular disease

Variable	Percent	(n) Total = 1411
Age	>65 years 85.55% < 65 years 14.45%	1405
Gender	Male 56.14% Female 43.86%	1409
Height	Mean 166.35 (SD 11.30832)	1316
Weight	Mean 78.31843 (SD 24.05)	1336
Body Mass Index	Underweight 1.84% Normal 25.23% Overweight 39.42% Obesity 33.51%	1304
Heart rate	Mean 75.62069 SD (16.45)	1350
Smoker current	4.03%	1364
Smoker previous	8.94%	1376
Family history of hypertension	13.85%	1379
Family history of myocardial infarction	0.44%	1378
Left ventricular hypertrophy on ECG	28.88%	1354
Left ventricular hypertrophy on echocardiogram	23.67%	1352
Left ventricular ejection fraction on echo < 40 %	4.03%	1340
Systolic blood pressure, mmHg	Mean 132.67 SD (26.53)	1372
Diastolic blood pressure, mmHg	Mean 80.40 SD (16.51)	1372
Hypertension	Normal 25.57 % Prehypertension 39.79% Stage 1 hypertension 22.25% Stage 2 hypertension 12.38%	1357
Isolated systolic hypertension	10.61%	1357

One thousand four hundred and eleven patients participated in the study, of which 85.5% were above 65 years, while 14.5% were below age 65. Male participants were 56% while female where 44%. Of note 72% had BMI of above 25. (Over weight and obese). Thirteen percent had family history of hypertension, in 1st or 2nd degree relatives. 8.9% had history of smoking with only 4% currently smoking. So the top 5 risk factors identified include age above 65, excess body weight, male gender, family history and smoking based on the overall incidences.

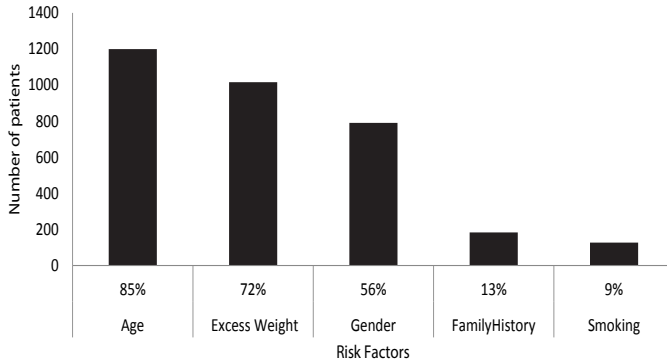


Figure 2: Number of patients versus risk factors

In light of other preexisting comorbidities, it was found that majority had dyslipidemia at 29.3%, with diabetes second at 13.9%. Atrial fibrillation was noted in 12% and hyperuricemia in 10.3% of the participants. The other cormobidities were less than 3% in the participants (thyroid disease, HIV, coronary artery disease, peripheral arterial disease and kidney disease).

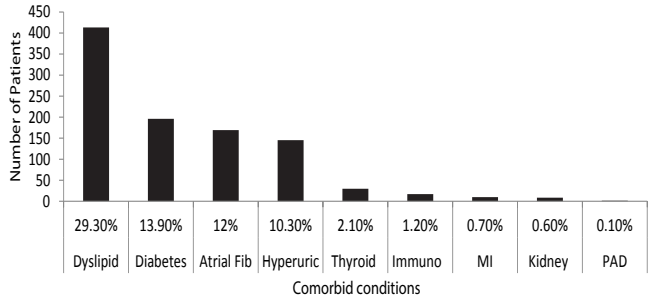


Figure 3: Number of patients versus comorbid conditions

Discussion

A significant percentage of the study population are obese or overweight (72%), and prehypertensive (38%). Blood pressure control for hypertensive patients was suboptimal (24.5%) and a concerning number of patients with hypertension were not on medication. Majority of patients had no family history of hypertension, signifying that we are at the beginning of hypertensive pandemic and identification of at risk populations and lifestyle interventions need to be targeted to them.

Conclusion

It is important to have local data to facilitate the adoption of appropriate actions including decision-making in prevention, surveillance and management. A larger prospective study is required to further evaluate the scale of prehypertension.

References

1. Lore W. Epidemiology of cardiovascular diseases in Africa with special reference to Kenya. *East Afr Med J.* 1993; **70**(6):357-361.
2. Kahugu W. Hypertension--rare or not in the African? Some interesting observations HYPERLINK. *Kenya Nurs J*. 1972; **1**(2):96-98.
3. Lodenyo HA, McLigeyo SO, Ogola EN. Cardiovascular disease in elderly in-patients at the Kenyatta National Hospital, Nairobi-Kenya. *East Afr Med J*. 1997; **74**(10):647-651.
4. Jowi JO, Mativo PM, Pathological sub-types, risk factors and outcome of stroke at the Nairobi Hospital, Kenya. *East Afr Med J*. 2008; **85**(12):572-581.
5. Ogeng'o JA, Olabu BO, Ong'era D, *et al*. Pattern of acute myocardial infarction in an African country. *Acta cardiologica.* 2010; **65**(6):613-618.
6. van de Vijver SJ, Oti SO, Agyemang C. Prevalence, awareness, treatment and control of hypertension among slum dwellers in Nairobi, Kenya. *J Hypertension*. 2013; **31**(5):1018-24.
7. Ogeng'o JA, Gatonga P, Olabu BO, *et al*. Pattern of hypertensive kidney disease in a black Kenyan population. *Cardiology*. 2011; **120**(3):125-129.
8. Nguchu HK, Joshi MD, Otieno CF. Acute coronary syndromes amongst type 2 diabetics with ischaemic electrocardiograms presenting to accident and emergency department of a Kenyan tertiary institution. *East Afr Med J*. 2009; **86**(10):463-468.
9. Otieno CF, Vaghela V, Mwendwa FW, *et al*. Cardiovascular risk factors in patients with type 2 diabetes mellitus in Kenya: levels of control attained at the an outpatient in Nairobi*. East Afr Med Jl*. 2005; **82**(12 Suppl):S184-190.
10. Poulter N, Khaw KT, Hopwood B.E, *et al*. Blood pressure and associated factors in a community. *Hypertension.* 1984; **6**(6 Pt 1):810-813.
11. Carvalho JJ, Baruzzi RG, Howard PF, *et al.* Blood pressure in four remote populations in the INTERSALT Study. *Hypertension.*1989; **14**(3):238-246.
12. Hendriks ME, Wit FW, Roos MT, *et al*. Hypertension in sub-Saharan Africa: cross-sectional surveys in four rural and urban communities. *PLoS One.* 2012; **7**(3):e32638
13. Peagyie F, Hypertension in Kitui district: a comparative study between urban and rural population. *East Afr Med J.* 1991; **68**(7):531-538.

14. Stringhini S, Viswanathan B, Gédéon J, *et al*. The social transition of risk factors for: Evidence from three cross-sectional surveys in the Seychelles. *Intern J Cardiol.* 2012; Nov 30
15. Jenson A, Omar AL, Omar MA, *et al*. Assessment of control in a district of Mombasa, Kenya. *Global Public Health.* 2011; **6**(3):293-306.
16. Mathenge W, Foster A, Kuper Urbanization, ethnicity and cardiovascular risk in a population in transition in Nakuru, : a population-based survey. *BMC Public Health.* 2010; **22**(10):569.
17. Pastakia SD, Ali SM, Kamano JH, *et al*. Screening for diabetes and in a rural low income setting in western utilizing home-based and community- based strategies. *Global Health.* 2013; **16**(9):21.
18. Mwita CC, Akello W, Sisenda G, *et al*. Assessment damage among adult patients with primary hypertension in Level 5 Hospital, Kenya: a criteria-based clinical audit. *Intern J Evidence-Based Healthcare*. 2013; **11**(2):115-120.
19. Ploubidis GB, Mathenge W, De Stavola B, *et al*. Socioeconomic position and later life prevalence of diabetes and visual impairment in Nakuru, Kenya. *Intern J Public Health.* 2013; **58**(1):133-141.

Original paper

Dysglycaemia among Kidney Transplant Recipients at a National Referral Hospital in Kenya

Faraj FA, Kayima J, Otieno CF, Were A, Ngare S

Department of Clinical Medicine and Therapeutics, College of Health Sciences, University of Nairobi, P.O. Box 19676 – 00202, Nairobi, Kenya

***Address for correspondence*:** Dr Faraj A. Amir. Email: docfaraj@gmail.com

Abstract

Background: Kidney transplantation is the best treatment for end stage kidney disease. Dysglycaemia makes Kidney Transplant Recipients (KTRs) more susceptible to fatal cardiovascular events.

Objective: The primary objective of our study was to determine the prevalence of dysglycaemia among KTRs at Kenyatta National Hospital (KNH) in Kenya and to describe the clinical characteristics of the KTRs with dysglycemia.

Design: A cross-sectional study

Setting: Transplant clinic at the renal unit of Kenyatta National Hospital.

Materials and methods: Selected KTRs were recruited and their weight, height and waist circumference were measured and blood samples in non-diabetic patients were taken for fasting blood sugar and Oral Glucose Tolerance Test (OGTT) to determine presence of dysglycemia.

Results: One hundred and five KTRs were recruited and found a prevalence of 13.3% for New Onset Diabetes after Transplantation (NODAT), 14.29% for impaired glucose tolerance (IFG) and 6.67% for Impaired Fasting Glucose (IGT). The prevalence of pre-transplant Diabetes Mellitus (DM) was 23.81%. Important risk factors noted at univariate analysis were female gender, longer duration post transplantation, BMI more that 25kg/m^2, higher waist hip ratios and family history of diabetes.

Conclusions*:* The study found a high prevalence of dysglycaemia in KTRs in our set up. This calls for improved screening programs on KTRs who previously were non-diabetic.

Key words*:* Dysglycaemia, Kidney Transplant Recipients (KTRs) and Oral Glucose Tolerance Test (OGTT)

Introduction

Dysglycaemic states encompass overt diabetes, Impaired Fasting Glucose (IFG) and abnormal glucose tolerance. There is variability in the natural history of IFG and Oral Glucose Tolerance (OGT) but approximately 25% develop diabetes in three to five years (1). Kidney transplantation has been proven to improve the health related quality of life and also reduces cardiovascular disease effect by removing the kidney failure adverse effects (2) but also on the other hand there is an increased risk of cardiovascular events in the group of patients with dysglycaemia as compared with other kidney transplant recipients (3).

Diabetes mellitus is an important risk after renal transplantation and it has been implicated to be a cause of increased mortality due to cardiovascular events (4), deleterious effects on allograft survival (5) and high incidence of infection rates (6). Several factors have been associated with the impairment of glucose metabolism, for example, the use of certain immunosuppressive medications such as glucocorticoids and Calcinuerin Inhibitors (CNI).

Early dysglycemia, that is, period of hospitalization post- transplant is common. This should always be taken seriously as majority of this patients are at risk of developing New Onset Diabetes After Transplantation (NODAT) such that day 7 FBS may be predictive at year one (7). A study which was done recently (8) measured continuous capillary blood sugar levels for the first 4 days post-transplant in 43 patients. There was an increased level of hyperglycaemia and 43% of patients spent more than 12 hours per day with blood sugar levels above 7.7mmol/l. After a mean follow up of 72 months, NODAT was frequently seen. Moreover, a normal OGTT within the first week has been shown to have a high negative predictive value of 97.6% for future development of NODAT (9). Early hyperglycaemia does not necessary predict future permanent dysglycaemic states.

Studies done by the World Health Organisation/American Diabetes association, (WHO/ADA) diagnostic criteria suggest that up to one third of non-diabetic KTRs develop persistent dysglycaemia by six month post transplantation. In a study done by Valderhaug et al (10) they found the incidence of NODAT to be 14-17%. This was by using OGTT at 10 weeks. A retrospective South African study on 221 KTRs showed an incidence of 22.6% of NODAT (11).

Post transplantation data showing the status in terms of burden of dysglycaemia in KTRs and the quality of glycemic

control in diabetic KTRs at KNH is unavailable. Data generated from this study will sensitize the clinicians on the magnitude of the disease thereby improving strategies for early detection and treatment thereafter prevention of complications.

The main aim of our study was to determine the prevalence of dysglycaemic states among KTRs at KNH (National referral facility in Kenya). The secondary objective was to describe clinical characteristics of KTRs with dysglycaemia.

Materials and methods

The study design was hospital based descriptive cross-sectional study. The Kenyatta National Hospital, the largest referral facility in East and Central Africa situated in Nairobi City County in Kenya. It has various specialist units, renal unit being one of them. Kidney transplantation started many years ago in Kenya (1980).

This clinic is attended by consultant physicians/ nephrologists, fellows in nephrology program, residents in internal medicine and the transplant coordinator nurse. The study subjects were all post KTRs, aged eighteen years and above, who attended the kidney transplant follow up clinic at KNH and consented to participate. We excluded all those transplanted and had come for dialysis (failed graft). Using the Daniel's formula for finite population, the minimal sample needed was calculated to 103 patients and we used consecutive sampling method.

The data collections process involved administration of a study structured questionnaire to obtain social, demographic details and medical history. The Principal investigator (PI) later undertook the clinical assessment using standard procedures (that is, height weight, waist and hip circumferences to compute body mass indices, and waist hip ratios). Fasting blood sugars and oral glucose tolerance testing were done to patients not known to have diabetes.

The dependent variables were the dysglycaemic states, that is, presence of diabetes mellitus {(pre transplant and post transplantation), Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT)}. The independent variables were age, gender, obesity, waist circumference, WHR, cigarette smoking, family history of DM, inactivity and current immunosuppressive therapy.

Pre transplantation diabetes was defined as presence of documentation in patient's file of diabetes which started before transplantation or being on hypoglycaemic agents before transplantation.

New Onset Diabetes after Transplantation (NODAT) was defined as of presence documentation in patient's file of diabetes which started after transplantation or started hypoglycaemic agents after transplantation, FBS greater than 7.0mmol/l or 2 hour blood sugar more than 11.1mmol.l, during OGTT. Impaired Fasting Glucose (IFG) was defined as fasting blood sugar between 5.6 and 6.9mmol/l while IGT was defined as 2 hour blood glucose between 7.8 and 11.0mmol/l during an OGTT.

Questionnaires were coded, entered and managed in Microsoft Access 2013 database. Statistical analysis was done using SPSS version 21.0. The study population was described using their socio-demographic and clinical characteristics. Analysis involving descriptive statistics such as mean, median and standard deviation were used for continuous data and frequency distribution for categorical with their corresponding 95% confidence intervals. T test method was used for comparison for continuous data and chi-square test for categorical data. The level of statistical significance was $P \leq 0.05$.

This study was carried out after a written approval had been issued by the Department of Clinical Medicine and Therapeutics, University of Nairobi (UON), and KNH/UON Ethics and review committee based at KNH.

Results

***Participants*:** The data collection commenced in the month of September 2016 and ended in May 2017. One hundred and seven patients were interviewed at the KNH transplant renal clinic thereafter two were excluded. One of whom had a failed graft and haemodialysis had been started and the other one was 17 years old, one year younger of the inclusion age. Therefore, 105 KTRs were recruited fulfilling the target minimum sample of 103.

The mean age of the participants was 45 ± 12.4 years with youngest and oldest being 19 and 69 years old respectively. Males made up to two thirds of the study participants making 64.8%. Three commonest causes of ESRD were chronic glomerulonephritis (56%), diabetes mellitus (25%) and hypertension (15%). Majority of the patients also had hypertension irrespective of their primary cause of ESRD (68.6%). All patients recruited had undergone dialysis before transplantation with a minimum period of half a month to a maximum of 96 months (8 years) and median duration of 12 months. The maximum graft age was 25 years and a minimum of one month. Mean and median duration post transplantation were 35 months and 29 months respectively. All the patients were on prednisone as part of their immunosuppressive drugs and 72% were using tacrolimus the rest were on cyclosporine or neither. Mycophenolate usage was more at 90.5 % than of azathioprine (7.6%). Only 28% were engaging in manual activities or exercise and 35.2% reported to be trying to adhere to nutritional advice. All grafts were from live donors and 67% of donors were male. The rest of clinical characteristics are shown in Table 1.

Prevalence of dysglycaemia: Among the study participants, 23.81% had diabetes before transplantation, 41.9% of the participants were normoglycaemic and almost one third had a form of dysglycaemia post-transplant, that is, 13.33% had New Onset Diabetes after Transplantation (NODAT), 14.29% had impaired glucose tolerance (IGT) and 6.67% had Impaired Fasting Glucose *(IFG).*

Table 1: Clinical characteristic of all study participants

Study variable	Total study participant n=105
Cause of ESRD	No. (%)
HTN	15 (14.3)
DM	25 (23.8)
CGN[1]	56 (53.3)
PKD[2]	3 (2.9)
Others[3]	6 (5.7)
Dialysis period months: Median (IQR)	12 (8-24)
Duration after transplant months: Median (IQR)	29 (10-51.5)
Graft source: Living no. (%)	105 (100)
Previous graft: None no. (%)	104 (99)
Donor sex: Male no. (%)	67 (63.8)
BMI Mean SD[4]	24.6±4.13
min/max	(15.5/39.5)
BMI categories	No. (%)
Underweight	4 (3.8)
Normal	56 (53.3)
Overweight	35 (33.3)
Obese	10 (9.5)
WHR Mean SD,	0.901±0.07,
min/max[5]	0.78/1.05
Higher WHR[6] no. (%)	46 (43.8)
Family H/O DM no. (%)	34 (32.4)

1.CGN chronic glomerulonephritis, 2. PKD Polycyctic kidney disease,3. Others: SLE, severe malaria, eclampsia, chronic NSAID use, unknown and 4.SD: Standard deviation, 5.min: minimum, max: maximum. 6.Higher WHR= Female >0.85, male> 0.9

Table 2: Dysglycaemia (Pre-DM) and NODAT and some risk factors

Risk factor	Pre-DM		NODAT	
	Odds ratios	P value	Odds ratios	P value
Age >45 years	1.59(0.56-4.46)	0.380	1.59(0.47-5.33)	0.454
Female Sex	5.25(1.74-15.85)	0.003	7.8(1.92-31.68)	0.437
Duration post-transplant (years) >1year	1.38(0.45-4.25	0.576	1.90(0.46-7.85)	0.375
Family history of DM	2.29(0.59-8.98)	0.230	7.80(1.92-31.68)	0.002
Tacrolimus usage	0.73(0.25-2.17)	0.545	2.51(0.49-12.86)	0.256
Cyclosporine usage	1.0(0.33-3.00)	1.0	0.36(0.70-1.82)	0.201
BMI >25kg/m^2	11.22(3.30-38.11)	0.0001	3.85(1.04-114.1)	0.042
WHR (>0.85 female, >0.90 male)	5.25(1.74-15.85)	0.003	2.25(0.64-7.93)	0.201
Exercise status(less active)	19.28(1.09-341.54)	0.044	0.56(0.16-1.93)	0.359
Dietary advice non adherence	0.69(0.24-1.94)	0.476	0.97(0.28-3.41)	0.965

(NODAT), 14.29% had impaired glucose tolerance (IGT) and 6.67% had Impaired Fasting Glucose

Table 3: Clinical characteristics of the participants with dysglycaemia

Study variable	Dysglycaemia Post-transplant		
	NODAT N=14	IFG N= 7 IGT N=15	
Age mean SD min/max	46±12.7 (30/67)	44.6±13 (31/60)	44±14 (21/60)
Sex Male no. (%)	9(64.3)	2(28.6)	6(40)
Cause of ESRD no.(%)			
HTN	3 (21.4)	2 (28.6)	3 (20)
DM	-	-	-
CGN	10 (71.4)	2 (28.6)	11 (73.3)
PKD	0 (0)	1 (14,3)	1 (6.7)
Others	1 (7.1)	2 (28.6)	0 (0)
Dialysis period months: Median (IQR)	11.5 (8-24)	7 (7-26)	12 (7-26)
Duration after transplant : months: Median (IQR)	17 (12.25-33.75)	10 (1-46)	53 (28-62)
Graft source: Living no. (%)	14 (100)	7 (100)	15 (100)
Previous graft: None no. (%)	13 (92.9)	7 (100)	15 (100)
Donor sex: Male no. (%)	8 (57.1)	5 (71.4)	8 (53.3)
BMI Mean SD min/max	24.6±4.8 (16.6/33)	27±2.5 (23/28.9)	27.4±4 (21/34)
BMI categories no. (%)			
Underweight	1 (7.1)	0 (0)	0 (0)
Normal	6 (42.9)	2 (28.6)	3 (20)
Overweight	5 (35.7)	5 (71.4)	8 (53.3)
Obese	2 (14.3)	0 (0)	4 (26.7)
WHR Mean SD, min/max	0.903±0.086 0.78/1.06	0.887±0.011 0.88/0.91	0.893±0.075 0.8/1.06
Higher WHR no. (%)	6 (42.9)	5 (71.4)	9 (60)
Family H/O DM no. (%)	7 (50)	2 (28.6)	3 (20)
Immunosuppressant no. (%)			
Prednisone	14 (100)	7 (100)	15 (100)
Cyclosporin	2 (14.3)	0 (0)	7 (46.7)
Tacrolimus	12 (85.7)	7 (100)	7 (46.7)
Mycophenolate	12 (85.7)	7 (100)	14 (93.3)
Azathioprine	2 (14.3)	0 (0)	0 (0)
Lifestyle no. (%)			
Smoking (Ex-smokers)	3 (21.4)	0 (0)	2 (13.3)
Alcohol (Previous)	1 (2.8)	0 (0)	2 (5.6)
Exercise/manual activity	6 (16.7)	0 (0)	0 (0)
Diet advice adherence	5 (35.7)	7 (100)	3 (20)

The mean ages were comparable (44-46) but the sexes were different with predominantly male in the NODAT group (64%) and female sex was commoner in the IFG and IGT category 71.4% and 60% respectively. One patient in both NODAT and IFT had SLE, and one in IFG had eclampsia as the cause of ESRD. Apart from the IFG group who had a lower median duration of dialysis, there were no much differences in the median duration of dialysis before transplantation across the dysglycaemic group and comparing with the total. Majority of the participants had at least undergone dialysis for 1 year. All participants had received grafts from live donors and predominantly of male gender. All of them were on prednisone while tacrolimus and mycophenolate were main drugs in other categories of immunosuppressive regimen. Half of the patients who had NODAT had at least a close family member with DM while only 28.6% and 20% in participants were found to have IFG and IGT respectively. Participants found to have NODAT and IGT had poor adherence to dietary advice (Table 3).

When combining the pre-DM status, that is, IFG and IGT, the odds ratios of risks factors were increased, especially female sex, BMI above normal and increased WHR and they were statistically significant (Table 2) but there was none which was independently significant on multivariate analysis. The odds ratio for ages more than 45 years, duration post transplantation and family history of DM were higher but they were not statistically significant. The risk factors for NODAT which were statistically significant were family history of DM and increased BMI of more than 25Kg/M^2. Table 2 illustrates other risk factors with odds ratio and p value.

Discussion

Our study was set to determine primarily the prevalence of NODAT, IFG, IGT and also pre-transplantation DM. We found that a third of the KTRs had a form of new onset dysglycemia and when including the pre-transplant DM status (which was found to be as the second commonest cause of ESRD following CGN) a total of 58.10% was witnessed. We got a prevalence of 13.3% for NODAT with a median duration post-transplant of 29 months and a mean age of 45±12.4. Bapoo *et al* (11) in South Africa got an incidence of 17% at 36 months for NODAT only with a mean time post-transplant and age of 18 months and 41 years respectively. It is fairly comparable and the slight difference could be attributed by different population and may be the bigger sample size with the South African study (n=221) while ours was n=105. Cosio *et al* (12) at Mayo Clinic and foundation, USA found an incidence of 10% at 3 years and 13% at 5 years. Porrini *et al* (13) in Spain study on NODAT and prediabetes states using OGTT found a prevalence of 33% of prediabetes with IGT being the abnormality most frequently observed (25% at 1 year) and 20% of the participants had NODAT at 1 year. The study found a prevalence of 14.29% for IGT and 6.67% for IFG. The difference in prevalence could be due to other risks which weren't factored in. These include race, infection such as hepatitis C virus, human leucocyte antigen mismatching or deceased donors.

Several factors have been studied and showed causative effect for dysglycemia. Immunosuppressive therapies are mainly implicated. Steroids and more so prolong exposure and intermittent pulsing due to episodes of acute rejections with high doses predispose the KTRs to diabetes mellitus. Combining it with tacrolimus which is a CNI with more diabetogenic effect than cyclosporine (14) it augments the risks of getting dysglycemias. The study done by Porrini *et al* (13) was a multicenter, prospective study (n=154) and all patients studied were on tacrolimus based immunosuppressive regimen with mycophenolate and low dose steroids. This is also the case in our setup as majority of the participants were on tacrolimus (72.4%) and all were on prednisone. This is due to the effects on insulin resistance and suppression of insulin secretion (β cell toxic effects) by the steroids and tacrolimus respectively. We did not find any significant associations with any immunosuppressive drug but this was beyond the scope of our study. SAILOR study group, an in progress multicenter study evaluating whether a steroid free immunosuppressive protocol based on ATG induction and low tacrolimus dose will reduce the incidence of NODAT may give us a clear guidance once it is completed (15).

Increasing age, higher BMI, dyslipidemia (13), duration post transplantation (9) and family history of DM (17) are other risks which have been shown to be independently associated with increased dysglycaemia (16). Some of these were evident in our study as the duration post transplantation; higher BMI, higher WHR and family history of DM related to the dysglycemic status were statistically significant at univariate analysis. There were no independent associations at multivariate analysis. Cosio *et al* (16) found up to 2.2 times higher risks of developing NODAT in KTRs older than 45 years compared with younger population. Despite that, we did not find any significant association though our mean age of the participants was 45±12.4. Our study design wasn't powered to show any associations/causative effects. Improved quality of life and appetite after transplantation make the KTRs gain weight and because they do minimal manual activities due to fear of the post operational pain and graft failure they tend to become obese and this keeps them at a higher risk of getting dysglycaemia (18). We found a population which was less active (only 28.6%), and had poor adherence to dietician advice (35.2%). This imposes a bigger problem than imagined. Family history was significantly associated with NODAT (p =0.002) in our study at univariate analysis and a study done by Hjelmesaeth *et al (*17) found a similar association. Our limitation was the design of the study, that is, cross sectional and it may not bring out causal effect in an on-going disease process.

Conclusion

This study showed a high prevalence of dysglycaemia post kidney transplantation in our setup and this implicates a significant danger to the KTRs in terms of developing cardiovascular events. This calls for improved screening protocols for all recipients for these conditions to enable early detection and institution of appropriate measures to prevent progression of pre-diabetic states to overt diabetes. The prevalent risk factors found in our study merit further exploration in longitudinal studies to determine correlations with risks of getting dysglycaemia among KTRs.

References

1. Nathan DM, Davidson MB, DeFronzo RA, Heine RJ, Henry RR, Pratley R, *et al*. Impaired fasting glucose and impaired glucose tolerance: implications for care. *Diabetes Care*. 2007; **30**(3):753–759.
2. Meier-Kriesche H-U, Schold JD, Srinivas TR, Reed A, Kaplan B. Kidney transplantation halts cardiovascular disease progression in patients with end-stage renal disease. *Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg.* 2004; **4**(10):1662–8.
3. Lindholm A, Albrechtsen D, Frödin L, *et al*. Ischemic heart disease--major cause of death and graft loss after renal transplantation in Scandinavia. *Transplantation*. 1995; **60**:451.
4. Boudreaux JP, McHugh L, Canafax DM, *et al.* The impact of cyclosporine and combination immunosuppression on the incidence of posttransplant diabetes in renal allograft recipients. *Transplantation.* 1987; **44**:376.
5. Cole EH, Johnston O, Rose CL, Gill JS. Impact of acute rejection and new-onset diabetes on long-term transplant graft and patient survival. *Clin J Am Soc Nephrol.* 2008; **3**:814.
6. Miles AM, Sumrani N, Horowitz R, *et al*. Diabetes mellitus after renal transplantation: as deleterious as non-transplant-associated diabetes? *Transplantation*. 1998; **65**:380.
7. Joss N, Staatz CE, Thomson AH, Jardine AG. Predictors of new onset diabetes after renal transplantation. *Clin Transplant*. 2007; **21**(1):136–43.
8. Wojtusciszyn A, Mourad G, Bringer J, Renard E. Continuous glucose monitoring after kidney transplantation in non-diabetic patients: early hyperglycaemia is frequent and may herald post-transplantation diabetes mellitus and graft failure. *Diabetes Metab*. 2013; **39**(5):404–410.
9. Kuypers DRJ, Claes K, Bammens B, Evenepoel P, Vanrenterghem Y. Early clinical assessment of glucose metabolism in renal allograft recipients: diagnosis and prediction of post-transplant diabetes mellitus (PTDM). *Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc*. 2008; **23**(6):2033–42.
10. Valderhaug TG, Jenssen T, Hartmann A, Midtvedt K, Holdaas H, Reisaeter AV, *et al*. Fasting plasma glucose and glycosylated hemoglobin in the screening for diabetes mellitus after renal transplantation. *Transplantation*. 2009; **88**(3):429–434.
11. Bapoo NA, Nel JD. New onset diabetes after transplantation in renal transplant recipients at Tygerberg Hospital. *Afr J Nephrology*. 2014; **17**(1).
12. Cosio FG, Pesavento TE, Kim S, Osei K, Henry M, Ferguson RM. Patient survival after renal transplantation: IV. Impact of post-transplant diabetes. *Kidney Int*. 2002; **62**(4):1440–6.
13. Porrini E, Moreno JM, Osuna A, *et al*. Prediabetes in patients receiving tacrolimus in the first year after kidney transplantation: a prospective and multicenter study. *Transplantation*. 2008; **85**:1133.
14. Heisel O, Heisel R, Balshaw R, Keown P. New onset diabetes mellitus in patients receiving calcineurin inhibitors: a systematic review and meta-analysis. *Am J Transplant*. 2004; **4**:583.
15. Ekberg J, Ekberg H, Jespersen B, Källen R, Skov K, Olausson M, *et al*. An in-progress, open-label, multi-centre study (SAILOR) evaluating whether a steroid-free immunosuppressive protocol, based on ATG induction and a low tacrolimus dose, reduces the incidence of new onset diabetes after transplantation. *Transplant Res*. 2014; **13**(3):12.
16. Cosio FG, Pesavento TE, Osei K, Henry ML, Ferguson RM. Post-transplant diabetes mellitus: increasing incidence in renal allograft recipients transplanted in recent years. *Kidney Int.* 2001; **59**(2):732–737.
17. Hjelmesaeth J, Hartmann A, Kofstad J, Stenstrøm J, Leivestad T, Egeland T, *et al*. Glucose intolerance after renal transplantation depends upon prednisolone dose and recipient age. *Transplantation*. 1997; **64**(7): 979–983.
18. Kasiske BL, Snyder JJ, Gilbertson D, Matas AJ. Diabetes mellitus after kidney transplantation in the United States. *Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg*. 2003; **3**(2):178–185.

Original paper

Prevalence, Severity and Short Term Outcomes of Patients with Community Acquired Acute Kidney Injury in The General Medical Wards at Kenyatta National Hospital

Taiyebali MM, Kayima J, Were AJO, Ogutu E

Department of Clinical Medicine and Therapeutics, College of Health Sciences, University of Nairobi, P.O. Box 19676 – 00202, Nairobi, Kenya

Address for correspondence: Dr MM Taiyebali. Email: mohmd.dr2011@gmail.com

Abstract

Objective: To determine the prevalence, severity and 2 week outcomes of patients with community acquired Acute Kidney Injury (AKI).
Design: Cross-sectional study.
Setting: The general medical wards at Kenyatta National Hospital, Nairobi County, Kenya.
Subjects: A randomly selected sample of 136 patients aged 13 years and above.
Results: A total of 136 patients were enrolled during the 3 month study period. We found a period prevalence of 8.1% at admission. Most of the patients had stage 1 AKI (51.5%) while the rest had stage 2 and stage 3 AKI (48.6%). Only 2 patients underwent RRT. The median Length of Hospital Stay (LOHS) was 9 days in stage 1 disease, 11 days in stage 2 and 10 days in stage 3 disease. There was no association between severity and LOHS. Sixty percent had non-recovery while 21 patients (18.6%) recovered fully and severity was associated with non- recovery (p- value=0.045). The in-hospital all- cause mortality was 16.9%. The severity of AKI was associated with mortality (p-value= 0.012). The commonest risk factors were sepsis (50.5%), nephrotoxic medications (45.6%) and gastrointestinal losses (42.6%).
Conclusion: AKI is common in our environment. Similar findings have been noted in developed countries. Most of our patients are younger than those seen in developed countries. Mortality in patients with AKI is high. The severity of AKI was associated with non- recovery, mortality and need of renal replacement therapy with no association in the length of hospital stay.

Introduction

Acute Kidney Injury (AKI) is a widespread problem of epidemic status and the new consensus term for acute renal failure. It is a clinical syndrome characterized by a rapid (hours to days) decrease in renal excretory function (1). The replacement of the term acute renal failure to acute kidney injury is to emphasize that a continuum of kidney injury exists that begins long before sufficient loss of excretory kidney function can be measured with standard laboratory tests. It also suggests a continuum of prognosis, whereby even small rises in serum creatinine leads to increasing mortality, and a further increase in mortality as the serum creatinine continues rising (2).

If left untreated, the condition has a high risk of multiple organ failure and, potentially, death. The increasing prevalence of AKI in developing and developed countries is strongly associated with increased early and long term patient morbidity and mortality, as well as the subsequent development of Chronic Kidney Disease (CKD) and accelerated progression to end-stage renal disease and those who remain on renal replacement therapy, often have reduced quality of life and consume substantially greater health-care resources than the general population as a result of longer hospitalizations, unplanned intensive care unit admissions and re-hospitalizations (3).

The aetiology of AKI in tropics is different from that seen in other countries. Trauma, surgery and sepsis contribute to a majority of the cases in developed countries. In the developing countries, especially in rural areas or smaller cities in the countryside, AKI is usually a community-acquired disease, affecting younger and previously healthy individuals (4).

In Africa, CAAKI is a challenging problem because of the disease burden especially HIV related AKI, malaria, nephrotoxins mainly from herbal remedies and diarrhoeal diseases, late presentation of patients to health facilities, lack of resources to support such kind of patients and paucity of data on the epidemiology (5).

The aim of this study was to determine the prevalence, severity, outcomes and risk factors of community-acquired AKI (com-AKI) in general medical wards at a tertiary hospital in Kenya, a country in sub-Sahara Africa.

Materials and methods

This was a cross sectional study involving 136 patients (68 males and 68 females) aged 13 years and above from the general medical wards at Kenyatta National Hospital,

Nairobi County. It was carried out between August and November 2016. Random sampling was done to determine prevalence, severity and outcomes of patients with community acquired acute kidney injury.

AKI was defined and categorized into three stages based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria as follows:

Stage 1 – Serum creatinine 1.5 – 1.9 times baseline or ≥ 26.5µmol/l increase OR urine output < 0.5ml/kg/hr for 6 – 12 hours.

Stage 2 – Serum creatinine 2 – 2.9 times baseline OR urine output < 0.5ml/kg/hr for 12 hours.

Stage 3 – Serum creatinine 3.0 times baseline or increase in serum creatinine to ≥ 353.6µmol/l OR initiation of dialysis OR urine output < 0.3ml/kg/hr for >24 hours OR anuria for >12 hours.

All the subjects with a diagnosis or suspicion of AKI admitted into the medical ward of Kenyatta National Hospital were included in the study. Oral and/or written informed consent were obtained from all the participants in the study. Using a structured pretested data sheet, we collected demographic information including age and gender. Clinical data included date of admission, date of discharge, medications including herbal use and radio contrast used in the prior one week of admission, primary diagnosis and treatment administered including haemodialysis.

For all patients, data on laboratory tests on admission included serum renal function tests, calcium and phosphate levels, a full blood count and urinalysis. A renal ultrasound was also done on admission to exclude chronic kidney disease. For patients whose baseline creatinine were unknown we used MDRD formula for estimation assuming a GFR of 75ml/min per 1.73m^2. Subsequently, the patient was reviewed after every 72 hours with serum creatinine to establish the modalities of management applied, the degree of renal dysfunction reached as well as outcome. The duration during which the subjects were in hospital was determined and subject's outcome assessed at 2 weeks of recruitment or at discharge or death.

Standard operating procedures for specimen collection and transport were followed with timely delivery to the laboratory to minimize pre-analytical errors. The blood and urine specimen were taken to the renal laboratory. This laboratory undergoes both internal and external quality control measures.

Data was analyzed using SPSS software version 21 for windows. Point prevalence of AKI was calculated as the percentage number of patients admitted with AKI out of all the admissions in the period of the study. Severity, risk factors, treatment modalities and outcomes of AKI was analyzed and presented using percentages with 95% confidence intervals. Outcomes were associated with severity of AKI using chi square test of associations. Statistical tests was performed at 5% level of significance. The study was approved by the Ethics and Research Committee of the Kenyatta National Hospital and University of Nairobi.

Results

A total of 1687 patients were admitted during the study period. Of these, 175 patients were screened for the presence of AKI. We excluded thirty nine patients who did not meet the study criteria leaving us with 136 (8.1%) patients with AKI. There was equal distribution between males and females. The mean age was 44.7 years. Most patients were in the 30 – 39 years age group and over 70% of the patients were under 60 years of age. Patients from rural areas predominated at 63.2%. Most of the patients had stage 1 AKI (51.5%) and the rest had stage 2 and stage 3 AKI (48.6%). Table 1 depicts the severity of AKI at presentation.

Table 1: Severity of AKI

Variable	Frequency (%)	95% CI
Severity of AKI		
Stage 1	70 (51.5)	43.4-59.6
Stage 2	33 (24.3)	17.6-31.6
Stage 3	33 (24.3)	17.6-31.6

2 week outcome in form of need of RRT, LOHS, degree of and time to renal recovery and death

a) *Need of RRT:* Fourteen patients had either one or multiple indications for renal replacement therapy. From those fourteen patients, ten patients had stage 3 AKI, three patients had stage 2 AKI and one had stage 1 AKI. Only 2 patients (14%) from our study population underwent haemodialysis and both the patients were in stage 3 disease with uremic encephalopathy. The most common indications for dialysis in our study were pronounced azotemia and uremic complications. The indications which warranted RRT are summarized in Table 2.

Table 2: Indications of RRT

Indications	No. of patients
Hyperkalemia	3
Severe metabolic acidosis	1
Volume overload	2
Pronounced azotemia	4
Uremic complications	4

b) *Length of hospital stay:* The median length of hospital stay was 9 days in patients with stage 1 AKI, 11 days with stage 2 AKI and 10 days with stage 3 and thus the severity did not affect the LOHS.

Table 3: Length of hospital stay

Variable	Severity of AKI			P value
	Stage 1	Stage 2	Stage 3	
Length of hospital stay, median (IQR)	9.0 (7.0-11.0)	11.0(8.0-14.0)	10.0 (9.0-14.0)	0.233

c) *Degree of renal recovery:* At 2 weeks, 60% had not recovered from AKI while 21 patients (18.6%) and there was an association with severity of AKI and non- recovery with a p value of 0.045 (Table 4).

Table 4: Degree of renal recovery

Variable	Frequency (%)
Degree of recovery	
None	60 (53.1)
Partial	32 (28.3)
Full	21 (18.6)

Table 5: Degree of renal recovery and severity of AKI

Variable	Stage 1	Stage 2/3	P value
Degree of recovery: No. (%)			
None	40(63.5)	20(40.0)	0.045
Partial	14 (22.2)	18 (36.0)	
Full	9 (14.3)	12 (24.0)	

d) *Death:* The in-hospital all- cause mortality during the study period was 23 patients (16.9%)

Table 6: In- hospital all-cause mortality

Variable	Frequency (%)
In-hospital all-cause mortality dead	23 (16.9)
Discharged or alive in 2 weeks	113 (83.1)

The more severe the AKI, the higher chances of mortality. There were 11 patients (33.3%) with severe AKI who died and that was statistically significant (p value of 0.012). Most of the patients who were given a discharge had stage 1 AKI.

Table 7: Mortality and severity of AKI

Variable	Severity of AKI			P value
	Stage 1	Stage 2	Stage 3	
In-hospital mortality: n (%)	7 (10.0)	5 (15.2)	11(33.3)	0.012
Dead discharged/ alive in 2 weeks	63 (90.0)	28 (84.8)	22 (66.7)	

AKI risk factors: The primary causes and other risk factors are outlined in Tables 8 and 9. The three most common risk factors for CA-AKI were sepsis at 50.5% followed by nephrotoxic medication use at 45.6%, and lastly gastrointestinal losses at 42.6%.

Table 8: AKI causes

Pre-renal factors	Frequency No. (%)
Gastro-intestinal losses	58 (42.6)
Significant bleeding	9 (6.6)
Left heart failure	20 (14.7)
Sepsis	70 (50.5)
Skin losses	0 (0)
3rd space losses	2 (1.5)
Renal factors	
Tubular	18 (13.2)
Acute glomerulonephritis	5 (3.6%)
Interstitial	1 (0.7)
Vascular	0
Obstructive factors	
Benign prostatic enlargement	9 (6.6%)
Metastatic cervical cancer	1 (0.07%)
Renal stones	1 (0.07%)

Table 9: Intrinsic AKI risk factors

Drugs used before admission	
Number of patients on medications	62 (45.6)
Aminoglycosides	8 (5.9)
NSAIDS	14 (10.3)
ACE-1	19 (14.0)
ARVs	25 (18.4)
Sulfonamides	23 (16.9)
Diuretics	19 (14.0)
Amphotericin B	1 (0.7)
Penicillin	16 (11.8)
Herbal medications	
Yes	6 (4.4)
No	130 (95.6)
Contrast within 5 days	
Yes	2 (1.5)
No	134 (98.5)

Discussion

The mean age in our cohort was 44.7 years with 36% of patients between the ages of 30 to 39 years. Similar mean age has been seen in other developing countries and have ranged between 35 to 50 years (6,7). However, studies from the developed countries have a higher mean age like a study done in Korea by Han *et al* (8) reported a mean age of 68 years and another one by Chertow *et al* (9) done in

the USA had a mean age between the ranges of 52.8 to 58.8. This difference in age could be due to the fact that developing countries have a relatively younger population than that in the developed countries.

We found an equal distribution between male and female. This may have been by chance as most studies have reported a male preponderance (6, 10). We got an admission period prevalence of 8.1%. The prevalence was much higher than what Munyu (6) got from his study done at a private facility in Nairobi with prevalence of 1.05% and similarly Kaufman *et al* (11) reported CA-AKI prevalence of 1% of all hospital admissions. However, a much higher prevalence of 17.2% was seen in a study done by Evans *et al* (12). The differences may have been due to the different geographical area, criteria for defining AKI and study designs used.

Most of the patients had mild (stage 1) disease while the rest had moderate to severe disease at 48.6%. Similarly a study done by Wei et al (13) in China found 46.1% with stage 1, 25.0% with stage 2 and 28.9% with stage 3 AKI. This was in contrast to what Evans et al (12) found in his study where there were 33 patients in stage 1 (21·6%), 27 in stage 2 (17·7%), and 93 in stage 3 (60·8%). This may signify our patients seeking healthcare earlier.

We reported only 2 (14.3%) patients from a total of 14 patients who underwent RRT. Similar findings were reported by Munyu *et al* (6) at 13.37%. Ogiator *et al* (14) in Nigeria found 61 patients (58.7%) in need of dialysis and out of those 56 (53.8%) were dialysed. It is possible that for our patients there may have been a delay in being reviewed by a nephrologist and therefore a delay in deciding on whether to be started on RRT although this was just based on an assumption as it was not part of our study objectives.

The severity of AKI in our study was not associated with the length of hospital stay (p-value= 0.233). The median length of stay was 9 days in stage 1 disease, 11 days in stage 2 and 10 days in stage 3 disease (6, 11). This was different from other studies (8, 15,16) which showed a significant association between severity of AKI and LOHS. The difference may have been due to the fact that our study was a short term study while the studies quoted above were for at least 3 months. The other reason may have been due to the different AKI definitions used to categorize severity.

Full recovery was observed in 21 patients, partial recovery in 32 and non-recovery in 60 (53%) individuals. There was no statistical difference among the three groups. The severity of AKI affected the rate of recovery, that is, the more severe the AKI, the less chances of recovery and this was statistically significant (p-value=0.045). This was similar to what Evans *et al* (12) found in their study done in Malawi. The non-recovery was comparable to what Bagasha *et al* (18) found in their study. Ali *et al* (16) reported full renal recovery in 321 (68%), 24 (5%) with partial recovery and recovery in the severe category being significantly lower. Most of our patients had non recovery and fewer had full recovery. This non recovery may have been high in our setup due to a delay in managing these patients as supported by a comparison study done by Gatuma *et al* (17) which found that patients with AKI secondary to hypovolemia who were intervened early as compared to those that were not had higher chances of renal recovery and reduced mortality.

The overall mortality in our patients with CA-AKI was 16.9% and of note was that with increasing severity, the mortality increased (p-value = 0.012). This was similar to what Munyu *et al* (6) got; an overall mortality of 16.6%. There were higher mortalities in studies done by Kiiru *et al* (21) at 52%. Evans *et al* (12) in a Malawi hospital reported a mortality of 44.4% and almost half of patients with stage 3 AKI died. Ogiator *et al* (14) found a mortality of 25% in a retrospective study done in Nigeria on medical admissions..

The higher mortalities observed in the above studies maybe due to the difference in study areas for example ICU versus medical wards, more patients with more severe disease. When we compare the mortality with other 2 week outcome studies done in different set of patients, more people died from AKI. A study done by Karanga *et al* in 2016 found a mortality rate of 13.5% in heart failure patients with hyponatremia. This was lower than what we found thus confirming the burden of the disease.

Mortality was also seen to increase significantly with increasing severity of AKI in our study as most deaths were observed in stage 3 disease at 33.3% which has been reported in other studies as well (21, 22).

The three most common risk factors for CA-AKI which we found in our study was sepsis at 50.5%, followed by nephrotoxic medications at 45.6% and lastly gastrointestinal losses at 42.6%. Similar findings have been reported in other studies as well (6). An important observation from our study was that we found AKI being multifactorial for example a patient would be on nephrotoxic medications, have gastroenteritis and be in heart failure in the same instance. It's a known fact that AKI is a multifactorial disease and sometimes establishing a single cause proves to be a daunting task. There was a high use of antibiotics (penicillins, aminoglycosides, sulfonamides) known to cause nephrotoxicity as well as the use of ACE I and non-steroidal anti-inflammatory drugs reported in 14% and 10% of patients. This highlights the need for clinicians to closely monitor and adjust patient's prescriptions to prevent adverse effects. Sepsis is associated with high morbidity and mortality and therefore requires timely empirical antibiotics within an hour of seeing the patient with proper fluid management and control of fevers. Gastrointestinal losses were the third most common risk factor. The vomiting and diarrhoea may have led to dehydration, hypotension and renal dysfunction. It is therefore important to target patients with these symptoms for prompt and proper fluid status management.

Some of the limitations to this study were that we did not use urine output as an additional criteria for defining AKI, obstructive uropathy is mainly a surgical admission and some cases may have been missed, some CKD patients have a normal sized kidneys on an ultrasound and may have been included in the study and most of our baseline creatinine were based on estimation.

Conclusion

This study showed a high prevalence of CA-AKI in patients admitted in the general wards at KNH and the severity of AKI was associated with non- recovery, mortality and need of renal replacement therapy with not much difference in the length of hospital stay. The most common risk factors were sepsis, nephrotoxic drug use and gastrointestinal losses.

References

1. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guidelines for Acute Kidney Injury. *Kidney Inter*. 2012; **2** (Suppl); 1-138.
2. Bellomo R, Kellum J, Ronco C. Acute kidney injury. *Lancet*. 2012; **380**: 756–766.
3. Rewa O, Bagshaw SM. Acute kidney injury—epidemiology, outcomes and economics. *Nature Reviews Nephrology*. 2014; **10**:193–207 (2014) doi:10.1038/nrneph.2013.282
4. Santos WJ, Zanetta DM, Pires AC, Lobo SM, Lima EQ, Burdmann EA. Patients with ischaemic, mixed and nephrotoxic acute tubular necrosis in the intensive care unit - a homogeneous population? *Crit Care*. 2006; **10**: R68.
5. Naicker S, Aboud O, Gharbi MB. Epidemiology of acute kidney injury in Africa. *Semin Nephrol*. 2008; **28**: 348-355.
6. Munyu PW. Prevalence, risk factors and outcomes in Aga Khan University Hospital, Nairobi 2008 (unpublished).
7. Hadidy S, Asfari R, Shammaa MZ, Hanifi MI. Acute renal failure among a Syrian population. Incidence, aetiology, treatment and outcome. *Int Urol Nephrol.* 1989; **21**(5):455-461.
8. Han SS, Kim S, Ahn SY, Lee J, Kim DK, Chin HJ, Chae DW, Na KY. Duration of acute kidney injury and mortality in critically ill patients: a retrospective observational study. *BMC Nephrology.* 2013; **14**:133 DOI: 10.1186/1471-2369-14-133.
9. Chertow GM, Burdick E, Honour M, Bonventre JV and Bates DW. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol*. 2005; **16**: 3365-3370.
10. Wang HE, Muntner P, Chertow GM, Warnock DG. Acute kidney injury and mortality in hospitalized patients. *Am J Nephrol*. 2012; **35**(4): 349–355.
11. Kaufman J, Dhakal M, Patel B, Hamburger R. Community-acquired acute renal failure. *Am J Kidney Dis*. 1991; **17**: 191-198. PubMed.
12. Evans RD, Hemmilä U, Craik A, Mtekateka M ,Hamilton F, *et al*. Incidence, aetiology and outcome of community-acquired acute kidney injury in medical admissions in Malawi. *BMC Nephrology*. 2017; **18**:21 DOI 0.1186/s12882-017-0446-4.
13. Wei Q, Liu H, Yan- Tu, Tang R, Wang Y,Pan M & Liu B. The characteristics and mortality risk factors for acute kidney injury in different age groups in China—a cross sectional study. *Renal Failure.* 2016; **38**(9): 1413–1417.
14. Ogiator, Chinyere I. Okpara , Mbaave P , Achinge G , Okopi J and Adaora B. Aetiology and outcome of Aki in Benue State University Teaching Hospital Makurdi, Nigeria - A three (3) year review. *Asian J Med Health*. 2017; **2**(4): 1-7 Article no.AJMAH.31579
15. Bedford M, Stevens P E, Wheeler TW, Farmer CK. What is the real impact of acute kidney injury? *BMC Nephrology.* 2014; **15**:95 **DOI:** 10.1186/1471-2369-15-95.
16. Ali T, Khan I, Simpson W, *et al*. Incidence and outc omes in acute kidney injury: a comprehensive population based study. *J Am Soc Nephrol.* 2007; **18**: 1292-8.
17. Gatuma PN, *et al.* Hypovolemia associated acute renal failure as seen in the medical wards at the Kenyatta National Hospital. 1998 (unpublished)
18. Bagasha P, Nakwagala F, Kwizera A, Ssekasanvu E, Kalyesubula R. Acute kidney injury among adult patients with sepsis in a low-income country: clinical patterns and short-term outcomes. *BMC Nephrology*. 2015; **16**:4 doi: 10.1186/1471-2369-16-4.
19. Mehta RL, Pascual MT, Soroko S, Savage BR, Himmelfarb J, *et al*. Spectrum of acute renal failure in the intensive care unit: The PICARD experience. *Kidney Int*. 2004; **66**: 1613– 1621.
20. Kiiru B, *et al*. Interleukin 18 as an early biomarker of acute kidney injury in critically ill patients. 2012
21. Thakar CV, Christianson A, Freyberg R, Almenoff P, Render ML. Incidence and outcomes of acute kidney injury in intensive care units: a Veterans Administration study. *Crit Care Med*. 2009; **37**:2552–2558.
22. Bagshaw S. Short- and long-term survival after acute kidney injury. *Nephrol Dial Transplant.* 2008; **23**: 2126–2128 doi: 10.1093/ndt/gfn300.

Original paper

Prevalence and Factors Associated with *Helicobacter Pylori* Infection in Adults attending Medical Out Patient Unit at Aden Abdulle Hospital, Mogadishu, Somalia

Dhiblawe AOH[1,2], Ponsiano O[1], Opio K[1], Osman D[3]

[1]Department of Internal Medicine, College of Health Sciences, School of Medicine, Makerere University, Uganda
[2]Aden Abdulle Hospital, Mogadishu, Somalia
[3] Benadir University, Mogadishu, Somalia

Address for correspondence: Dr Abdirahman OH Dhiblawe, Department of Internal Medicine, College of Health Sciences, School of Medicine, Makerere University, Uganda. Email: draoh2014@gmail.com

Abstract

***Background*:** Prevalence of *H. Pylori* infection is high in developing countries. It is a risk factor for peptic ulcer disease, gastric carcinoma and B-cell Mucosa-Associated Lymphoid Tissue (MALT) lymphoma. Despite its significant morbidity and mortality, data on prevalence in Somalia is not available.

Objectives: To determine the prevalence and factors associated with *H. pylori* infection among patients attending Aden Abdulle Hospital medical outpatient unit.

Methods: In this cross sectional study, patients aged 18 years and above were recruited by systematic random sampling. *Helicobacter pylori* was determined using H. *pylori* test kit cassette (Pylori K-SeT cassette, Gembloux**,** Belgium). Patients on proton pump inhibitors, H2 receptor blockers, bismuth salts or antibiotics were excluded.

Results: A total of 323 patients were studied, 131 (40.5%) were male and 192 (59.5%) were female. The median age was 38 years (IQR= 26). There were 2 age group peaks, 18 to 29 and ≥ 50 years. Among all patients, 138 (42.7%) of them were *H. pylori* positive and 61.6% of these were female. None of the factors (age, gender, residence, crowding, smoking, chewing Khat and clinical presentations) were associated with *H. pylori* infection in this study.

***Conclusion and recommendation*:** The prevalence of *H. pylori* in this study was 42.7%. None of the factors studied associated with *H. pylori* infection. Given the high prevalence, doctors should consider their patients could be affected. A large-scale epidemiological survey needs to be conducted in the community.

Key words: *Helicobacter pylori*, Stool antigen

Introduction

Helicobacter Pylori is a risk factor for peptic ulcer disease, gastric cancer, and B-cell Mucosa-Associated Lymphoid Tissue (MALT) lymphoma (1). Over 50% of world's population is infected with H. *pylori* (2). The prevalence varies by geographical location, ethnic background, and socioeconomic conditions (2).

Prevalence of *H. pylori* is high in developing countries (3). Mode of transmission of *H. pylor*i infection is poorly understood, but oral-oral, gastro-oral and faecal-oral routes are all possible (4). Water from streams, rivers and wells are also found as source of infection (4). This infection is usually acquired early in life (5).

In Somalia there was limited data about the prevalence of *H. pylori* infection. The aim of this study, therefore, was to investigate the prevalence of *H. pylori* infection and associated factors among patients attending AAH medical outpatient unit in Mogadishu-Somalia.

Materials and methods

This was a cross sectional study conducted among patients aged 18 years and above who attended AAH outpatient unit from August to October 2015. Three hundred and twenty three patients were studied, systematic random sampling was done and every 4th patient was recruited into the study after consenting. *Helicobacter pylori* was determined using *H. pylori* test kit cassette (Pylori K-SeT cassette, Gembloux**,** Belgium). Patients on proton pump inhibitors, H2 receptor blockers, bismuth salts or antibiotics were excluded.

A structured questionnaire was administered to obtain clinical socio-demographic characteristics of the patients. Stool antigen was requested from the participants and tested immediately using *H. pylori* test kit cassette described above. The data was entered into EPI-DATA 3.1 and analyzed using STATA 12. Approval was sought from Department of Medicine, School of Medicine Research Ethics Committee (SOMREC), Makerere University College

of Health Sciences and administration of Aden Abdulle Hospital.

Results

During the months of August to October 2015, 339 patients who were attending Aden Abdulle Hospital Medical outpatient unit in Mogadishu, Somalia were screened. Three hundred and twenty three participants were recruited into the study. Sixteen patients were excluded, of these six of them were less than eighteen years while ten others had taken PPIs within two weeks (Figure 1).

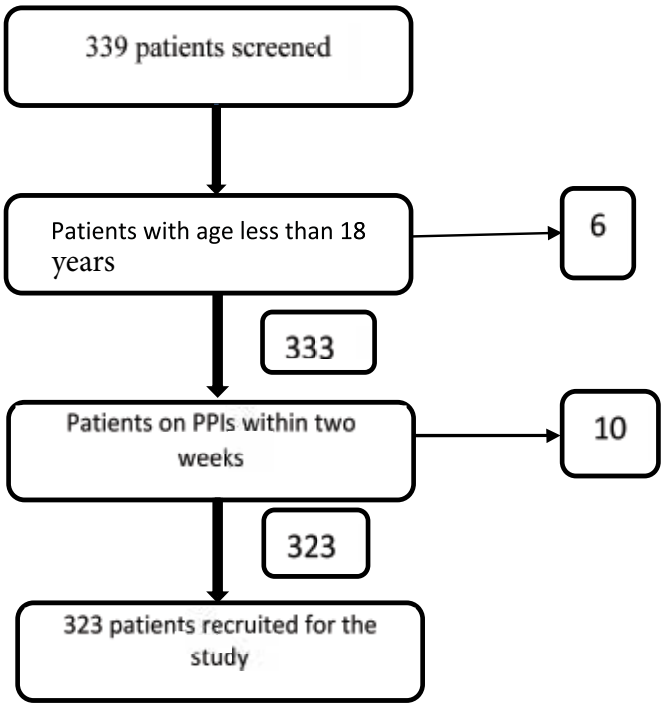


Figure 1: Study flow chart

Socio demographic characteristics of the study participants (JN=323): The majority of the study participants were female 192 (59.5%). The median age of the study participants was 38 (IQR=26). The majority of the participants lived in the urban areas 288 (89.2%) and half of the total participants (50%) had no formal education. The socio-demographic characteristics are summarized in Table 1.

Table 1: Socio-demographic characteristics and dyspeptic complaints of the study (n=323)

Variable	Frequency No. (%)
Age (years)	
18 – 29	98 (30.3)
30 – 39	69 (21.4)
40 – 49	50 (15.5)
≥ 50	106 (32.8)
Gender	
Female	192 (59.5)
Marital status	
Married	252 (78.0)
Single	71 (22.0)
Residence	
Urban	288 (89.2)
Rural	35 (10.8)
Level of education	
University	46 (14.2)
Secondary	63 (19.5)
Primary	53 (16.4)
No formal education	161 (49.8)
Type of accommodation	
Villa house/Flat**	205(63.5)
Refugee/Shanty house***	118 (36.5)
Number of people per room (crowding)	
1 – 2	98 (30)
≥2	225(69.7)
Sewage system*	
Good	14(4)
Fair	200(62)
Poor	109(34)
Source of water	
Treated wells	79 (25)
Untreated wells	220 (68)
Water dam	24 (7)
Ever smoked cigarettes	
Yes	30(13)
No	293(74)
Smoke cigarette now	
Yes	15(5)
No	18(6)
Chewing Khat	
Yes	14(4)
No	309(96)
Wash hands before eating	
Yes	113(34)
No	210(65)
Epigastric burning/pain	
Yes	252 (78)
No	72 (22)
Acid regurgitation	
Yes	190 (59)
No	133(41)
Excessive belching	
Yes	153(47)
No	170(53)
Feel early satiety	
Yes	181(56)
No	142(44)
Unexplained weight loss in last 6 months	
Yes	143(44)
No	180(56)

*Good when the sewage system is covered, fair when sewage is collected and disposed off in another place, Poor

when sewage is everywhere around the home uncovered
** Villa house/ Flat is a permanent house with 4 Rooms, kitchen and toilet
*** Refugee/ shanty houses is temporary houses poorly made

Dyspeptic complains of the study 323 participants: These dyspeptic complains were either prior or during this presentation. Most frequent complaints were epigastric pain 252 (78%), acid regurgitation 190 (59%) and early satiety 181 (56%). These symptoms are summarized in Table 2.

Prevalence of H. pylori infection in the 323 study: Prevalence of *H. pylori* infection was 42.7% (95% CI 37.3 – 48.1). Of the 138 patients with *H. pylori* infection, 61.6% (n=85) were female.

Distribution of H. pylori by age of study participants: Of all the participants, *H. pylori* was seen mainly in patients in the age groups between 18-39 years and above 50 years of age. This is shown in Figure 2.

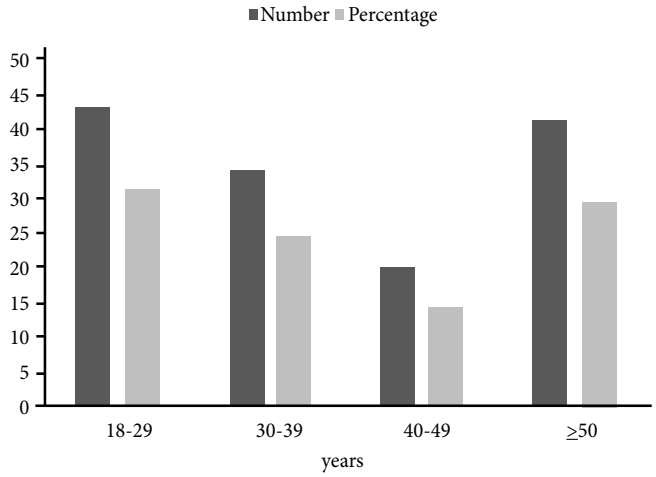


Figure 2: Distribution of *H. pylori* by age in the study population

Socio-demographic factors associated with H. pylori in the 323 participants in bivariate analysis: At bivariate analysis statistically significant association, that being in a rural residence reduced risk of infection (p-value=0.01) was observed. Other Socio-demographic factors are not associated with *H. pylori* infection at this level (Table 3).

Table 2: Bivariate analysis showing association of dyspeptic complains with the occurrence of H. *pylori* infection in the study 323 participants

Variable	Presence of *H. pylori*		OR (95% CI)	P-value
	Negative (n=185(57.3%) (%)	Positive (n=138(42.7%) (%)		
Epigastric burning/pain				
Yes	144(78)	108(78)	1.0	-
No	41(22)	30(22)	0.97 (0.57 – 1.66)	0.93
Acid regurgitation				
Yes	103(56)	87(63)	1.0	-
No	82(44)	51(37)	0.73 (0.47 – 1.16)	**0.18***
Excessive belching				
Yes	87(47)	66(48)	1.0	-
No	98(53)	72(52)	0.97 (0.62 – 1.50)	0.89
Feel early satiety				
Yes	103(56)	78(57)	1.0	-
No	82(44)	60(43)	0.97 (0.62 – 1.51)	0.88
Unexplained weight loss in last 6 months				
Yes	81(44)	62(45)	1.0	-
No	104(56)	76(55)	(0.61 – 1.49)	0.84

**p-value≤0.20 and therefore carried forward to multivariate analysis.*

Table 2a: Bivariate analysis showing association of socio-demographic characteristics with the occurrence of *H. pylori* infection in 323 participants.

Variable	Presence H. *pylori*		OR (95% CI)	P-value
	Negative (n=185 (57.3%) (%)	Positive (n=138 (42.7%) (%)		
Age (years)				
18 – 29	55 (30)	43 (31)	1.0	-
30 – 39	35 (19)	34 (25)	1.24 (0.67 – 2.30)	0.49
40 – 49	30 (16)	20(15)	0.85 (0.43 – 1.70)	0.65
≥ 50	65 (35)	41(30)	0.81 (0.46 – 1.44)	0.45
Gender				
Male	78(42)	53(38)	1.0	-
Female	107(58)	85(62)	1.17 (0.75 – 1.83)	0.50
Marital status				
Married	149(80)	103(75)	1.0	-
Single	36(20)	35(25)	1.41 (0.82 – 2.39)	**0.20***
Residence				
Urban	158(85)	130(94)	1.0	-
Rural	27(15)	8(6)	0.36 (0.16 – 0.82)	**0.01***
Level of education				
University	24(13)	22(16)	1.0	-
Secondary	35(19)	28(20)	0.87 (0.41 – 1.87)	0.73
Primary	29(16)	24(17)	0.90 (0.41 – 1.99)	0.80
No formal education	97(52)	64(46)	0.72 (0.37 – 1.39)	0.33
Type of accommodation				
Villa house/Flat	112(61)	93(67)	1.0	-
Refugee/Shanty house	73(39)	45(33)	0.74 (0.47 – 1.18)	**0.20***
Number of people per room (crowding)				
1 – 2	52(28)	46(33)	1.0	-
≥2	133(72)	92(66)	0.78 (0.48 – 1.26)	0.31
Source of water				
Treated wells	50(27)	29(21)	1.0	-
Untreated wells	120(65)	100(72)	1.44 (0.85 – 2.44)	**0.18***
Water dam	15(8)	9(7)	1.03 (0.40 – 2.66)	0.94
Sewage system				
Good	10(5)	4(3)	1.0	-
Fair	107(58)	93(67)	2.17 (0.70 – 1.76)	**0.20***
Poor	68(37)	41(30)	1.51 (0.44 – 1.59)	0.51
Ever smoked cigarettes				
Yes	16(9)	14(10)	1.0	-
No	169(91)	124(90)	0.84 (0.39 – 1.78)	0.65
Smoke cigarette now				
Yes	10(5)	5(4)	1.0	-
No	8(4)	10(7)	2.50 (0.60 – 10.34)	**0.20***
Chew Khat				
Yes	8(4)	6(4)	1.0	-
No	177(96)	132(96)	0.99 (0.34 – 2.93)	0.99
Wash hands before eating				
Yes	58(31)	55(40)	1.0	-
No	127(69)	83(60)	0.69 (0.43 – 1.09)	**0.11***

**p-value ≤0. 20 and therefore carried forward to multivariate analysis.*

Dyspeptic complains with the occurrence of H. pylori infection in the study 323 participants at bivariate analysis: Association of *H. pylori* to epigastric pain, acid regurgitation, excessive belching, early satiety and unexplained weight loss were studied. None of these factors were statistically significant at bivariate analysis as shown in the Table 3.

Socio-demographic and clinical factors associated with H. pylori infection at multivariate analysis: At multivariate analysis, eight factors with less than 0.2 p-value at bivariate were analyzed using logistic regression. Two of them (accommodation and source of water) dropped from the model because of similarity to other factors (collinearity). Being single (not married) reduced risk of having infection by 94% at a distinct trend towards significance (p-value 0.07).
None of the socio-demographic and clinical factors were statistically significant. Table 4 is a summary of multivariate analysis.

Table 3: Socio-demographic and presentations of 323 participants at multivariate analysis

Variable	OR (95% CI)	P-value
Residence		
Urban	1.0	-
Rural	18.88 (0.26 – 135.90)	0.26
Marital status		
Married	1.0	-
Single	0.06 (0.003 – 1.21)	0.07
Rating of the sewage system		
Good		
Fair	1.0	-
Poor	6.15 (0.50 – 79.80)	0.16
	0.72 (0.02 – 25.31)	0.85
Ever felt acid regurgitation		
Yes	1.0	-
No	1.24 (0.19 – 7.87)	0.82
Do you smoke now?		
Yes	1.0	-
No	1.01 (0.16 – 6.24)	0.99
Wash hands before eating		
Yes	1.0	-
No	2.94 (0.32 – 26.71)	0.34

Discussion

This was a cross sectional study to determine the prevalence and factors associated with H. pylori infection in patients attending medical out patient at Aden Abdulle Hospital in Mogadishu, Somalia.

Prevalence: The prevalence of *H. pylori* infection in the study population is 42.7% (95% CI 37.3 – 48.1). However 71 participants reported that they had previously taken *H. pylori* eradication therapy. Although 44 of these patients had negative test results in this study, we assumed the treatment could have eradicated the infection. This prevalence represents what had been seen in developing countries.

A cross sectional study done in Mulago Hospital, Uganda by Segamwenge *et al* (6) reported prevalence of 33.5% and 32.5% using *Helicobacter pylori* stool antigen test and histology respectively. This is lower than what we found in our study. The reason could be that Uganda has better health facilities and infrastructure than Somalia.

However in Addis Ababa, Ethiopia, a *Helicobacter pylori* stool antigen test based study found a prevalence of 81%. This prevalence is high than what both this study and the study in Uganda found (7). This study is not comparable to our study because they were recruiting patients with symptoms consecutively.

Shmuely *et al* (8) also reported a prevalence of 71% and 70% among symptomatic and asymptomatic participants respectively in Nakuru, west Kenya in a hospital based study. In Nigeria and Egypt, studies done found a prevalence of 64% and 60% respectively, which are higher than what this study reports (9, 10). Both studies used different method of testing hence they may not be comparable to our study.
In a meta-analysis in early 1990s, Khalifa et al (10) found that the overall prevalence of *H*. *pylori* infection was significantly higher in developing countries, averaging 60%; compared to 41.9% in the developed countries. However some of these studies used serum *H*. *pylori* antibody testing, which is an exposure test and could potentially lead to higher rates than would be if an antigen test is used as in our study.
Although some of these studies looked at symptomatic patients, it is difficult to benchmark the prevalence of *H. pylori* infection across geographical settings, even if the population characteristics seem similar and the method of diagnosis is the same.

This study was conducted in a private hospital setting and in a predominantly urban population. Because of the lifestyles in the urban setting, the observed prevalence could be a result of better living conditions than could be seen if this study was conducted in a rural setting of Somalia.

Factors associated with H. pylori infection: At bivariate analysis, the residence was significantly associated with *H. pylori* infection OR=0.36 (95% CI 0.16 – 0.82; p-value=0.01), this shows being in the rural areas reduced the risk of infection by 64%.

However, in multivariate analysis, it was insignificant. Other than that, no other factor in this study showed a significant association at both bivariate and multivariate logistic regression. Again this could be explained by the fact that there were very few participants from the rural population in our study.

In contrary to this study, a community based survey in Mexico found that age and low educational status were

associated with *H. pylori* infection. They also found no difference in prevalence between the rural and the urban populations hence no association (11).

In India, a case control study found a host of factors to be associated with *H. pylori* infection namely low social economic status, eating meat, eating restaurant food and drinking non-filtered water. However, this study included only participants that had either peptic ulcer or cancer of the stomach and was therefore likely to have introduced selection bias (12).

A hospital based cross sectional study in Sudan reported that only rural residence increased risk of infection and therefore the only factor associated with *H. pylori.* The diagnosis was also based on serology (13).

Limitations of the study

The fact that this was a hospital based study means there was a filtering effect that introduces a selection bias. In this study, some of the participants who had had *H*. *pylori* eradication prior to two weeks were analyzed as if they were positive for *H*. *pylori*. This could have potentially led to over or under reporting of the prevalence as this was done on the assumption that the therapy could have led to eradication of infection. The majority of participants were from urban population, so the study results cannot be generalized to the rural setting.

Conclusion

The prevalence of *H*. *pylori* infection in this study was 42.7%. None of the socio-demographic and current or previous dyspeptic symptoms were associated with the infection.

Acknowledgements

The authors thank everyone who participated in this study. This study was a dissertation for masters of medicine and was supported financially by Aden Abdulle Hospital.

References

1. Sipponen P, Hyvärinen H. Role of Helicobacter pylori in the pathogenesis of gastritis, peptic ulcer and gastric cancer. *Scandinavian J Gastroenterol.* 1993; **28**(S196):3-6.
2. Brown LM. Helicobacter pylori: epidemiology and routes of transmission. *Epidemiol Reviews.* 1999; **22**(2):283-297.
3. Bardhan PK. Epidemiological features of Helicobacter pylori infection in developing countries. *Clin Infect Dis*. 1997; **25**(5):973-978.
4. Miyaji H, Azuma T, Ito S, Abe Y, Gejyo F, Hashimoto N, *et al.* Helicobacter pylori infection occurs via close contact with infected individuals in early childhood. *J Gastroenterol Hepatol.* 2000; **15**(3):257-262.
5. Akcan Y, Ersan S, Alper M, Bicik Z, Aytug N. The transmission of Helicobacter pylori via exposure to common sources outweighs the person-to-person contact among spouses in developing countries. *Am J Gastroenterol.* 2000; **95**(1):317-319.
6. Segamwenge IL, Kagimu M, Ocama P, Opio K. The utility of the Helicobacter pylori stool antigen test in managing dyspepsia: an experience from a low resource setting. *Afr Health Sci.* 2015; **14**(4):829-834.
7. Asrat D, Nilsson I, Mengistu Y, Ashenafi S, Ayenew K, Al-Soud WA, *et al*. Prevalence of Helicobacter pylori infection among adult dyspeptic patients in Ethiopia. *Annals Trop Med Parasitol.* 2004; **98**(2):181-189.
8. Shmuely H, Obure S, Passaro DJ, Abuksis G, Yahav J, Fraser G, *et al.* Dyspepsia symptoms and Helicobacter pylori infection, Nakuru, Kenya. *Emerg Infect Dis*. 2003; **9**(9):1103.
9. Jemilohun AC, Otegbayo JA, Ola SO, Oluwasola OA, Akere A. Prevalence of Helicobacter pylori among Nigerian patients with dyspepsia in Ibadan. *Pan Afr Med J.* 2010; **6**(1).
10. Khalifa MM, Sharaf RR, Aziz RK. Helicobacter pylori: a poor man's gut pathogen. *Gut Path*. 2010; **2**(2):2-12.
11. Torres J, Leal-Herrera Y, Perez-Perez G, Gomez A, Camorlinga-Ponce M, Cedillo-Rivera R, *et al*. A community-based seroepidemiologic study of Helicobacter pylori infection in Mexico. *J Infect Dis*. 1998; **178**(4):1089-94.
12. Mhaskar RS, Ricardo I, Azliyati A, Laxminarayan R, Amol B, Santosh W, *et al*. Assessment of risk factors of Helicobacter pylori infection and peptic ulcer disease. *J Global Infect Dis.* 2013; **5**(2):60.
13. Abdallah TM, Mohammed HB, Mohammed MH, Ali AAA. Sero-prevalence and factors associated with Helicobacter pylori infection in Eastern Sudan. *Asian Pacific J Trop Dis.* 2014; **4**(2):115-119.

Original paper

The Utility of Physiochemical and Modified Physiological Approach in Metabolic Acidosis at a Tertiary Level Hospital in Kenya

Essaji LT[1], Kayima J[2], Joshi MD[2], Otieno CF[2], Amayo A[3], Achieng L[2], Gacii M[4]

[1]PGY3 Internal Medicine Resident, University of Nairobi, Kenya
[2]Department of Clinical Medicine and Therapeutics, University of Nairobi, Kenya
[3]Department of Clinical Chemistry, University of Nairobi, Kenya
[4]Department of Anaesthesia, University of Nairobi, Kenya

Address for correspondence: Dr. Lallet T Essaji, Internal Medicine Resident, University of Nairobi, Kenya. Email: tasneem-nurdin@hotmail.com

Abstract

Introduction: Metabolic acidosis is a poor prognostic marker it is therefore imperative that they be diagnosed early and underlying mechanism understood. The physiological approach and the base excess approach are the most frequently used by clinicians. However, Anion Gap (AG) not corrected for serum albumin has been shown to be misleading in the classification of metabolic acidosis. Of growing interest is the physiochemical approach which, though complicated, has been shown to be superior in detecting acid base derangements missed by the other two approaches.

Methodology: This was a cross sectional study done over three months at the Kenyatta National Hospital critical care units. Two hundred and forty two consecutive patients admitted to the critical care units were recruited and demographic and clinical information recorded, blood drawn for an arterial blood gas, urea, sodium, potassium, magnesium, phosphate, creatinine, full blood count and liver function tests and an APACHE II score determined. Prevalence of metabolic acidosis was calculated using Base Excess (BE), physiological and physiochemical approach. Prevalence of high anion gap metabolic acidosis was calculated using the anion gap, anion gap corrected for albumin (AGcor) and the Strong Ion Gap (SIG). Diagnostic utility of AG, AGcor and SIG was assessed by calculating their sensitivity and specificity.

Results: Prevalence of metabolic acidosis was 77.7% using BE approach, 76.9% using physiological approach and 87.2% using physiochemical approach. Physiochemical approach detected metabolic acidosis in 24 patients classified as having no acidosis using BE and physiological approach. Sixteen out of these 24 patients had hypoalbuminemia causing an alkalotic effect. High anion gap acidosis was greater for AGcor than for AG (77.4% vs 62.9% p = <0.001). Using the physiochemical approach 78.7% had SIG acidosis. Uncorrected AG resulted in misclassifying 20 out of every 100 subjects as normal anion gap acidosis. However its high specificity (93%) and low false positive results suggests its diagnostic ability as a rule in test. AGcor performed well against AG as well as against Strong Ion Gap (SIG) sensitivity of 100% and 95.8% respectively and thus could be useful to rule out high anion gap acidosis. Area under the curve for AGcor was higher than SIG, 0.921 vs 0.896 suggesting that AGcor outperforms SIG in the classification of metabolic acidosis into high anion gap acidosis.

Conclusion: The study shows that there is high prevalence of metabolic acidosis as well as high anion gap acidosis in the ICU. The physiochemical approach is able to pick up metabolic acidosis in patients with hypoalbuminemia and thus outperforms the BE and physiological approaches. Once anion gap is corrected for albumin levels, it performs equally well as the physiochemical approach in diagnosing high anion gap metabolic acidosis. Correcting anion gap for albumin levels might be the compromise solution between the more complicated physiochemical approach and the poorly performing uncorrected physiological approach.

Key words: Anion gap, Corrected anion gap, Strong ion gap, Physiochemical, Base excess, bicarbonate, Physiological, Metabolic acidosis

Introduction

How we analyse acid base disorders has undergone evolution depending on how we define an acid or base (1). The primary diagnostic acid base approach used by clinicians at the KNH is the physiological and base excess approach. AG, when calculated is not corrected for hypoalbuminemia. Uncorrected AG has been shown to be misleading in the diagnosis of acid base disorders (2, 3). An elevated anion gap can masquerade as a normal anion gap e.g. Low serum albumin reduces the AG and has an alkalinizing effect. In this situation a clinician might wrongly interpret and classify the patients as to having a normal anion gap metabolic acidosis.

Current acid base measurements has gaps and not only affects accuracy in diagnosis but is also unreliable as a prognostic factor. This study may potentially change how we analyse acid base status in our patients and this will enable us to better understand the underlying mechanisms associated with the acid base disorders.

Materials and methods

This was a cross sectional analytical study done over three months at the Kenyatta National Hospital critical care units which included the 21 bed mixed medical and surgical ICU, 5 bed medical ICU and 6 bed Accident and Emergency CCU. The study was approved by the Department of Clinical Medicine and Therapeutics University of Nairobi and the KNH/UON ethics committee. All patients above the age of 13 years admitted in any of the critical care units at the KNH were consecutively screened and recruited after an informed consent.

Demographic and clinical data was then recorded as well as an APACHE II score determined. Five mls of blood was collected from the cubital fossa for urea, electrolytes, creatinine calcium, magnesium, phosphate, albumin and total blood count. Two mls of blood was also drawn aseptically for an Arterial Blood Gas (ABG) from the radial artery into a pre-heparinised syringe. Blood was transported to the respective laboratory in cooler boxes with ice packs at approximately 4ºC. ABGs were analysed in the ICU laboratory using the Siemens Rapid Point 500 analyser. UECs calcium, magnesium, phosphate and albumin were measured using Boleki - Biolis 50i superior at the renal laboratory. Total blood count was analysed using the Roche - Cell Dyn 3700 automated machine at the haematology laboratory.

Anion gap was calculated as follows (4):

$$AG\ mmol/L = (Na^+ + K^+) - (HCO_3^- + Cl^-) \quad (1)$$

AG was corrected to albumin levels as follows (5):

AG_{cor} mmol/L= AG + 0.25 x (lower limit of normal albumin – observed albumin) (in g/L) (2)

Apparent strong ion difference calculated as (4):

$$SID_{app}\ mmol/L = Na^+ + K^+ + Ca^{2+} + Mg^{2+} - Cl^- \quad (3)$$

Effective strong ion difference was derived as follows (4):

SID_{eff} mmol/L = HCO_3^- + {albumin g/dL x (0.123 x pH – 0.631)**} + {**HPO_4^{2-}mmol/L x (0.309 x pH – 0.469)**}** (4)

Strong ion gap was calculated as (4):

SIG =SID_{app} - SID_{eff} (5)

Acid base analysis was performed using the physiological, physiochemical and base excess approaches. Using the physiological approach metabolic acidosis was defined as reduced pH < 7.35 or a reduced HCO_3 < 22mmol/L and the calculated $PaCO_2$ using the formula 1.5 × [HCO3-] + 8 ± 2 will be equal to or greater than the measured $PaCO_{2)}$. The physiochemical approach used the diagnostic criteria by Fencl *et al* to determine metabolic acidosis (6):

1. Dilutional acidosis: ↓SID, ↓Na
   Hyperchloremic acidosis: ↓ SID, ↑ Clcorrected
   Unidentified anions excess: ↓ SID, ↑ SIGcorrected
2. Nonvolatile weak acids
   Hyperalbuminemic acidosis: ↑ albumin
   Hyperphosphatemic acidosis: ↑ PO4
3. Unidentified anions excess: ↓ SID, ↑ SIG
   Using the base excess approach, SBE less than -2mmol/L was considered as metabolic acidosis (7).

Normal ranges for AG, AGcor and SIG were calculated from 14 healthy volunteers and abnormal values were considered as those that were 2 SD above or below the mean. These were then used to classify the metabolic acidosis into high anion gap acidosis.

Data was coded, entered and managed in a password protected Microsoft database. Statistical analysis was performed in SPSS version 21.0 software.

Results

Two hundred and forty two patients were recruited, 52.1% were from the Accident and Emergency CCU. The study subjects comprised of 138 males (57%) and 104 females (43%) with mean age of 39.71 years (SD 16.77) (Table 1). Majority of the patients (74%) were aged below 50 years. The biochemical and acid base profiles of the study subjects are shown in Table 2.

Table 1: Study subjects characteristics

Variable	Frequency	
	No.	(%)
Unit of admission		
AE CCU	126	52.1
Main ICU	80	33
Medical ICU	36	14.9
Medical patients[1]	140	57.9
Surgical patients[2]	102	42.1
Gender		
Female	104	43
Male	138	57
Age		
Mean (SD)	39.71 (16.77)	
Median (IQR)	35.5 (27.75 – 51.25)	
Min – Max	13 - 91	

Parallel testing was utilised to determine the prevalence of metabolic acidosis which was 77.7% (CI 71 – 84%) using base excess approach, 76.9% (CI 71 -82%) using physiological approach and 87.2% (CI 83 – 91%) using physiochemical approach. Combining BE and physiological approach gave a 80.2% prevalence which was higher than the individual BE and physiological approaches.

Physiochemical approach was able to detect metabolic acidosis in 24 study subjects who were classified using the combined BE and physiological approach as not having metabolic acidosis. 37.5% of those classified as having no metabolic acidosis had either lactic acidosis, acute kidney injury, Acute Decompensated Heart Failure (ADHF) or sepsis, these conditions present with metabolic derangements. Hypoalbuminemia was present in 66.7% and hypophosphatemia in 37.5% of those classified as no metabolic acidosis using either the BE or physiological approaches.

High Anion Gap (HAG) acidosis prevalence was 62.9% (CI 56 – 70%) of those classified as having metabolic acidosis using the physiological approach. Once anion gap was adjusted for albumin levels the High Anion Gap (HAGcor) acidosis prevalence increased to 77.4% (CI 70 – 84%). The prevalence of High Anion Gap (SIG) acidosis using physiochemical approach was 78.7% (CI 70 – 84%). The difference in proportions between HAG and HAGcor acidosis using the physiological approach was statistically significant p =<0.001 using the Chi square test.

Since there has been no gold standard test to metabolic acidosis, the diagnostic utilities of SIG and AG_{cor} were tested by calculating their sensitivity, specificity and predictive value against AG. AGcor had a sensitivity of 100%, specificity of 60.9%, positive predictive value of 81.3% and negative predictive value of 100% (Table 14).

SIG had a sensitivity of 97.4%, specificity of 58%, positive predictive value of 79.7% and negative predictive value of 93%. Using SIG as the gold standard, AG had a sensitivity of 79.7%, specificity of 93%, positive predictive value of 97.4% and negative predictive value of 58% (Table 16) while AGcor had a sensitivity of 95.8%, specificity of 83.7%, positive predictive value of 95.1% and negative predictive value of 85.7%

Table 2 : Biochemical and acid base profile of study subjects

	Mean (SD)
Sodium mmol/L N = 135 - 145	135.97 (9.67)
Potassium mmol/L N = 3.5 – 5.0	3.9 (1.00)
Chloride mmol/L N = 95 - 105	101.19 (9.5)
Calcium mmol/L N = 2.25 – 2.75	2.18 (0.39)
Magnesium mmol/L N = 0.67 – 1.04	0.89 (0.42)
Phosphorous mmol/L N = 0.81 – 2.30	1.32 (0.77)
Albumin g/L N = 37 - 52	34.45 (8.05)
pH N = 7.35 – 7.45	7.36 (0.14)
PaO^2 mmHg N = 75 - 90	102.34 (45.66)
PaO2 mmHg N = 35 - 45	31.72 (10.84)
Bicarbonate mmol/L N = 22 - 26	18.02 (6.04)
BE mmol/L N = -2 - 2	-6.73 (8.58)
Lactate mmol/L N = 0.5- 2.22	2.18 (1.42)
AG mmol/L N1 = 11.92 – 19.12	20.71 (9.27)
AGcor mmol/L N1 = 9.56 – 16.76	20.85 (9.05)
SIDapp mmol/L N1 = 36.39 – 46.39	39.64 (8.4)
SIDeff mmol/L N1 = 33.78 – 43.78	29.79 (6.54)
SIG mmol/L N2 = 1.20 – 5.80	9.8 (9)

1 – reference values as per 2 SD above and below the mean.
2 – reference values at 10^{th} and 90^{th} percentiles

Discussion

Prevalence of metabolic acidosis was 77.7% using the base excess approach, 76.9% using the physiological approach and 87.2% using physiochemical approach. Combining the use of both the base excess and physiological approaches gave an 80.2% prevalence. Metabolic acidosis is a common problem in the ICU, however epidemiological data is scarce as a result of the various different approaches used

to describe acid base status (8). A Brazilian study of ICU admissions by Park *et al* (7) found a similar metabolic acidosis prevalence (77.4%) using the BE approach. A retrospective study by Gunnerson *et al* (9) on ICU patients showed that metabolic acidosis as defined by SBE < -2mmol/L was present in 64% of patients recruited. However, their sample population included only those patients who had an arterial lactate done therefore their sample population was just 9% of the total admissions. Most literature has been based on physiological approach and the uncorrected anion gap. Currently there is no agreement to what approach is best in identifying acid base disorders, some authors state that the physiochemical approach is more sensitive and thus able to pick up metabolic acidosis better than physiological approach, however most agree that it is a more cumbersome method (3,10).

Our study showed that the physiological approach detected lower numbers of metabolic acidosis while the physiochemical approach had the highest cases of metabolic acidosis 76.9% (CI 0.71 – 0.82) vs 87.2% (CI 0.83 – 0.91). Dubin *et al* (3) compared the diagnostic ability of all three approaches in diagnosing metabolic acidosis and had similar results showing that physiochemical approach was able to identify metabolic acidosis in 14% of patients admitted to ICU with normal BE and bicarbonate. The higher prevalence using the physiochemical approach could be attributed to the fact that the approach considers all three buffer systems i.e the carbonic acid bicarbonate buffer, the protein buffer and the phosphate buffer while the other two approaches are based entirely on carbonic acid bicarbonate buffer system.

The physiochemical approach was able to detect metabolic acidosis in 24 patients classified as having no metabolic acidosis by both the Base Excess (BE) and physiological approach. Hypoalbuminemia was present in 66.7% and hypophosphatemia in 37.5%. McAuliffe *et al* (11) showed that a decrease of 1g/dL in albumin level correlates to a proportional increase in bicarbonate of 3.4mmol/L and a proportional decrease in the anion gap by 3mmol/L thus low albumin levels has an alkalotic effect which could therefore mask an underlying metabolic acidosis.

Metabolic acidosis was classified into high anion gap acidosis using the anion gap (HAG), using the corrected anion gap (HAGcor) and using the Strong Ion Gap (SIG). HAG acidosis using the anion gap was 62.9%. Once corrected for albumin levels, high anion gap corrected (HAGcor) acidosis increased to 77.4%. The difference in proportions of HAG and HAGcor acidosis was statistically significant p = <0.001. The physiochemical approach gave a strong ion gap acidosis of 78.7% this approach considers albumin levels and thus does not need correction. This therefore suggests that in the critically ill patient, low albumin level can mask a high anion gap acidosis.

In our study, using Anion Gap (AG) to classify metabolic acidosis into high and low and high anion gap acidosis resulted in classifying 20 out of every 100 subjects as normal anion gap acidosis. However its high specificity (93%) and low false positive results suggests its diagnostic ability as a rule in test.

Anion Gap corrected for albumin levels (AGcor) performed well against AG as well as against Strong Ion Gap (SIG) sensitivity of 100% and 95.8% respectively. This suggests that AGcor identifies true positives well and thus could be useful to rule out high anion gap acidosis. Area under the curve for AGcor was higher than SIG, 0.921 vs 0.896 this suggests that AGcor outperforms SIG in the classification of metabolic acidosis into high anion gap acidosis. Dubin *et al* (3) found that SIG and AGcor were tightly correlated and showed excellent agreement in their patients (r^2= 0.97). A study done by Moviat *et al* (10) also showed a very strong correlation between AGcor and SIG (r^2 = 0.934, P < 0.001). AGcor does not require complex mathematical formula and therefore this could be a compromise solution between the poorly performing AG and the more sophisticated SIG.

Conclusion

This study shows that metabolic acidosis and high anion gap acidosis is quite common in the critical care units. The physiochemical approach is much better at detecting metabolic acidosis even in patients with hypoalbuminemia and thus outperforms the BE and physiological approaches.

Once anion gap is corrected for albumin levels, it performs equally well in diagnosing high anion gap metabolic acidosis. This might be the compromise solution between the more complicated physiochemical approach and the poorly performing physiological approach.

References

1. Story DA. Bench-to-bedside review: a brief history of clinical acid-base. *Crit Care*. 2004; **8**(4):253-258.
2. Salem MM, Mujais SK. Gaps in the anion gap. *Arch Intern Med*. 1992; **152**(8):1625-1629.
3. Dubin A, Menises MM, Masevicius FD, Moseinco MC, Kutscherauer DO, Ventrice E, *et al.* Comparison of three different methods of evaluation of metabolic acid-base disorders. *Crit Care Med*. 2007; **35**(5):1264-1270.
4. Morris CG, Low J. Metabolic acidosis in the critically ill: part 1. Classification and pathophysiology. *Anaesthesia*. 2008; **63**(3):294-301.
5. Figge J, Jabor A, Kazda A, Fencl V. Anion gap and hypoalbuminemia. *Crit Care Med*. 1998; **26**(11):1807-1810.
6. Fencl V, Jabor A, Kazda A, *et al*. Diagnosis of metabolic acid-base disturbances in critically ill patients. *Am J Respir Crit Care Med.* 2000; **162**:2246–2251.

7. Park M, Taniguchi LU, Noritomi DT, Libório AB, Braga AL, Maciel AT, Cruz-Neto LM: Clinical utility of standard base excess in the diagnosis and interpretation of metabolic acidosis in critically ill patients. *Braz J Med Biol Res* 2008, **41**:241–249.
8. Gunnerson KJ. Clinical review: The meaning of acid–base abnormalities in the intensive care unit part I – epidemiology. *Critical Care*. 2005; **9**(5):508-516. doi:10.1186/cc3796.
9. Gunnerson K, Saul M, He S, Kellum J. Lactate versus non-lactate metabolic acidosis: a retrospective outcome evaluation of critically ill patients. *Critical Care*. 2006: **10**(1):R22.
10. Moviat, M., van Haren, F., & van der Hoeven, J. Conventional or physiocochemical approach in intensive care unit patients with metabolic acidosis. *Critical Care*. 2003; **7**(3): R41–R45.
11. McAuliffe JJ, Lind LJ, Leith DE, Fencl V. Hypoproteinemic alkalosis. *Am J Med*. 1986; **81**(1):86-90.

Original paper

Thyroid Function among Pregnant Women Attending Antenatal Clinic at Kenyatta National Hospital

Mungla P[1], Ong'ech J[2], Joshi MD[3]

[1]Department of Clinical Medicine and Therapeutics, University of Nairobi, Nairobi, Kenya
[2]Department of Reproductive Health, University of Nairobi, Kenya
[3]Department of Clinical Medicine and Therapeutics, University of Nairobi, Kenya

Address for correspondence: Dr P Mungla, Department of Clinical Medicine and Therapeutics, University of Nairobi, Nairobi, Kenya. Email: pmungla@yahoo.co.uk

Abstract

Background: Maternal thyroid hormone levels are an important determinant of pregnancy and fetal outcomes. Both hyperthyroidism and hypothyroidism have been shown to have adverse maternal and fetal outcomes. There is no data on the magnitude and profile of thyroid dysfunction among pregnant women in Kenya.

Methods: This was a descriptive cross- sectional study involving consenting pregnant women attending ANC aged 18 years and above. One hundred and eight participants were recruited using consecutive sampling. The study set out to determine the prevalence of thyroid dysfunction among pregnant women Attending Antenatal Clinic (ANC) at the Kenyatta National Hospital (KNH) and to determine association between thyroid dysfunction in pregnancy to fetal well-being status using a trimester specific obstetric ultrasound. A focused history and physical examination was carried out using the study proforma. Analysis of TSH and FT4 was carried out in the KNH biochemistry laboratory using an automated cobas machine which applied electro-chemiluminescence immunoassay technique and thereafter a trimester specific ultrasound was performed to assess fetal well-being.

***Results*:** An analysis of the complete data of 107 participants was performed, one participant was excluded due to intrauterine fetal death based on ultrasound. The median age was 29 years. The median gestational age was 32.2 weeks with majority (61.7%) in the third trimester. Only eight (7.5%) had previously tested thyroid function while twelve (11.2%) had a family history of goiter. Six had thyroid dysfunction giving a prevalence of 5.6% (95% CI 1.9-10.2) with majority (5/6) being diagnosed with subclinical hypothyroidism. Only one participant had overt hypothyroidism and none with either overt or subclinical hyperthyroidism. Only one participant who had reported history of previous pregnancy loss had subclinical hypothyroidism. Ten participants who had a history of pregnancy loss had normal thyroid function tests. Study directed obstetric ultrasounds were carried out on 83 (77.6%) participants among whom eight (9.6%) had abnormal fetal well-being which was classified as being small for dates using trimester specific parameters. There was no significant association (p=0.646) between thyroid dysfunction and fetal well-being. However, the significance of this finding needs further evaluation to determine impact on fetal and maternal outcomes.

Conclusion: The prevalence of thyroid dysfunction among pregnant women attending ANC was at 5.6% with majority (5/6) diagnosed with subclinical hypothyroidism. There were very few study participants with thyroid dysfunction and hence this study was not able to assess any association with markers of fetal well-being.

Introduction

The thyroid gland is an important endocrine gland that has a lot of influence on the reproductive system. Due to the normal physiological changes that happen in pregnancy, the thyroid gland is under a lot of hormonal influence. In the first trimester, the rise in Beta Human Chorionic Gonadotropin (BHCG) leads to a rise in Free Thyroxine (FT_4) and Free Tri-iodothyronine (FT_3), and by negative feed-back to a suppression of Thyroid-Stimulating Hormone (TSH). Estrogen leads to an increase in Thyroxine-Binding Globulin (TBG), which leads to decreased FT4 levels. There is also altered iodine clearance in the kidneys and placental metabolism of thyroid hormone (1).

The most common disorder in pregnancy has been noted to be hypothyroidism with sub-clinical more prevalent than overt hypothyroidism. Nutritional deficiency most notable iodine is the most common factor involved in thyroid disease followed by autoimmune thyroiditis then others like thyroid nodules and malignancies which are rare (2). These conditions are difficult to diagnose in pregnancy as they have symptoms that mimic the normal physiological changes that occur in pregnancy. Risk factors associated with thyroid disease in women include: age more than 30 years, family history of thyroid disease, Body Mass index (BMI) more than 40kg/m^2, history of infertility, history of any other autoimmune disorder, use of amiodarone, lithium or recent neck radiation (2). Thyroid

dysfunctions are most prevalent in women between 15 – 35 years when a woman is considered most fertile and are associated with a lot of fetal and maternal complications if left untreated. The most feared complication has been neurocognitive problems in children born by mothers who suffered hypothyroidism. There is lack of data on the burden of thyroid dysfunction among pregnant women in Kenya and hence the need to undertake this study.

This study will form a definite foundation for future studies that will inform strategy or influence screening and management of thyroid dysfunction among pregnant women in Kenya.

Materials and methods

Between 1st and 30th September 2016 we enrolled all pregnant women attending the ante-natal clinic, we excluded, obstetric emergencies that warrant hospitalization and documented multiple pregnancy. The pregnant women provided written informed consent. The trial was approved by the ethics committee and University of Nairobi.

Study design: Consecutive sampling procedure used with each pregnant woman attending the ANC who fulfilled inclusion criteria being included in the study in order to achieve the sample size of 108. A study proforma was administered to capture demographic data, relevant history and a focused physical examination of the thyroid gland and the fundal height assessment was carried out by the principal investigator and the findings recorded. The TSH and FT4 estimation was by use of electro-chemiluminescence immunoassay using cobas machine. The study used the American Association Thyroid reference ranges for TSH and FT4 (3).

The ultrasound was performed at a study designated center (Plaza imaging) using General Electronics scan that uses a curvilinear probe with a frequency of 3-5 MHz. The scans were trimester-specific as this allowed assessment of the fetal well-being at different gestational ages.

Fetal well-being was assessed using all the following parameters:

(i) Estimated Fetal Weight (EFW) using Shepherd's formula (4) which was compared against the expected weight and if less than 10th percentile was noted as small for gestational age.

(ii) Head to abdominal circumference ratio: was calculated and a ratio greater than 2 Standard Deviations (SD) above the mean for GA was considered abnormal (5).

(iii) Doppler studies- were done at a gestation age of 28 weeks and above. The umbilical artery was evaluated and recorded as a ratio/ index. A systolic/ Diastolic (S/D) ratio >3.0 or RI (Resistive Index) >0.6 was considered abnormal (6).

(iv) Biophysical profile.

Fetal well-being was summarized as small for gestational age or normal-growth for gestational age based on parameters above, numbers 1-4. Any abnormal report of the numbers 1-4 above downgrades the fetal well-being and was classified as small for gestational age.

Results

The study participants were recruited between 1st and 30th September 2016. Approximately 400 pregnant women attended the ante-natal clinic during the study period. One hundred and thirty two consecutive pregnant women were approached and 24 who did not give informed consent were excluded. The final analysis included 107 participants due to exclusion of one due to intrauterine fetal demise based on obstetric ultrasound. The median age was 29 years, 100 (92.6%) were married, 86 (80.4%) had attained post primary education and 76 (71.0%) were employed.

Table 1: Baseline demographic characteristics of study participants

Characteristic	
Age	
Mean (SD)	29.3
Median	29
Range	18-39
Characteristic	Frequency (%) n=107
Education level	
Primary	21 (19.6)
Secondary	29 (27.1)
Tertiary	57 (53.3)
Employment status	
Yes	76 (71.0)
No	31 (29.0)

The median gestational age was 32.2 weeks (IQR 25-36.3) with a median fundal height of 32 centimeters (IQR 26.0-36.0). Sixty six(61.7%) were in the third trimester. The mean blood pressure recorded was 114.1/69.9 mmHg. Nine had abnormal blood pressure, among whom seven had a high blood pressure reading while two had a low blood pressure reading. Eight (7.4%) had previously been tested for thyroid function. Twelve had a family history of goiter. Only one participant was on follow up for goiter prior to pregnancy. Only one participant had history of previous neck radiation.

***Serum thyroid hormone profile*:** The median TSH and FT4 levels were at 1.85 mU/l (IQR 1.41-2.73) and 139.20 nmol/l (IQR-124-153.2) respectively and were within normal reference range as shown in Table 2. The reference levels used for TSH and FT4 were trimester specific as recommended by the ATA guidelines. The prevalence of thyroid dysfunction in this study was 5.6% (95% CI 1.9-10.2) as shown in Table 2. Six participants had elevated

TSH levels. Five had isolated elevated TSH levels with normal FT4 levels (sub-clinical hypothyroidism) while one had both elevated TSH levels and low FT4 levels (overt hypothyroidism). Among the six study participants with thyroid dysfunction two were in first trimester, one in second trimester and three in third trimester. The only study participant with overt hypothyroidism was in the third trimester. The participant with previous neck radiation exposure had subclinical hypothyroidism.

Table 2: Serum thyroid biochemical profile of study participants

Variable		
TSH (mU/l)		
Median (IQR)	1.85 (1.41-2.73)	
Range	0.31- 5.21	
FT4 (nmol/l)		
Median (IQR)	139.20 (124-153.2)	
Range	60.25- 193.20	
Variable	n=107 (%)	95% CI
Thyroid function status		
Dysfunction/ abnormal	6 (5.6)	1.9-10.2
Normal	101 (94.4)	89.8-98.1

Obstetric ultrasound results: Eighty four (77.8%) had fetal well-being assessment using study directed obstetric ultrasounds. The median gestational age (ultrasound derived) was 33 weeks. Only 9/84 (8.3%) had an obstetric ultrasound that did not correspond to clinical assessment; eight had small for gestational age fetus and one had Intra-Uterine Fetal Death (IUFD). The participant with IUFD was excluded in the analysis of the results (Table 3).

Table 3: Obstetric ultrasound findings of study participants

Variable	Frequency (%)
Gestation age (in weeks)	
Mean (SD)	30.0 (8.3)
Median (IQR)	33 (25.5-36.5)
Range	9 – 41
The overall fetal growth (n=84)	
Normal for gestational age	75 (69.4)
Small for gestational age	8 (7.4)
IUFD	1 (0.9)

There were very few study participants with thyroid dysfunction hence this study was unable to assess effect on fetal well-being.

Discussion

This is the first study carried out in Kenya that set out to evaluate thyroid function among pregnant women. Our study was able to demonstrate the prevalence of thyroid dysfunction at (5.6%); with subclinical hypothyroidism being the most common among pregnant women in third trimester attending ante-natal clinic at Kenyatta National Hospital, an urban tertiary public referral facility. This study was unable to demonstrate any association between thyroid dysfunction and fetal well-being due to the small sample size.

There are few studies carried out globally assessing thyroid dysfunction among pregnant women. Most of the studies have been carried out in Europe, Asia and few in Africa. A cross-sectional study in a referral hospital in Spain among 2509 pregnant women in the first trimester (median gestation 8 weeks, range 4–13 weeks) reported a prevalence of thyroid dysfunction at 16% (7). The high prevalence could be attributed to the use of national reference ranges used for TSH and FT4 which are higher than the reference ranges recommended by the American Thyroid Association (3).

A cross-sectional study among 1311 pregnant women within the first and third trimesters in Belgium documented a prevalence of thyroid dysfunction at 15.3%. The prevalence was higher in the first than third trimester. The study used the ATA trimester specific reference ranges. The high prevalence of thyroid dysfunction was attributed to iodine deficiency (8).

There have been only three African studies carried out on the prevalence of thyroid dysfunction among pregnant women. In Sudan, cross sectional hospital based study among 500 pregnant Sudanese women aged 15-45 years in all trimesters, found a prevalence of 9.4% which is higher than our study and this could be attributed to the use of national reference ranges instead of the American Thyroid Association trimester specific reference ranges (9).

A cross-sectional study carried out in Tunisia among 1519 pregnant women in all trimesters demonstrated a high prevalence of thyroid dysfunction at 9.7% which was attributed to iodine deficiency. This study used the ATA trimester specific reference ranges (10).

In Nigeria, a prospective case control study among 300 pregnant women and 100 age-matched non-pregnant controls reported a prevalence of thyroid disorders at 5.3% and 5%, respectively (11). This study used trimester specific population reference values. Majority of the participants were in the second and third trimester. The high prevalence of thyroid disorders could be attributed to the fact that the TSH upper reference value used in that study was high at 4.0 µIU/L irrespective of trimester.

Our study found a prevalence of thyroid dysfunction at 5.6% among pregnant women in the third trimester, using the ATA reference ranges. Other studies (9 -11) have reported a prevalence of between 9.4-15.3%. These high prevalence ranges are mainly attributed to use of population-specific reference ranges as opposed to ATA trimester specific reference ranges and also due to iodine deficiency. Unfortunately, here in Kenya national trimester specific reference ranges are not yet available. Despite the

high prevalence of thyroid dysfunction among pregnant women in this study we cannot recommend universal screening due to the small sample size.

This study was not able to demonstrate association between thyroid dysfunction and fetal well-being. The low rate of small for gestational age fetus and thyroid dysfunction in this study can be attributed to the small sample size. However other studies in Europe and Asia have been able to show associations between thyroid dysfunction and poor fetal and maternal outcomes (12).

Subclinical hypothyroidism has been associated with an increased risk of adverse maternal and fetal outcomes (13). On the other hand, overt hypothyroidism which is not as common as subclinical hypothyroidism has invariably been associated with an increased risk of poor pregnancy outcomes such as premature birth, low birth weight, pregnancy loss and impaired fetal neurocognitive development (14,15). This risk of poor fetal and maternal outcomes necessitates the need for close follow up and initiation of appropriate treatment in pregnant women with thyroid dysfunction

Conclusion

The prevalence of thyroid dysfunction among pregnant women attending ANC was 5.6%, majority (5/6) with subclinical hypothyroidism. Association between thyroid dysfunction and fetal well- being could not be established. This study establishes a useful platform for conducting further research in thyroid function among pregnant women in Kenya, because thyroid dysfunction is treatable thus potential fetal events are preventable.

Recommendations

The findings of this study are able to highlight the high prevalence of thyroid dysfunction but was unable to demonstrate the association with fetal well-being and hence a larger cross-sectional/longitudinal follow up study may be required to be able to demonstrate this association. Secondly, further studies to assess thyroid dysfunction among pregnant women in the first and second trimesters as these two groups were under represented in this study.

This is the first study to evaluate thyroid profile among pregnant Kenyan women and is able to highlight the magnitude of thyroid dysfunction among this population.

Limitations

The limitations of this study were firstly the study directed obstetric ultrasound were done once at point in time as opposed to serial to asses fetal well-being due to financial constraints. Secondly the study was carried out among a high-risk population of pregnant women who attend ante-natal clinic at Kenyatta National Hospital, a tertiary referral hospital and cannot be generalized to all the pregnant women in Kenya. Finally, due to the cross-sectional study design it was not possible to establish association between thyroid dysfunction and fetal well-being because the fetal changes associated thyroid dysfunction may be more functional than structural ultrasound detectable changes.

Acknowledgement

I would like to appreciate my supervisors, the staff at Kenyatta National Hospital at the reproductive clinic and patients who accepted to participate in my study.

References

1. Burrow GN, Fisher DA, *et al*. Maternal and fetal thyroid function. *N Engl J Med*. 1994; **331**:1072-1078.
2. Vaidya B, Anthony S, Bilous M, *et al*. Detection of thyroid dysfunction in early pregnancy: universal screening or targeted high-risk case finding? *J Clin Endocrinol Metab*. 2007; **92**:203-207.
3. Stagnaro-Green A, Abalovich M, Alexander E, *et al*. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. American Thyroid Association Taskforce on Thyroid Disease during Pregnancy and Postpartum. *Thyroid*. 2011; **21**:1081-1125.
4. Shepard MJ, Richards VA, Berkowitz RL, *et al*. An evaluation of two equations for predicting fetal weight by ultrasound. *Am J Obstet Gynecol*. 1982; **142:** 47-54.
5. Campbell S, Thoms A. Ultrasound measurement of the fetal head to abdomen circumference ratio in the assessment of growth retardation. *Br J Obstet Gynaecol.* 1977; **84**:165.
6. Maulik D, Yarlagadda P, Youngblood JP, *et al.* The diagnostic efficacy of the umbilical arterial systolic/diastolic ratio as a screening tool: a prospective blinded study. *Am J Obstet Gynecol*. 1990; **162**:1518.
7. Marta Diéguez *et al*. Prevalence of thyroid dysfunction in women in early pregnancy. *Clin Endocrinol*. 2016; **84**(1):121-126.
8. Moreno-Reyes R, Glinoer D, Van Oyen H, *et al*. High prevalence of thyroid disorders in pregnant women in a mildly iodine-deficient country: A population-based study. *J Clin Endocrinol Metab*. 2013; **98** (9): 3694-3701.
9. Saeed AK, Yassin K, Elmahdi EMA, *et al*. The prevalence of thyroid dysfunction among Sudanese pregnant women. *SOJ Gynecol Obstet Womens Health*. 2015; **1**(1): 5.
10. Feki M, Omar S, Menif O, *et al*. Thyroid disorders in pregnancy: frequency and association with selected diseases and obstetrical complications in Tunisian women. *Clin Biochem*. 2008; **41**:927–931.

11. El-Bashir JM, *et al*. Prevalence of gestational thyroid disorders in Zaria, north-western Nigeria. *Ann Nigerian Med.* 2015; **9**:51-55.
12. León, *et al*. Maternal thyroid dysfunction during gestation, preterm delivery, and birthweight. The Infancia y Medio Ambiente Cohort, Spain. *Paediat Perinat Epidemiol.* 2015; **29**: 113–122.
13. Männistö T, Mendola P, Grewal J, *et al*. Thyroid diseases and adverse pregnancy outcomes in a contemporary US cohort. *J Clin Endocrinol Metab*. 2013; **98** (7): 2725-2733.
14. Allan WC, Haddow JE, Palomaki GE, Williams JR, Mitchell ML, *et al*. Maternal thyroid deficiency and pregnancy complications: implications for population screening. *J Med Screen*. 2000; **7**:127-130.
15. Casey BM, Dashe JS, Wells CE, McIntire DD, *et al*. Subclinical hypothyroidism and pregnancy outcomes. *Obstet Gynecol*. 2005; **105**:239-245.

East, Central and Southern Africa College of Physicians

A constituent college of the ECSA College of Health Sciences

Background: Over a billion people worldwide have little or no access to health services and the help and advice of health workers. As a result, millions die or are disabled every year. Health workers are the cornerstone and drivers of health systems. And yet the world is facing a serious shortage of health workers – a shortage that is identified as one of the most critical constraints to the achievement of health and development goals. This crisis is impairing the provision of essential, life-saving interventions such as childhood immunization, safe pregnancy and delivery services for mothers, and access to treatment for HIV/AIDS, malaria and tuberculosis. New and innovative initiatives are urgently needed to increase the numbers of trained health workers (WHO *Scaling Up Saving Lives* Report).

The challenge*:* The current number of health workers being educated and trained in Africa is too small to make a difference. This is compounded by the fact that there is little international coordination of effort and, all too often, differential salary scales between public sector, international and private organizations, which drive up costs and lead to movement from the public sector, and significant international migration of health workers.

East, Central and Southern Africa Health Community

As a result, the lack of access to well-trained physicians in the countries of the East, Central and Southern Africa Health Community remains stark (<10 doctors per 100,000 population). Most graduates of existing health training programs choose to stay in large cities due to the lack of clinical support, poor pay and working conditions in rural hospitals; all of which leads to a major rural–urban disparity. Meanwhile, Africa struggles to retain its precious health workers. Approximately 65,000 African-born physicians, or about one-fifth of those trained, have migrated to high-income countries within 5 years of completing their training.

Our solution: ECSACOP is rewriting the way in which post-graduate medical education is delivered and assessed in East, Central and Southern Africa. With a common curriculum and standardised training methodologies, our post-graduate medical qualification will be accepted as gold standard throughout the region. Blended learning, using the best of the new technologies, will radically change the way in which trainers and trainees interact.

This is a 'College without Walls', with faculty from a multitude of nations learning and developing together, sharing experience, and refining curricula for the emerging cadre of physicians that will go on to lead health systems across the region. This new cadre of physicians will be better equipped to lead, to manage and to steward the vital resources that can dramatically improve health outcomes for all, especially those in remote or difficult-to-reach communities.

Expanding the number of health workers, and transforming their education at the same time, has the potential to accelerate health equity and inclusive economic growth. Employing these additional health workers in national programmes to deliver universal health coverage can be a trigger for economic revival. ECSACOP itself is designed to be self-sustaining after a number of years. Once established, ECSACOP examinations, courses and workshops will become income earners for the College, allowing us to reinvest in scholarships. Our focus on equipping physicians with the requisite skills to become effective teachers and leaders - as much as effective clinicians - will radically improve the management of health systems in the region.

Local, regional and international organizations are working together to build South–South, South–North, regional and public–private partnerships, to deliver

increased investment; build up the necessary infrastructure of knowledge and expertise in basic science, public health and management; create centers of excellence; and deliver innovative education and training, based on countries' burdens of disease and healthcare systems, and with support from developed countries. The guiding principles for our model of training are to:

- address country health needs and embed education and training in the health system;
- increase equity and efficiencies of scale through innovation in curriculum design and delivery; and
- enhance quality through leadership and collaboration.

Aims and objectives: ECSACOP aims to improve access to well-trained physicians across the region by establishing a network of dedicated training centers and implementing an internationally recognized postgraduate medical qualification.

Aim 1 - We will work in partnership with governments, universities and healthcare providers to expand and improve postgraduate training and provision of quality healthcare.
Goals - Expand the current annual output from internal medicine postgraduate training programs in the region by 50% by 2025, doubling capacity by 2030.
- Develop a core, common curriculum in internal medicine across the region, training that is formally recognized by all relevant accrediting, government and regulatory bodies.
- Develop a high-quality assessment and examination programme, involving all relevant stakeholders.
- Identify, support and accredit training centers and trainers to deliver the curriculum.
- Implement continuous quality improvement of programs, building on learning and experience as well as harnessing new innovations.

Aim 2 - We will be a voice for the patient and the profession, recognized as a regional leader in advocating for healthcare improvement and disease prevention.
Goals - Build relationships with governments, healthcare providers and training institutions to advocate on access to well-trained physicians, workforce planning and healthcare financing.

Aim 3 - We will support physicians' lifelong learning and career development.
Goals - Develop a programme of high-quality Continuing Professional Development (CPD) for physicians, using innovative models of delivery to facilitate access for all.
- Establish partnerships with the public, charitable and private sectors where innovative approaches are being used to deliver lifelong learning.
- Support physicians delivering postgraduate training with professional development, leadership training and mentoring

ECSACOP will move learning closer to the community, using modular education and action learning. We will increase use of information and communication technologies and provide improved education through quality assurance programmes. Furthermore, we will build institutional capacity by: expanding teaching capacity; fostering twinning and partnerships; maximizing our impact through a regional approach; and harnessing public–private partnerships.

Indeed, ECSACOP will improve access to well-trained physicians across the region through establishing a network of dedicated training centers and implementing an internationally recognized postgraduate medical qualification, delivered by our faculty, a group of highly qualified 'master physicians'. Our ultimate goal is to double the output of physicians being trained in the region by 2030.

Fellowship: The East Central and Southern Africa College of Physicians (ECSACoP) awards Fellowships through instruction and examinations. Enrolled trainees participate in full-time instruction in approved training institutions.

The Fellowship (Part 1) examination leads to admission into the final part of training. The Fellowship (final) examination leads to the qualification of Fellow of the East Central and Southern Africa College of Physicians, FCP (ECSA). This qualification is a recognition that the candidate has reached the level of knowledge and practice of internal medicine sufficient to practice independently at a consultant or specialist level.

The Physician will be skilled in the management of acute unselected medical emergencies, patients with multiple conditions and the management of patients with chronic diseases. The management includes all medical and psychosocial factors that contribute to preserving life and to improving the quality of life. Emphasis will be placed upon how the environment influences both disease manifestations as well as the capacity of the patient (and care givers) to effectively manage health issues.

In order to attain these attributes, the Physician will be trained in common diseases affecting various body systems or medical sub-specialties, including but not limited to: Infectious and tropical diseases; Cardiology; Respiratory medicine; Gastro-enterology and hepatology; Endocrinology and diabetes; Neurology; Genito-urinary medicine; Nephrology; Rheumatology and rehabilitation; Medical oncology; Palliative medicine; Dermatology; Clinical pharmacology; Therapeutics and toxicology; Geriatrics; Psychological medicine and intensive care. The trainee will be expected to acquire a sound understanding of basic sciences that underlie the practice of medicine, that include anatomy, physiology, biochemistry and pathology.

Applicants for training towards the FCP(ECSA) must have completed the requisite internship and compulsory post internship training in approved posts (as required by the respective registration authority in their countries). The duration and learning content will vary from country to country. Certification of satisfactory completion of internship is determined by the individual national registration authority in a given country. In many countries,

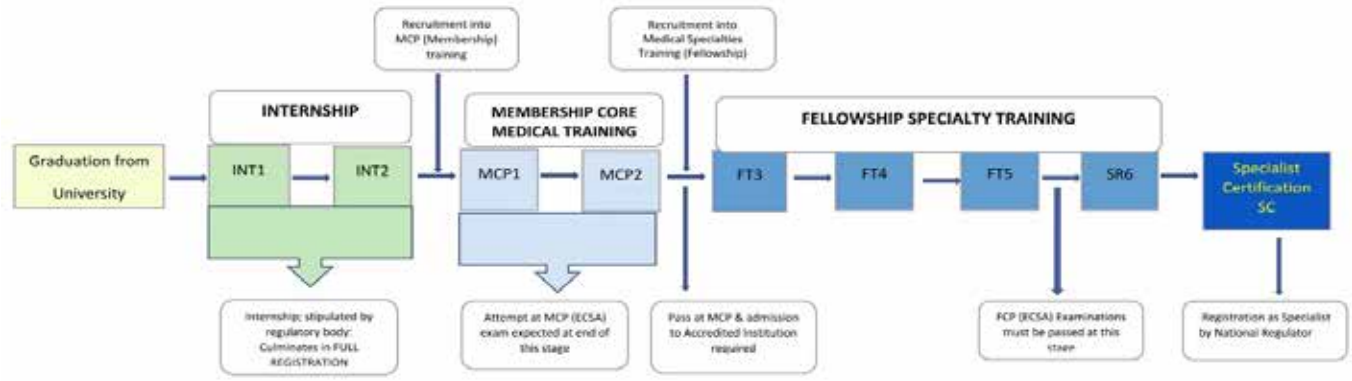
this period covers internship or "housemanship" rotations and, in addition, other postings are compulsory before the doctor is eligible for registration as an unrestricted practitioner.

Duration and organization of training: The total duration of training is four years following admission into the FCP(ECSA) training programme. All years of training are directed and supervised. The trainees will follow a spiral curriculum, where certain concepts and skills are taught every year, but in increasing complexity of the subject matter as well as requiring higher levels of proficiency in the student's capacity to deal with any given topic. Thus the topics during different periods of training may appear to be similar from year to year, but the ways these topics are addressed and the complexity of concepts will vary greatly.

ECSACOP admits applicants from a wide variety of educational backgrounds. It is an important aspect of the training programme that all trainees must achieve a uniform minimum level of competence during the first half of training. The first two years of training culminates in the Part 1 examination and is designed to achieve a minimum level of competence with regards to basic applied science, diagnostic methods and patient holistic approach to management. Emphasis is placed on integrating these components into the student's ability to deal with important as well as common clinical presentations. The FCP (1) examination, the passing of which is a prerequisite for advancing to the second half of the training, is designed to assess understanding of the basic principles of medicine, the ability to evaluate and manage common/important ways of presentation in an ill person and broad knowledge in general medicine. On completion of Part 1 training, successful candidates are expected to competently manage medical emergencies as well as to provide a defined level of care in wide variety of important conditions. Passing of the Part 1 FCP examination does not confer specialist status, but empowers the individual in dealing with the more complex and more demanding part of the training.

All trainees are required to register with, and to work in, health institutions that are accredited by ECSACOP. Training will be carried out both in Designated Health Institutions (DHI) and in teaching hospital(s) or other major centers that have at least two designated teaching consultants (Educational Supervisors). In addition, one consultant within the same country will act as Programme Director to the trainee. Initially, all trainees will enter the programme for Internal Medicine specialty alone. In years to come, many trainees will train for dual certification with another specialty (e.g. cardiology, nephrology etc.). However, even at that time, specialist training in Internal Medicine alone will be a perfectly acceptable (even encouraged) option.

An important and large component of training will be work-based, under the supervision of designated teachers, supervisors and coordinators. The faculty will participate from different localities, including local institution, national and regional members. In addition, trainees will attend compulsory courses, participate in regular eLearning programmes as well as small group seminars.



KEY: PROPOSED ECSACOP TRAINING PATHWAY: SPECIALTY OF GENERAL INTERNAL MEDICINE

INT	Internship Years (they vary according to country from one to three years)
MCP	Core Medical (formal, supervised) training in Medicine; culminating in Membership examination
FT	Fellowship Specialty Training in Medical Specialities
SR	Senior Registrar year: Post-exams year, working within a team, under senior consultant
SC	Specialist Certification: recognition by national regulatory body of status of independent specialist practitioner

March, 2016

During the first 2 years, whilst the trainee will be working towards the FCP Part 1 examination, he/she will be resident for at least 4 days per month for acute unselected medical intake. It is essential that the trainee is responsible (i.e. involved in decision making) for the continued care of general medical patients.

The correct use of diagnostic tests forms an important part of training. Trainees are expected to master these competences in different contexts including work-based activity, didactic sessions and e-learning platforms. It is essential that trainees must acquire practical skills which may be needed at any time in the management of medical emergencies.

Regional workshops may need to be arranged in order to cater for core training requirements that are difficult to provide on an individual country basis. Details of the requirements for training in Internal Medicine are set out in this document.

Assessment: During the first 2 years of training, and in preparation for the Part 1 examination, trainees are required to cover all 5 competencies groups, to a level 2 of attainment in all topics unless otherwise. Competence to at least level 2 descriptors will be expected prior to progression into year 3 of ECSACOP specialty training. The first three common competencies cover the simple principles of history taking, clinical examination, decision making and clinical reasoning and therapeutics and prescribing.

Since there is a hierarchy of competencies within the curriculum, it is expected that emphasis in the Part 1 (as measured by depth and breadth of knowledge) will be placed on the common competences, emergency presentations and top presentations as indicated in the syllabus below, and will be greater than that for the other important presentations. In Part 2 of the instruction and examination, the entire syllabus is given uniform importance. An e-Portfolio curriculum record should be used to present evidence in an organized way to enable the educational supervisor and the relevant College committees to determine whether satisfactory progress is being achieved. These include supervised learning events, evaluation of clinical cases and personal performance. In addition, the record will indicate activity to directed e-learning modules, literature review, workshops, audit or quality improvement and assessments. Teaching attendance should be recorded.

Procedures should be assessed using direct observation modules; initially formative for training then summative direct observational procedural skills modules to confirm competence where required. Summative sign off for routine procedures is to be undertaken on one occasion with one assessor to confirm clinical independence. Summative sign off for potentially life threatening procedures should be undertaken on two occasions with two different assessors (one assessor per occasion).

An educational supervisor's report covering the whole training year, accompanied by the e-Portfolio curriculum should be submitted to the appropriate committees of the College. The educational supervisor will receive feedback on a trainee's clinical performance from at least one other clinician through direct discussion and the use of the multiple consultant report. Great emphasis is placed on the educational supervisor confirming that satisfactory progress in the curriculum is being made compared to the level expected of a trainee at that stage of their training. This report should bring to the attention of the committee anything of concern e.g. patient safety issues, professional behaviour issues, poor performance in work-place based assessments, and issues reported by other clinicians. It is expected that a seriously adverse report would trigger a formal committee review. Each candidate requires a satisfactory review by the committee before he/she can sit either FCP Part 1, or FCP Part 2 examinations.

Faculty Development: Will involve a combination of residential and distance learning activities, focused on developing the leadership, project management and programme evaluation skills of participants, as well as teaching the key principles of health profession education-curriculum design, teaching and learning and assessment**.**

Given the paucity of teachers, it is important that the curriculum, particularly at the in-service level, prepares learners to teach those who follow. Including teaching as a core competency, as is the case in countries such as Australia, Canada, the United Kingdom and the United States, and providing learners with the opportunity to develop their teaching skills, will add significantly to the stock of teachers.

There are many ways of improving collaboration and sharing of information among education leaders to stimulate and sustain innovation. These include, among others, networks of academic partners in developing and developed countries, 'clearing houses' for open consultation and advice on specific problems, and more systematic global partnerships for sustained linkages, learning and support.

Training the Educators: ECSACOP has started bringing together and training a cohort of senior physicians from across the region to ensure that those enlisted to teach at ECSACOP Training Centers have excellent, current skills in transferring knowledge to adults. This group of African medical leaders - the faculty - is learning and training together, familiarizing itself with the newly developed ECSACOP training curriculum, while adopting the same regional training methodologies - an essential step before training can begin at the identified sites. Senior physicians first assembled in Lusaka, Zambia in May 2017, to undertake an intensive 3-day Educational Leaders' course, which led to:

- 21 educational leaders with a refreshed and reinvigorated sense of what being an educator entails
- Self-awareness around educational capabilities and competencies across the group
- A community of practice – a coherent faculty, networked and collegiate
- Shared values and ambitions for the future of ECSACOP
- Co-developed written documents – Accreditation tool-kit; refinements to syllabus and curriculum

A second course was carried out between 1st-3rd October 2017 in Entebbe, Uganda, immediately after our second AGM and Scientific Conference. Around 20 participants attended each course, delivered by 3-4 specialist trainers who have been recruited through the Royal College of Physicians (London).

Faculty Development Coursework will enable faculty to write teaching objectives, plan and structure teaching sessions, select appropriate evaluation techniques and perform work-place based assessments. Specific sessions on good supervisory practice, mentoring and apprenticeship learning skills will be highly relevant.

Presently, many educators within the region's MMed programmes have received little, if any, training in how to be an effective teacher. Our curriculum is designed to prepare learners to teach those that follow. ECSACOP teachers will be regularly assessed alongside ECSACOP training sites by cross-border assessors. Course content will be continuously updated and tools (e.g. real-time messaging) will be put in place to encourage ECSACOP teachers and trainers to interact and share learnings, thus building a truly regional faculty.

Partners: ECSACOP's principal 'champion' and sponsor thus far has been the Royal College of Physicians in London. As the RCP moves towards its 500th Anniversary in 2018, it was wanting to initiate something purposeful in commemoration of this occasion. As such, it determined to help establish a new College of Physicians in the region of the world that might most benefit from such an organization. The RCP contributes staff time and expertise, financial support, logistical and finance management, and general cheer-leading.

The Infectious Diseases Institute (IDI), located in Kampala, Uganda, is our 'host' in the region. IDI has trained over 19,000 health workers from Uganda and 27 other African countries and we are grateful for their guidance, their mentorship and for housing our staff.

The National Associations of Physicians in our six member states are our principal collaborators when it comes to the identification and recruitment of training sites and trainers, curriculum design, accreditation and quality control.

Outputs: Number of accredited training sites - 12 sites operational within 3 years (2020/21); 18 sites operational by 2025.

Number of physicians who have participated in our Faculty Development Program - 40 individuals in 2017 and 2018.

Number of faculty teaching the new qualification - 24 faculty trained and teaching by 2020/21, with around 50 faculty in place by 2025.

Number of physicians trained - starting with 2-3 trainee physicians per site initially, eventually becoming 4-6 per site; thus, circa 72-108 trainee physicians enrolled in our postgraduate medical qualification by 2025.

For More Information Contact
Secretariat: 5th Floor
IDI- McKinnel Knowledge Centre
Makerere University, Kampala
P.O.Box 22418, Kampala
Tel: +256 41 4307000
www.ecsacop.org

Instructions to authors

The *Journal of Kenya Association of Physicians (JOKAP)* is a quarterly journal published by the Kenya Association of Physicians.

Authors submitting manuscripts to JOKAP do so on the understanding that if accepted they surrender all copyright to the journal. No part of this journal may be reproduced or transmitted in any form without the written permission of the Editor-in-Chief.

The following categories of manuscripts will be considered for publication;

(i) **Original articles**: The article must contribute further to the existing knowledge of the subject. This must follow the IMRAD format with the following sub-headings: Title; Structured abstract with the following sub-titles; background, objective(s), study design, methods, results and conclusion(s); Introduction; Materials and Methods; Results; Discussion; Conclusion(s), Recommendations (if any) and References (not exceeding 25. The article should not exceed 4000 words including text, figures, tables and references.

(ii) **Reviews**: This must be a critical analyses of the subject reviewed. Reviews should preferably be written by an expert in that particular area and can be commissioned by the Editor-in-Chief. Reviews should not exceed 6000 words including tables, figures and references. The format should be as follows; title, structured abstract (with the following sub-headings; objective(s); data source, conclusions), Introduction and sub headings where necessary, results and conclusion(s) and references not exceeding 40.

(iii) **Case reports:** This should be unique clinical syndromes or presentations. They should not exceed 2500 words. The format should be a Title, Abstract (prose form) not exceeding 200 words, Introduction, Case report, Discussion, Acknowledgement(s) and references not exceeding 15.

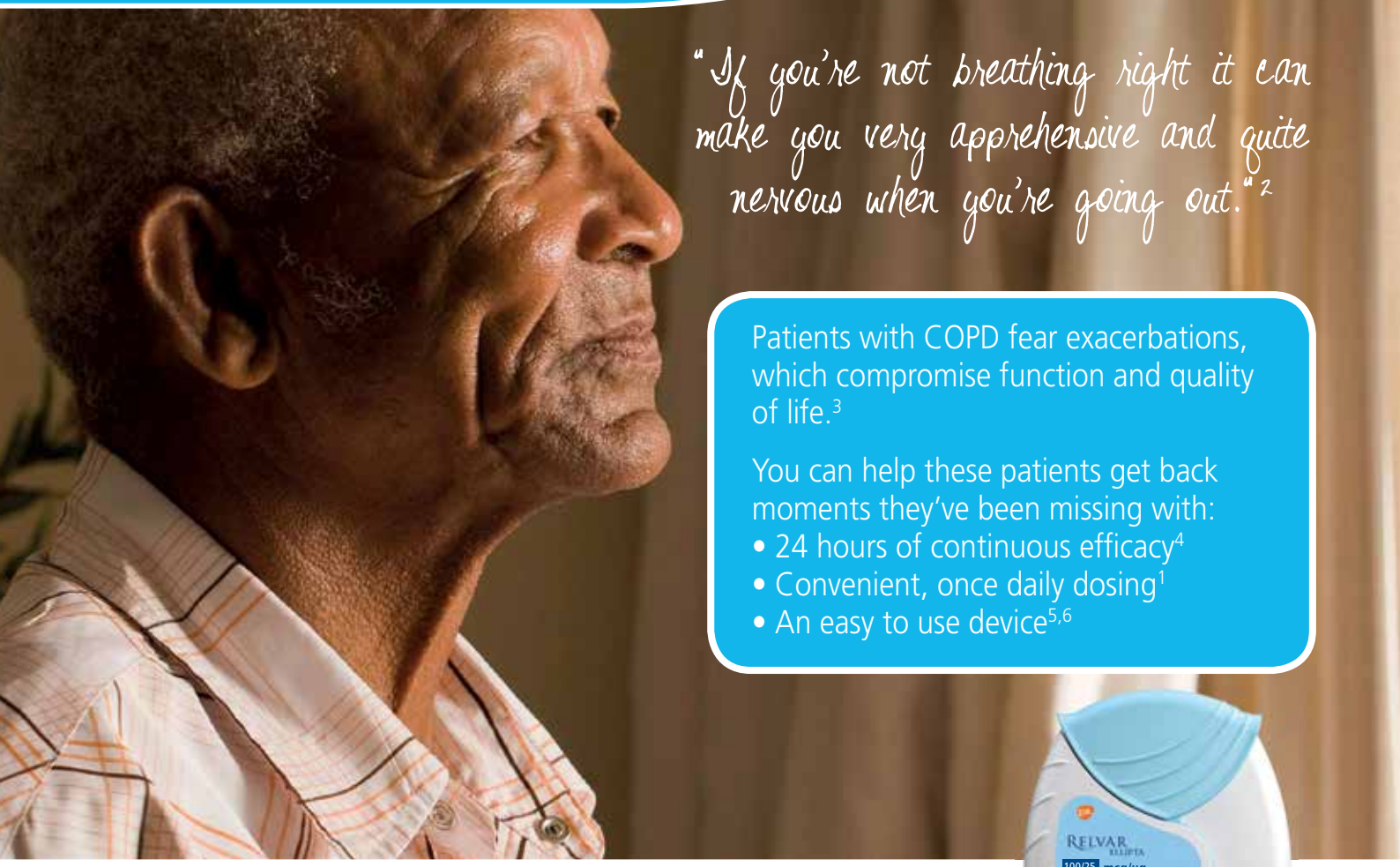
(iv) **Short communication:** This should possess all the elements of a scientific paper but should be presented in prose form without sub-headings. It should have not more than 1500 words and 10 references.

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

COPD

RELVAR ELLIPTA 100/25 µg is an ICS/LABA indicated for the maintenance treatment of airflow obstruction in adult patients with chronic obstructive pulmonary disease (COPD) including chronic bronchitis and/or emphysema and to reduce exacerbations of COPD in patients with an exacerbation history[1]



"If you're not breathing right it can make you very apprehensive and quite nervous when you're going out."[2]

Patients with COPD fear exacerbations, which compromise function and quality of life.[3]

You can help these patients get back moments they've been missing with:

- 24 hours of continuous efficacy[4]
- Convenient, once daily dosing[1]
- An easy to use device[5,6]

WARNINGS AND SPECIAL PRECAUTIONS: Not to be used to treat acute asthma symptoms or an acute exacerbation in COPD. Increasing use of short-acting bronchodilators to relieve symptoms indicates deterioration of control and patients should be reviewed by a medical practitioner. **CONTRA-INDICATIONS:** Patients with severe milk-protein allergy or who have demonstrated hypersensitivity to either fluticasone furoate, vilanterol or any of the excipients.

RELVAR ELLIPTA

(fluticasone furoate and vilanterol inhalation powder)

Practical efficacy[5,7]

SIDE EFFECTS: Very Common: headaches, nasopharyngitis. Common: pneumonia, upper respiratory tract infection, bronchitis, influenza, candidiasis of mouth and throat, oropharyngeal pain, sinusitis, pharyngitis, Rhinitis, Cough, Dysphonia, abdominal pain, arthralgia, back pain, fractures, pyrexia. Uncommon: extrasystoles.

COPD = Chronic Obstructive Pulmonary Disease
ICS = Inhaled corticosteroid
LABA = Long acting beta$_2$-agonist

References: 1. Relvar Ellipta Prescribing Information prepared in September 2017 based on GDS version 09/IPI 10 dated 30 May 2017. **2.** GSK data on file HO-15-15502. 2016. **3.** Rennard S, Higenbottam T. Exacerbation-free COPD: A goal too far? *Proc Am Thorac Soc.* 2007;4:583–585. **4.** Boscia JA, *et al.* Effect of once-daily fluticasone furoate/vilanterol on 24-hour pulmonary function in patients with chronic obstructive pulmonary disease: a randomized, three-way, incomplete block, crossover study. *Clin Ther.* 2012;34(8):1655–1666.e5. **5.** Svedsater H, *et al.* Qualitative assessment of attributes and ease of use of the Ellipta dry powder inhaler for delivery of maintenance therapy for asthma and COPD. *BMC Pulm Med* 2013;13:72. **6.** Riley JH, *et al.* Correct usage, ease of use, and preference of two dry powder inhalers in patients with COPD: analysis of five phase III, randomized trials. *Int J Chron Obstruct Pulmon Dis.* 2016;11:1873–1880. **7.** Vestbo J *et al.* Effectiveness of fluticasone furoate-vilanterol for COPD in clinical practice.. NEJM 2016. DOI: 10. 1056/NEJMoa 1608033.

RELVAR ELLIPTA. Fluticasone furoate/vilanterol. Each pre-dispensed dose contains either 100/25 micrograms or 200/25 micrograms of fluticasone furoate/vilanterol (as trifenatate). Inhalation powder. Each single inhalation of fluticasone furoate/vilanterol provides a delivered dose of 92/22 micrograms of fluticasone furoate/vilanterol or 184/22 micrograms of fluticasone furoate/vilanterol. Inhalation powder. **INDICATIONS: Asthma:** For the maintenance treatment of asthma. **COPD:** For the maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD) including chronic bronchitis and/or emphysema and to reduce exacerbations of COPD in patients with an exacerbation history. **Dosage and Administration:** *RELVAR ELLIPTA* is for inhalation only. *RELVAR ELLIPTA* should be administered once daily either morning or evening but at the same time every day. After inhalation, the patient should rinse their mouth with water without swallowing. **Asthma: Adults and adolescents aged 12 years and over.** One inhalation of *RELVAR ELLIPTA* 100/25 micrograms once daily. Or One inhalation of *RELVAR ELLIPTA* 200/25 micrograms once daily for patients who require a higher dose of steroid or patients inadequately controlled on *RELVAR ELLIPTA* 100/25 micrograms. **COPD (adults):** One inhalation of *RELVAR ELLIPTA* 100/25 micrograms once daily. *RELVAR ELLIPTA* 200/25 micrograms is not indicated for patients with COPD. **Special populations (Asthma and COPD):** ***Elderly:*** No dosage adjustment. **Renal impairment:** No dosage adjustment. **Hepatic impairment:** Caution should be exercised as patients with hepatic impairement may be more at risk of systemic adverse reactions associated with corticosteroids. **Contraindications:** Contraindicated in patients with severe milk-protein allergy or who have demonstrated hypersensitivity to either fluticasone furoate, vilanterol or any of the excipients. **Warnings and Precautions:** Not to be used to treat acute asthma symptoms or an acute exacerbation in COPD, for which a short-acting bronchodilator is required. Patients should not stop therapy with *RELVAR ELLIPTA*, in asthma or COPD, without physician supervision. Paradoxical bronchospasm may occur. Treat immediately with a short-acting inhaled bronchodilator. Discontinue immediately. The patient should be assessed and alternative therapy instituted if necessary. *RELVAR ELLIPTA* should be used with caution in patients with severe cardiovascular disease. For patients with moderate to severe hepatic impairment, the 100/25 micrograms dose should be used. Systemic corticosteroid effects such as HPA axis suppression, decrease in bone mineral density, growth retardation in children and adolescents, cataract and glaucoma may occur especially with high doses. Administer with caution in patients with pulmonary tuberculosis or in patients with chronic or untreated infections. An increase in pneumonia has been observed in patients with COPD. Risk factors for pneumonia in patients with COPD receiving *RELVAR ELLIPTA* include current smokers, patients with a history of prior pneumonia, patients with a body mass index <25 kg/m^2 and patients with a (forced expiratory volume) FEV$_1$<50% predicted. These factors should be considered when relvar is prescribed and treatment should be re-evaluated if pneumonia occurs. **Interactions:** Beta-adrenergic blockers may weaken or antagonise the effect of beta$_2$-adrenergic agonists. Concurrent use of both non-selective and selective beta-blockers should be avoided. Care is advised when co-administering with strong CYP 3A4 inhibitors (e.g. ketoconazole, ritonavir) as there is potential for an increased systemic exposure. **Pregnancy and Lactation:** Safety not established. **CLINICAL TRIALS: Adverse Reactions: Very common:** Headache, Nasopharyngitis. **Common:** Pneumonia, Upper Respiratory Tract Infection, Bronchitis, Influenza, Candidiasis of mouth and throat, Oropharyngeal pain, Sinusitis, Pharyngitis, Rhinitis, Cough, Dysphonia, Abdominal pain, Arthralgia, Back pain, Fractures, Pyrexia. **Uncommon:** extrasystole. **POST-MARKETING DATA: Adverse reactions: Common:** Muscle spasms. **Rare:** Hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticarial, Anxiety, Tremor, Palpitations, Tachycardia Paradoxical bronchospasm. **Ability to Drive and Use Machines:** No studies. **Management of overdose:** There is no specific treatment for an overdose with *RELVAR ELLIPTA*. If overdose occurs, the patient should be treated supportively with appropriate monitoring as necessary. Cardioselective beta-blockade should only be considered for profound vilanterol overdose effects that are clinically concerning and unresponsive to supportive measures. Cardioselective beta-blocking drugs should be used with caution in patients with a history of bronchospasm. Further management should be as clinically indicated or as recommended by the national poisons centre, where available. **List of Excipients:** Lactose monohydrate (which contains milk protein) (12.5 milligram lactose monohydrate per blister) Magnesium stearate. Storage condition depends on local registration requirements. **Following removal from tray, the product may be stored for a maximum period of:** 6 weeks: below 25˚C or 1 month: below 30˚C. Write the date the inhaler should be discarded on the label in the space provided. The date should be added as soon as the inhaler has been removed from the tray. If stored in the refrigerator, allow the inhaler to return to room temperature for at least an hour before use. ***GSK is committed to the effective collection and management of human safety information relating to our products and we encourage healthcare professionals to report adverse events to us on +254 20 693 3200/0722 742 998 or email us on ke.safety@gsk.com.*** Full Prescribing Information is available on request from GlaxoSmithKline Pharmaceutical Kenya Limited, P.O. Box 78392-00507, 23 Likoni Road, Industrial Area, Nairobi, Kenya. Abbreviated Prescribing Information prepared in September 2017 based on GDS version 09/IPI 10 dated 30 May 2017.

EA/FFT/0004/18a Date of preparation: February 2018

RELVAR ELLIPTA was developed in collaboration with INNOVIVA

GlucoWell®

VILDAGLIPTIN

GlucoWell®-MET

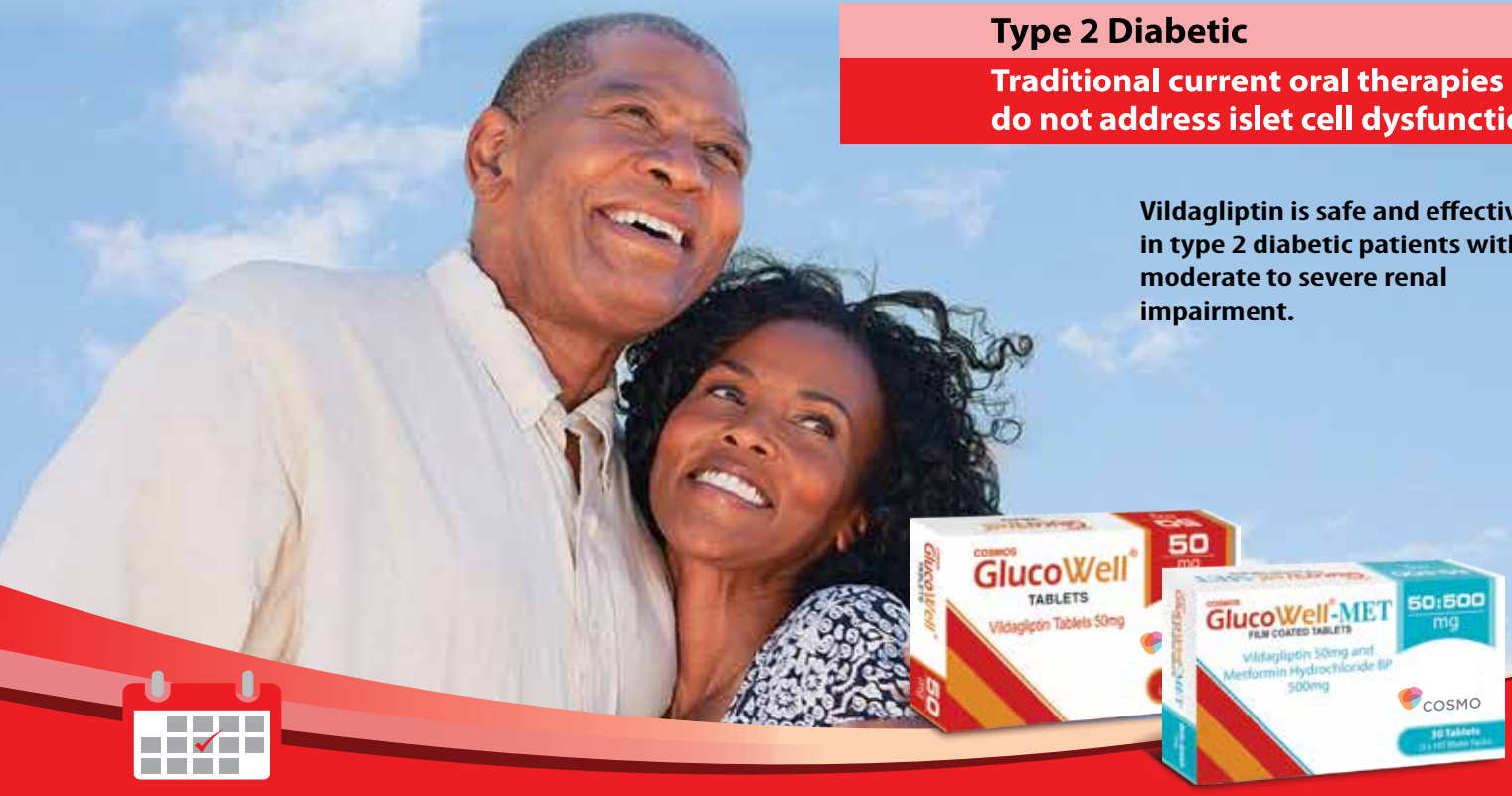
VILDAGLIPTIN AND METFORMIN HYDROCHLORIDE

COSMOS

Type 2 Diabetic

Traditional current oral therapies do not address islet cell dysfunction

Vildagliptin is safe and effective in type 2 diabetic patients with moderate to severe renal impairment.



PATIENT COMPLIANCE CALENDAR PACK

MEDICINE YOU CAN TRUST

Induric® SR

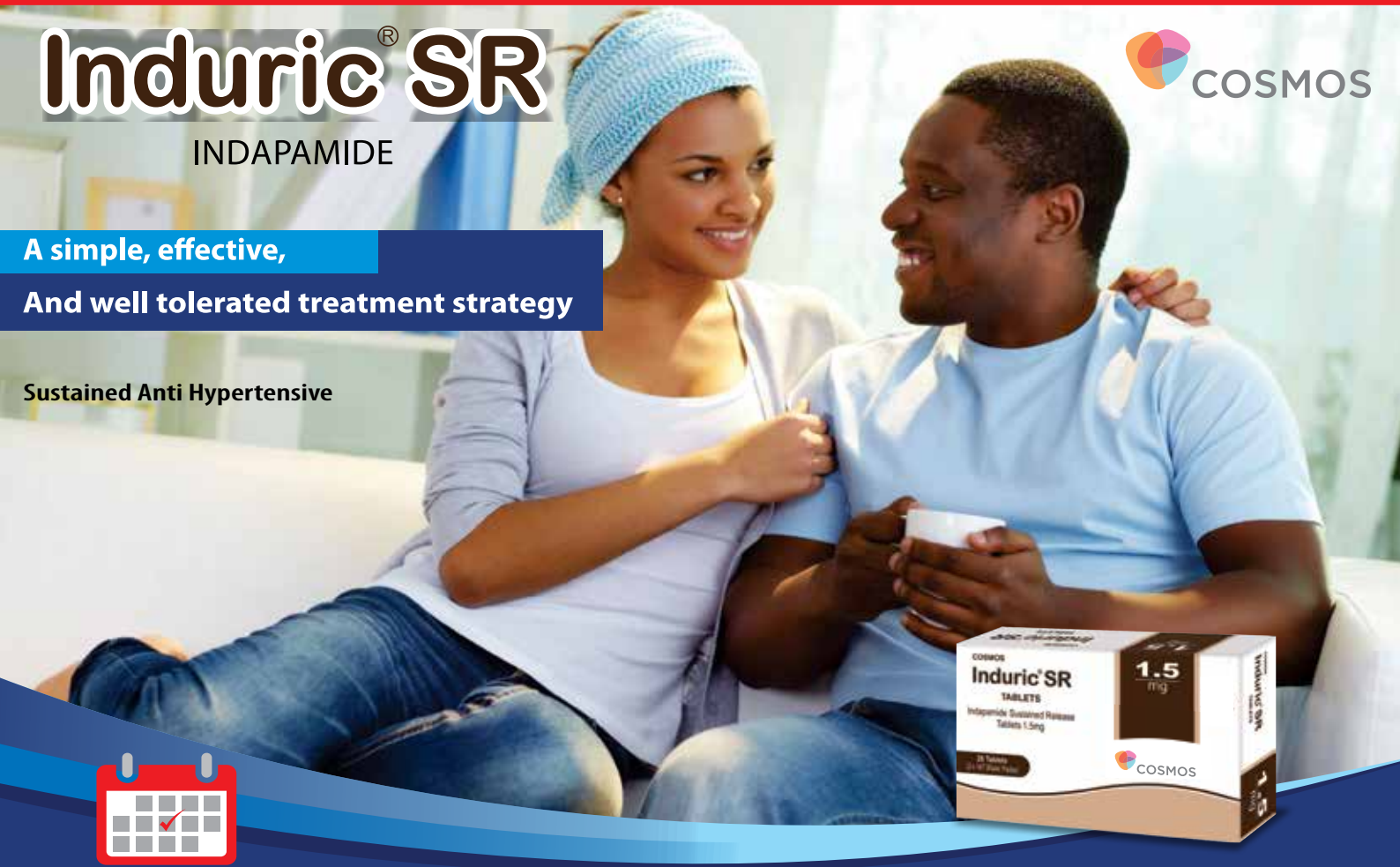
INDAPAMIDE

COSMOS

A simple, effective,

And well tolerated treatment strategy

Sustained Anti Hypertensive



PATIENT COMPLIANCE CALENDAR PACK

MEDICINE YOU CAN TRUST

Rangwe Close / Rangwe Road, Off Lunga Lunga Road, Industrial Area, Nairobi. | P.O Box 41433 GPO, Nairobi 00100, Kenya
Cell No.0722 333 834 /0733 666 834 Pilot Line: 0709 864000 E-mail:sales@cosmos-pharm.com www.cosmos-pharm.com