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GULU UNIVERSITY MEDICAL JOURNAL VOL 6



IN THIS ISSUE

The Odongo-Aginya Stain Shortgun sequencing of T.cruzi Thinking Mobile Health The Ebola Tragedy in Africa Outcome of Gulu-NAP Project Medical Picture Quiz And Much More



BEING PART OF THE STORY — THE LEGACY OF DR LUKWIYA

Since the beginning of this epidemic, I have been reflecting and it has brought about a change in my life as regards the medical profession. We chose it at some point in our lives. Maybe for the prestige it gives us, or we want to save lives. Now I understand more deeply that it is a call from God. This service cannot be separated from the willingness to give one's lifey – DR. MATTHEW LUKWIYA

The fearless field commander at the center of a biological war that threatened everyone in the country — New York Times



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Foreword

Mezirow (1996) described transformative learning as "the process of using a prior interpretation to construe a new or revised interpretation of the meaning of one's experience in order to guide future action". Transformative learning differentiates between a learner who is a receptacle of knowledge (rote learner) from that who is actively involved in critical thinking, deeper analysis and interpretation of knowledge and experiences in order to make new meaning and guide future action.

Transformative education is based on Mezirow's transformative learning theory which describes how learners understand, critically reflect, interpret and reformulate the meaning of their experiences in order to change their beliefs, attitudes and reactions. According to Mezirow, transformative education construes learning to be the process of using prior knowledge to construct a new idea or meaning in order to guide future action.

What is the influence of transformative education and transformative learning theory in medical education?

Medical education has experienced transformation especially in the western world through gradual progression and consolidation from 1910 to the end of the last century. In the 21st century medical education is entering a period of transformation focusing on competencies. The report of the Global Independent Commission on Education of Health Professionals in the 21st century (1996) states: "All health professionals in all countries should be educated to mobilize knowledge and engage in critical reasoning and ethical conduct so that they are competent to participate in patient and community-centered health systems as of locally responsive and globally connected learners". The report outlines 21st century learning outcomes of medical education to include: attitudes, professionalism, communication skills, critical thinking skills, lifelong learning, ability to evaluate research evidence, collaborative and cooperative learning and team work. The health care delivery system requires that medical graduates be endowed with knowledge, skills and attitude competencies which are differentiated from those that characterized a traditional medical curriculum.

Medical education in Uganda has historically been founded on the traditional curriculum and posited on a health care system focused on public health and primary care. Medical education must be responsive to the health needs of the population, the priorities of the national health system and to global health concerns. In 2010, the Faculty of Medicine, Gulu University together with four other medical schools in a consortium adopted the competence-based education (CBE) curriculum to transform medical education from the traditional curriculum to competence based in order to train doctors who would be responsive to the emerging health needs of the 21st century. The philosophy of the CBE curriculum is strongly based on educational philosophies of essentialism and progressivism with emphasis on the learner acquiring essential medical knowledge, skills and having academic rigor it is a learner-centered curriculum that focuses on active learning through active participation of the learner. The main objectives of the curriculum are to provide a sound scientific and professional basis for the production of a medical doctor who would work anywhere in Uganda and beyond to provide such training that equips the doctor with skills of rendering quality primary care health services to empower doctors with internationally acceptable standards and with abilities to undertake specialized medical training in all health sciences and to produce doctors with sufficient knowledge and skills in leadership and management of health care systems delivery.

The CBE curriculum emphasizes acquisition of competencies in medical knowledge, clinical skills and patient care, critical inquiry and scientific methods, professionalism and ethical practice, interpersonal and communication skills, leadership and management skills, population health, continuous improvement of care through reflective practice and health systems management. The content of the curriculum is organized in courses which are delivered at three incremental levels to enable students gain developmentally appropriate learning experiences by reinforcing their knowledge, skills and experiences across disciplines and grade levels. Medical students must, in addition to learning common disease conditions, be conversant with factors that influence public health in the 21st century such as global economy, poverty, environmental degradation, lifestyle, sedentary technology and insecurity resulting in fragmentation of family life and communities. The competence based curriculum is expected to transform medical education, clinic practice and research.

The 21st century is experiencing emerging health challenges of environmental and behavioral risks, gaps and inequities in health, changing patient and population needs and new infections like HIV/AIDS and Ebola. These challenges are coupled with a mismatch of competencies of health professionals. Transformative medical education fosters a professional education system that responds to these emerging challenges in order to improve health system performance, provide patient-centered care and ensure quality care and patient safety. To judge whether we are there or not in the implementation of the CBE curriculum pursuance of transformative medical education will require an indepth evaluation of the outcomes of transformative medical education as characterized by the competence based curriculum

Assoc. Prof. Emmanuel Moro Dean Faculty of Medicine

Preamble

Warm greeting to you the esteemed reader. It is a great honor to write to you on behalf of Gulu University Medical Students' Association (GUMSA). Since the inception of GUMSA in March 2005, six months after the start of the Faculty of Medicine in September 2004, the fraternity has prioritized in transforming the health in the country particularly northern Uganda.

GUMSA serves to link the students' fraternity of Faculty of Medicine to the University administration and other national and international Medical students' bodies as well as provision of health related pro bono services to communities in Northern Uganda while it adheres to its motto, "a passion for life".

Over the years we have ensured the coordination of students and University management for smooth running of academic programs, engaged with our respective partners like Gulu University, Local governments in Northern Uganda, Reproductive Health Uganda, AMREF, World Vision, TASO, Straight Talk Foundation, Comboni Samaritans of Gulu and Youth Alive among others to provide much needed health services to the nearby communities.

We have had several projects such as Run against Cervical Cancer, Northern Uganda Village Health Outreach Project, Pre-Medical Dinner and Pre- Conference health services to mention but a few.

We have also organized pleasurable activities like sports, dinners and symposia all to the holistic contribution to the society.

The fraternity has organized and participated in conferences of International Federation of Medical Students' Associations (IFMSA), Federation of African Medical Students' Associations (FAMSA), Federation of Ugandan Medical Students' Associations (FUMSA) and Uganda Psychiatrists' Association (UPA) to mention but a few. These tremendous achievements are due to the focused, goal oriented nature and team spirit of her members which I must appreciate.

Gulu University Medical Journal (GUMJ) serves to provide written account of what progresses in that walk of transforming health. It also helps us to deliver health information both to the profession and the populace.

The sixth volume of GUMJ is yet another evidence of the ultimate commitment and vision to archetypal medical learning. The students and the fraternity of scientists in the profession put onto paper astounding ideas, researches and the like, to save your curiosity.

We thank the staff of the Faculty for their guidance, mentorship and support for without them the students would not have achieved these high standards.

We appreciate our partner institutions and consortia, the BEMSA, MEPI MESAU, GULU-NAP and so many others involved in the ultimate success. All those who have financed this publication and hope for more support for the continuity of this noble initiative.

Finally, I thank the GUMSA executive 2014/2015, Editor in chief and his team, all those who contributed to the success of the journal and the entire members of the Faculty for the high level of cooperation which has made us a classical Medical School.

Thank you OCAKACON JAMES GUMSA PRESIDENT 2014/2015

Editorial Comment

It is with great esteem that I welcome you to the 6th edition of the Gulu University Medical Journal. This edition brings to you exciting articles from various fields of medicine. With the current disease and health care burden in Uganda, many factors can be stated for this deplorable yet amendable status quo. These include research into possible diagnostic criteria, new perspectives for the health workers to access information and among many more the political and advocacy role of the government and any other stakeholders. This particular issue explores such avenues from different health care workers and students. The theme is open however with a special focus on new discoveries, perspectives and insight on the current dilemma on health care delivery in Uganda,

Notable among the many high quality articles contained in this journal is an article about short gun sequencing of Trypanosoma cruzi the causative agent of Chagas disease and the Odong-Aginya method for quantification of helminthes eggs in human field. With the recent shift in technology, this journal contains a perspective on mobile health that will stimulate students and other health care workers to use the new hi-tech gadgets find health information during their practice.

Still in this exciting issue are snapshots of activities taking place at the faculty of medicine including new masters programs, perspectives into the future of health care in Uganda and many more articles that will keep you glued to this piece of literature

The faculty of medicine is taking great leaps in transforming the lives of the neighboring communities. This comes at a time when the region is recovering from the devastating effects of the over twenty year insurgency. Students are involved in a number of projects including comprehensive health outreaches, cervical cancer awareness drives and hepatitis B prevention campaigns.

Great thanks go to all members of the editorial committee with whom this daunting task was accomplished, kudos to you. Great thanks go to Prof. Odong-Aginya for the sacrifice made to read through the articles and guide the committee, Dr. Dan Elly Aniku for constant encouragement, the Dean Faculty of Medicine and Prof Luigi Greco for the immeasurable support and mentorship. Special thanks also go to all people who contributed articles. And finally we thank the Almighty God for His special protection during this period of hard work.

Thank you, OCHORA MOSES EDITOR-IN-CHIEF. mtochora@gmail.com

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FEATURED ARTICLE Odongo-Aginya Method for Quantification of Helminthes Eggs in Humans for Field Research A Modification of Kato/Katz

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ABSTRACT

INTRODUCTION

The Kato/Katz method is the research field method which has been recommended by World Health Organisation for quantitative estimation of Helminth eggs in humans. Nevertheless the method has some disadvantages which remained unsolved for a long time. The major problems are: a) the prepared slides need to clear for few hours for good visibility of the slides. b) During this period, the delicate eggs like those of hookworm over clear in glycerine and become difficult to identify under the microscope. c) Larvae of parasites like those of strongyloides and miracidium from hatched eggs of schistosome are difficult see. d) The method therefore becomes time consuming.

To develop a more reliable method for quantification of helminth eggs in human for field research a modification of kato/katz

Design

Purposive cross sectional

Kigungu Fishing village Entebbe Uganda

Fishermen and school children at Kigungu primary school

Method

In Odongo-Aginya method, the modification of the Kato/Katz method the stool smears on the slides are stained using a compound stain, a mixture of 5% eosin and 7.5% nigrosin in equal proportion both in 10% formalin base solvent. The stool sample is strained using sieve of 250 mesh size. The strained stool in filled in a template measuring 41.7mg of stool on the slide. Available drop of the compound stain, depending on the consistency of the stool sample is added on the smear and stirred in. A wettable cover slip pre-soaked in 50% glycerine is placed on the stained stool smear on the slide and the slide inverted on absorbing paper and pressed down. Excess of the stain is absorbed by the paper. Well prepared slides allow the back of the hand to be visible through the pinkish smears.

Results

The slides prepared using Odongo-Aginya can be examined immediately the slides are prepared and the visibility of the parasites eggs, even those of hookworm, larvae and miracidia if any remain good without compromising their clarity for a long time.

CONCLUSION

Odongo-Aginya method, the modification of the Kato/Katz method for the quantification of Helminth eggs stool smears is reliable diagnostic tool in field research.

INTRODUCTION

The Kato/Katz method is the long standing method recommended by World Health Organisation (WHO) for the diagnosis and quantification of Schistosoma mansoni and other intestinal helminth infections due to soil transmitted Helminth eggs or larvae⁽¹⁾.

The 50% glycerine in the 1% malachite green in Kato/Katz method functions as a clearing agent which improves the visibility of the slide after a long incubation at ambient temperature and the malachite green beside being a dye is also bactericidal^(2,3). The glycerine in Kato/Katz takes between one to two hours to clear the background of the stool smear on the slide for good visibility to allow accurate visualisation of most helminthes eggs⁽¹⁾. These long waiting hours for glycerine to clear the background of the slides, make delicate eggs of hookworm over clear and become difficult to detect and differentiate from other artefacts⁽¹⁾.

The aim of this paper is to show the pectoral appearance of different eggs, larvae, and cysts of different parasites in Odongo-Aginya method⁽⁴⁾. Several Field studies have shown that Odongo-Aginya method is simple, cost effective and the visibilities of the parasites are good immediately the slides are prepared and these can keep for a long time so long as the slides are kept at cool dry environment. This property makes a visual reference of the results of the method useful to facilitate the recognition of parasites eggs by researchers willing to adopt this method⁽⁵⁻⁹⁾.

MATERIAL AND METHOD

In Odongo-Aginya method, the 1% malachite green in 50% glycerine used in the Kato/Katz method is replaced by the compound stain 5% eosin yellow in 10% formalin mixed in equal parts 1:1 with 7.5% nigrosin also in 10% formalin. The cellophane cover slips used in Aginya method are cut in 25x40mm pieces and are pre-soaked in 50% glycerine before use. Like in Kato Katz method the stool sample is stained through a stainless steel sieve mesh size 250. Through a template delivering 41.7 mg of the sample, the strained stool sample is measured on the slide. About 10µl to 50µl of the compound stain (Odongo-Aginya Stain) depending on the consistency of the stool specimen, is added on the stool smear on the slide and stirred in using the corner of another slide or glass cover slips in a circular movement. The plain cellophane cover slip pre-soaked in the 50% glycerine is removed by a pair of forceps and the excess glycerine is blotted on an adsorbent paper and the cellophane cover slip is placed on the stained stool smear. The slide is inverted on the absorbent paper and gently pressed done to spread the smear evenly under the cellophane cover slip and to remove excess stain and air bubbles. A well prepared slide has a pinkish background and is possible to read the face of a wrist watch through it.

RESULTS

Photographs of different helminthes eggs, Isospora belli cysts and larvae of Strongyloides stercoralis in Odongo-Aginya method are present in the figures below. The photographs were taken using an Olympus Photomicroscope B20 in the Department of Pathology Makerere Medical School Kampala to illustrate time factors on the visibility of the helminth eggs, cysts and larvae of parasites at different time periods of immediately the slides were prepared, one hour later and one week and beyond. The specimens were obtained from the fishing village of Kigungu in Entebbe an area endemic for both Schistosoma mansoni and other soil transmitted helminthes.

ETHICS

Makerere University Faculty of Medicine for Higher Degree ethical committee, Uganda National Council of Science and Technology approved the study to collect the specimens from the subjects in Kigungu fishing village. Informed consent from participants was requested before they were recruited in the study. The results were released confidentially to individuals and all intestinal helminthes and Schistosoma mansoni cases detected were treated accordingly. Other ailments were referred to other health facilities.

DISCUSSION

The objectives of this short report is to illustrate pictorially the improvement made on Kato/Katz method on the visualisation on helminthes egg, cysts, and larvae by replacing the 1% malachite green in 50% glycerine with a compound stain 5% eosin and 7.5% nigrosin in 10% formalin use in Odongo-Aginya stain⁽⁴⁾. Odongo-Aginya method has several advantages over the Kato/Katz method in that:

a) it is fast because the prepared slides in Odongo-Aginya stain can be examined with great success immediately.

b) It is simple and easy to learn.

c) Hookworm eggs can be recovered from the slides for a much longer period unlike in the Kato/Katz where they over clear with two hours making the identification difficult⁽¹⁾.

d) Beside eggs of other parasites remain unaltered for a long time⁽¹⁾. The evaluation of Odongo-Aginya method tfo determine the reproducibility was done by WHO team of experts ^(6,7).

e) Further advantage of Odongo-Aginya method on Kato/Katz method is safety of the method when performing the test. Malachite green in Kato/Katz is weakly bactericidal which does not provide protection against most viral and other microbial pathogens in stool specimens as 10% formalin in Odongo-Aginya Method provides. At this concentration formalin acts as a fixative and it's a great advantage when working with stool specimens from Human Immunodeficiency Viruses (HIV) infected patient⁽⁴⁾.

Odongo-Aginya method is reliable and reproducible. Slides prepared using the eosin /nigrosin compound stain can be microscopically examined immediately after preparation. Hookworm eggs remain visible up to six months later⁽⁴⁾. Odongo-Aginya method is ideal in the study of intestinal helminthes especially where the examination of the slides cannot be performed immediately or shipped.

ACKNOWLEDGEMENT

I am indebted to study participants of Kigungu fishing village in Entebbe. Without their consent to participate in the study, I would not have got the specimens. The photographic work was done in Pathology Department Makerere Medical School, I am grateful. Without the clearance from the Makerere Faculty of Medicine Committee for Higher Education

FEATURED



Plate 1A: Ascaris lumbricoides Note the ease of differentiating parasite egg from artifacts



Plate 3: Hymenolepis nana From formalinised specimen, seven days after the slide was prepared



Plate 1B: Ascaris lumbricoides Immediately the slide was prepared



Plate 4: Trichuris trichuira



Plate 2: Taenia spp Note the contrast between the artifacts and the taenia egg



Plate 5A: Hookworm Immediately the slide was prepared



Plate 5B: Hookworm One day after the slide was prepared



Plate 6: Enteriobis vermicularis Immediately the slide was prepared



Plate 8A: Schistosoma mansoni Seven days after the slide was prepared, note the sharp spine revealed in the staining



Plate 8B: Schistosoma mansoni Immediately the slide was prepared, note the slope olf the spine revealed in the staining



Plate 7: Isospora belli cysts Oocysts Immediately the slide was prepared



Plate 9: Strongyloides stercoralis larva Immediately the slide was prepared

and the National Council of Science and Technology this study would not have taken place. Thanks for this.

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FEATURED ARTICLE

Shotgun Sequencing Analysis of Trypanosoma cruzi I Sylvio X10/1 and Comparison with T.

cruzi VI CL Brener

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ABSTRACT

Trypanosoma cruzi is the causative agent of Chagas disease, which affects more than 9 million people in Latin America. We have generated a draft genome sequence of the Tcl strain Sylvio X10/1 and compared it to the TcVI reference strain CL Brener to identify lineage-specific features. We found virtually no differences in the core gene content of CL Brener and Sylvio X10/1 by presence/absence analysis, but 6 open reading frames from CL Brener were missing in Sylvio X10/1. Several multicopy gene families, including DGF, mucin, MASP and GP63 were found to contain substantially fewer genes in Sylvio X10/1, based on sequence read estimations. 1,861 small insertion-deletion events and 77,349 nucleotide differences, 23% of which were nonsynonymous and associated with radical amino acid changes, further distinguish these two genomes. There were 336 genes indicated as under positive selection, 145 unique to T. cruzi in comparison to T. brucei and Leishmania. This study provides a framework for further comparative analyses of two major T. cruzi lineages and also highlights the need for sequencing more strains to understand fully the genomic composition of this parasite.

INTRODUCTION

The protozoan parasite Trypanosoma cruzi, causative agent of Chagas disease, infects 7.7 million people in Latin America and causes 12,500 deaths annually [1]. Transmission of the parasite most commonly occurs if infected faeces of the haematophagous triatomine insect vector makes contact with mucosae or abraded skin. Most morbidity is associated with the chronic stage of the disease, which can take several years to develop. There is no vaccine against T. cruzi infections and drug treatment is restricted to a small number of drugs with insufficient efficacy and potentially harmful side effects.

Multiple genotyping strategies support the subdivision of T. cruzi into six major phylogenetic groups, recently renamed discrete typing units (DTUs) I-VI by international consensus [2]. DTU distribution can be loosely defined by several parameters including ecology, vector and host preference, geography and disease association [3], although patchy sampling precludes definitive associations. Likewise, an accumulating number of in vitro and in vivo experiments indicate significant phenotypic variation between T. cruzi strains in terms of physiology, biochemistry and infectivity [4,5,6,7,8,9,10,11,12,13]. Again, however, there are few clear-cut correlations between genetic groups and pathogenic potential and the genetic determinants of such differences remain enigmatic. Genome sequencing can provide crucial data to facilitate such research.

Tcl is the predominant agent of Chagas disease in the Americas North of the Amazon e.g. [14] [15] [16], although it is by no means uncommon in patients in other regions (e.g. [17]). In contrast, TcII, TcV and TcVI are the predominant causes of Chagas disease in the Southern Cone countries, where megaoesophagus and megacolon are more common [18,19,20,21,22, 23,24,25]. Tcl shows spectacular abundance among wild hosts and vectors throughout the endemic range of T. cruzi, especially, but not exclusively, in association with Didelphis sp. opossums [3,26]. Whereas the other strains responsible for most human disease, TcII, V and VI, are rarely isolated from natural reservoirs or triatomines. Indeed, minimal diversity across multiple markers in putative TcII/TcIII hybrids TcV and TcVI, and their widespread southerly distribution, are consistent with a recent origin alongside domestic transmission cycles (Lewis et al, submitted). In phylogenetic terms TcI and TcII are most divergent and nucleotides models estimate their MRCA at 3-16 MYA [27]. Concurrent with substantial intraspecific genetic diversity, Chagas disease is characterized by a highly variable clinical presentation [1]. This has long been assumed to be, at least in part, a product of genetic differences between strains of T cruzi [15]. However, despite important advances in T. cruzi genotyping [28] [14] and population

AUTHOR SUMMARY

Chagas disease is a major health problem in Latin America and it is caused by the protozoan parasite Trypanosoma cruzi. The genome sequence of the T. cruzi strain CL Brener (TcVI) has revealed a genome with large repertoires of genes for surface antigens, among other features. In the present study, we sequenced the genome of a representative member of Tcl, the predominant agent of Chagas disease North of the Amazon and performed comparative analyses with CL Brener. Genetic variation between strains can potentially explain differences in disease pathogenesis, host preferences and aid the identification of drug targets. Our analysis showed that the two genomes have very similar sets of genes, but contain large differences in the relative size of several important gene families. Moreover, an abundance of allelic sequence variation was found in a large fraction of genes, and an evolutionary analysis indicated that many genes have evolved at different rates.

genetics [29,30], the genomic variation between lineages or individual clones of T. cruzi remains largely unexplored.

The haploid genome of T. cruzi CL Brener (TcVI) is approximately 55 Mbp in size [31]. Analyses of the sequence revealed a repeat-rich, hybrid genome, with long regions of conserved synteny to Leishmania major [32] and Trypanosoma brucei [33]. A strong signature of the putative TcII/TcIII hybridization that gave rise to TcVI remains. As such, CL Brener predominantly comprises two divergent haplotypes, named Esmeraldo-like (TcII) and non-Esmeraldolike (TcIII) (abbreviated to Esmeraldo and non-Esmeraldo here). The hybrid nature and repetitive content of this genome complicated its assembly, leaving the first T. cruzi genome incomplete by comparison to those L. major and T. brucei. A later effort to place the contigs and scaffolds into predicted chromosomes increased the length of scaffolds, although resolution still requires considerable improvement [34].

We considered the sequencing of a smaller, less repetitive, nonhybrid T. cruzi genome to be a sensible approach to improving resolution. Furthermore, an evolutionarily distinct genome, from a DTU with broader host preferences than TcVI, could provide an interesting basis for comparative genomics. Not only are Tcl parasites highly divergent from TcVI in ecology and evolution, but typically they have smaller genomes [28,35,36,37] and have relatively low levels of heterozygosity [30]. They are thus the ideal candidate for analysis. Here we describe shot-gun sequencing and partial genome assembly of Sylvio X10/1, originally isolated in 1983 from a male individual in Para' State, Brazil, suffering from acute Chagas disease [38]. Sylvio X10/1 is a common reference strain of TcI and is frequently used in both in vivo and in vitro experiments [39] [40] [41] [42]. The genomic contigs and sequence reads were subsequently compared to CL Brener. We found that the core gene content of the two T. cruzi lineages is highly similar, but that they harbor large differences in repetitive content and sequence, which may have functional and epidemiological implications.

MATERIALS AND METHODS

Accession numbers

This Whole Genome Shotgun project has been deposited at DDBJ/EMBL/GenBank under the accession ADWP00000000. The version described in this paper is the first version, ADWP01000000. The data will also be available at TriTrypDB [43].

Sequencing, assembly and annotation

Trypanosoma cruzi Sylvio X10/1 cells were cultured at 28uC in RPMI liquid medium supplemented with 0.5% (w/v) tryptone, 20 mM HEPES buffer pH 7.2, 30 mM haemin, 10% (v/v) heatinactivated foetal calf serum, 2 mM sodium glutamate, 2 mM sodium pyruvate and 25 mg/ml gentamycin. Genomic DNA was extracted using the Gentra Puregene Tissue Kit (Qiagen). Sequencing was performed using 454 technology (FLX/Titanium) and sequence assembly was performed de novo using the CELERA assembler (v5.4) [44].

Gene prediction and annotation was performed using GeneMarkS (v2.6p) [45] and best reciprocal BLAST hit to CL Brener. Annotations were manually inspected by alignment to CL Brener using Promer [46] and the Artemis Comparison Tool [47]. Gene models were manually added if found to be missing. In cases where genes were disrupted by sequencing errors, all fragments of the genes were annotated. Truncated genes located on contig ends were annotated when possible.

GENE SPECIFIC AND EVOLUTIONARY ANALYSIS

Individual genes were identified using reciprocal BLASTp and tBLASTn on both assembled and unassembled reads.

Alignments were created using ClustalW and used to call strainspecific differences both nucleotide differences and insertiondeletion (indel) events. Calculation of dN/dS was carried out using yn00 (PAML, v4.2) [48]. The McDonald-Kreitman test (MK-test), as implemented in BioPerl (v1.6), was used to evaluate protein adaptation [49], using alignments created by transAlign [50] with T. brucei used as the outgroup. Synonymous sites were assumed to be neutral while non-synonymous sites were assumed to be deleterious, neutral or confer an advantage. Positive selection was assumed to take place if the number of inter-species nonsynonymous changes was greater than the intra-species changes. A contingency table and Fisher's exact test was used to test for (N) =significance. The neutrality index (Pn/Ps)/(Dn/Ds)) was used to test the direction of adaptation, which is expected to be 1 under neutrality, .1 for positive selection and ,1 for purifying selection. Using NI, the proportion of adaptive substitutions can be estimated as a = 1 - NI.

Multigene family analysis

Sequence reads with similarity to known gene families in CL Brener were analyzed. Initially, homologous genes were collapsed into families using the clustering tool cdhit [51] at a 90% identity threshold. Subsequently clusters were subject to multiple alignments with ClustalW. Profile hidden markov models (pHMM) were created using hmmbuild (v3, with the parameter –symfrac 0), concatenated to a single file and compressed using hmmpress [52]. Sylvio X10/1 and CL Brener reads were translated into the six reading frames and hmmscan (with the parameters –nobias and – nonull2) was used to conduct searches. To make the results comparable to Sylvio X10/1, Sanger reads from CL Brener were cut into smaller pieces before the HMM search was conducted.

Results and Discussion

We used 454 technology whole genome shot-gun sequencing [53] to produce a partial assembly as well as a read-based analysis of the Tcl reference strain Sylvio X10/1 (Tcl) genome. We then conducted a comparison to the genome of the reference strain CL Brener (TcVI). This has allowed the first genomescale analysis of genetic diversity in T. cruzi. The architecture of the two genomes was highly similar, composed of large, co-transcribed, gene-dense "core" coding regions, which displayed highly conserved synteny interspersed with regions of repetitive sequence. The draft assembly has good coverage of these gene dense regions, but is more fragmented in repetitive regions due to the technical difficulties associated with accurate assembly of repeat sequences. However, we have complemented this assembly with a read-based analysis. Thus we were able to characterize comparatively the repeated genes in both genomes. The core gene content of the two genomes was virtually the same but we identified abundant nucleotide and amino acid sequence differences. Furthermore, in the comparison between Sylvio X10/1 and CL Brener we found large differences in the proportion of sequence with homology to multigene families. CL Brener was found to have approximately 5.9 Mbp more of haploid sequence related to the DGF, RHS, mucin, MASP, GP63, and transsialidase gene families. The expansion of these gene families underlies most of the genome size difference between Sylvio X10/1 and CL Brener.

SEQUENCING AND COMPARATIVE ANALYSES

Genome sequencing of the Tcl isolate Sylvio X10/1 was carried out using 454 technology [53], which generated 582 Mbp sequence data (nreads = 1,688,475, Table 1, Figure S1A), where 79 Mbp (nreads = 301,005) corresponded to maxi/mini circles. Sequence assembly resulted in 7092 contigs (N50= 5659 bp) yielding an average coverage of 11x Subsequently, contigs from the (Figure S1B). assembly were aligned to both CL Brener haplotypes [34] which revealed large blocks of synteny, representing the core gene content of these genomes (i.e. excluding repetitive regions). The amount of heterozygosity in the assembly was examined by counting the number of high quality mismatches between aligned reads, which estimated the heterozygosity to be less than 0.08% in the core genome.

In the coding regions the mean nucleotide identity was higher between Sylvio X10/1 and non-Esmeraldo i.e. TcIII (98.2%) than between Sylvio X10/1 and Esmeraldo i.e. TcII (97.5%) (Table 2, Figure 1 and 2).

Table 1. Data comparison Sylvio X10/1 and CL Brener.

	Sylvio X10/1	CL Brener
Data amount (10 ⁶ bp)	582 ^a	823 ^b
LINE content ^c	2.12%	2.27%
LTR content ^c	0.45%	0.50%
Unique ORFs	0	6
Intergenic distance ^d	500 bp	500 bp

^a454 sequencing.

^bSanger sequencing.

^cIdentified using RepeatMasker.

^dAverage intergenic distance. doi:10.1371/journal.pntd.0000984.t001

Table 2. Sylvio X10/1 compared to the individual haplotypes.

	non-Esmeraldo	Esmeraldo
Coverage *	66%	62%
Nucleotide identity	98.2%	97.5%
Nucleotide diversity	0.0241	0.0310

^aPercentage of the chromosomes that are covered by Sylvio X10/1 contigs. doi:10.1371/journal.pntd.0000984.t002

The mean nucleotide identity between the two CL Brener haplotypes Esmeraldo and non-Esmeraldo was 97.8%. This is independent genome-wide evidence of the generally closer phylogenetic relationship between Tcl (Sylvio X10/1) and TclII (non-Esmeraldo) than with TcII (Esmeraldo). The divergence between these three T. cruzi lineages is therefore greater than between T. brucei subspecies T. brucei brucei and T. brucei gambiense (99.2%) [54] but less than between two representatives of different Leishmania species complexes, L. major and L. infantum (94%) [55].

From the alignments, a total of 77,349 putative fixed differences were identified in the coding regions of a total of 5582 genes (8.6 Mbp of sequence). Of these nucleotide differences 52% were synonymous changes, 34% were non-synonymous changes giving rise to chemically similar amino acids and 23% were nonsynonymous changes associated with radical amino acid replacement. The average rate of nucleotide differences (ND) between Sylvio X10/1 and non-Esmeraldo was 18 ND/kb/gene and compared to Esmeraldo 25 ND/kb/gene (Figure 2A). In comparison, the average ND rate between non-Esmeraldo and Esmeraldo was 22 NT/kb/gene. This large number of nucleotide differences is consistent with independent evolution of the T. cruzi lineages over several million years [27], presumably due to ecological, geographic, and/or reproductive isolation, limiting homogenising forces that might act between lineages. Some of these changes may be adaptive, although one explanation for the high proportion of radical amino acid replacements might be low rates of sexual recombination in T. cruzi leading to the accumulation of mildly deleterious mutations over time (Muller's ratchet). Experimental phenotypic comparisons and associated in depth annotation of the potential functional implications of such radical amino acid changes may reveal biological consequences. Multiple CL Brener genes originally

thought to have a frame shift not observed in Sylvio X10/1 (n =169, Table S1) must now also be considered in such comparisons, because our alignments and confirmatory Sanger sequencing revealed they had been misassembled and incorrectly annotated as pseudogenes in CL Brener.

Nucleotide substitutions between CL Brener and Silvio X10/1 were not the only coding variations present. A search was also conducted to identify indel events. We identified 1861 coding indels dispersed in 1271 genes. The majority (n =1350, 72.5%) were caused by length variation in microsatellite tracts. Indels 3 bp in length were the most common, followed by 6 and 9 bp.

Multiple genes with a functional annotation (i.e. non-hypothetical genes) were found to contain indels, for example DNA topoisomerase genes, helicase genes, various metabolic genes and chaperones. Several functionally important genes contained relatively large indels, including the DNA repair protein BRCA2, which was found to contain a 44 codon N-terminal deletion in Sylvio X10/1 spanning amino acids 82-125. Although this deletion did not directly affect an evolutionarily conserved domain, it have functional consequences mav for BRCA2mediated homologous recombination capacity in this strain. Deletions were slightly more prevalent in Sylvio X10/1, which could possibly indicate reductive evolution in Sylvio X10/1, or, conversely, that sequence expansion has generally been more common in CL Brener. Similarly, the number of 195 bp satellite repeats was greater in CL Brener [56] [36] and the sum of total intergenic distances was marginally larger in CL Brener (Table 1). The overall content of retroelements, LINEs and LTRs, assessed across both genomes using RepeatMasker and conducted using reads, showed little variation (Table 1).

The clear size differences between the CL Brener and Sylvio X10/1 genomes were confirmed at the macro level. The Sylvio X10/1 haploid genome size was estimated to be 44 Mbp, using extrapolation from the combined length of the contigs from the Sylvio X10/1 assembly (23 Mb) and the unassembled data from repetitive regions (see following sections). Our estimate tallies with previous studies that have estimated the Sylvio X10 genome size at about 35–44 Mbp, using pulse-field gel electrophoresis [37] and flow cytometry [28]. This value for haploid genome size is considerably lower than that for CL Brener (,55 Mbp) [31]. The smaller genome size appears to be a general feature of Tcl strains[28].

GENOME-SPECIFIC SEQUENCES AND

EVOLUTIONARY ANALYSES

We found that Sylvio X10/1 and CL Brener have nearly the same core gene complement, including housekeeping genes, structural genes and genes of unknown function. Six annotated open reading frames (ORFs) in CL Brener were not found in Sylvio X10/1 (Table S2). As these ORFs were short (,350 aa) and without a functional annotation, it is unclear whether they are expressed at all. We were not able to identify any Sylvio X10/1-specific genes or significantly long ORFs. However, we note that minimal gene differences are also reported between



Identity (%)

Figure 1. Sequence identity of Sylvio X10/1 contigs compared to non-Esmeraldo and Esmeraldo. Shows the percentage identity (horizontal axis) of the best Sylvio X10/1 versus CL Brener BLAST hit and the combined alignment length on the vertical axis. The black line (triangles) represent Sylvio X10/1 compared to non-Esmeraldo and blue lines (circles) represent Sylvio X10/1 compared to Esmeraldo. Both comparisons have a similar overall distribution of identities but Sylvio X10/1 compared to non-Esmeraldo is shifted to a slightly higher sequence identity. Sylvio X10/1 compared to non-Esmeraldo has a peak at 97% sequence identity and Sylvio X10/1 compared to Esmeraldo has a peak at 96% sequence identity.

T. brucei subspecies genomes [54], as well as between those of Leishmania species [55]. A similar trend has been observed in Giardia lamblia [57,58]. Instead, the great majority of genetic differences between strains of all these parasite genera consist of SNPs and indels as well as, crucially, copy number (see following section).

In the absence of strain specific genes in our dataset, we also screened for those genes that might be under directional selection between Silvio X10/1 and CL Brener. dN/dS ratios (v) identified 336 genes under positive selection (v.1), a significant proportion of which (145) were unique to T. cruzi by comparison to T. brucei and Leishmania. The presence of these rapidly evolving T. cruzi specific genes could indicate important biological roles in American trypanosomes, for example, genes regulating interactions with hosts or vectors. Those genes that could be assigned function included two genes encoding cell-surface targeted proteins, one 90 kDa surface protein gene and one member of the ToIT family. MK tests (see Materials and Methods) for adaptive selection between T. cruzi and T. brucei identified other genes of known function and putative importance including transporters and various other membrane coupled proteins, as well as, surprisingly, some DNA repair proteins, chaperones and cyclins (Table S2).

ESTIMATION OF MULTIGENE FAMILY CONTENT

Many surface proteins involved in interaction with the host in T. cruzi are encoded by large repetitive gene families [31]. These regions represent a major area of interest for comparisons between CL Brener and Sylvio X10/1 genomes. Assembly of such repetitive sequences is problematic, therefore we applied a novel approach. The Sylvio X10/1 assembly contained only about 49% of the generated sequence data, leaving 710,109 reads (,236 Mbp) that did not enter the assembly. To evaluate these data, sequence reads were classified into pre-defined categories using profile hidden markov models. The size of each gene family was estimated using the combined alignment length and normalized to the total amount of sequence data (Figure 3). To provide an estimate of the relative repeat abundance, the same searches were performed on the CL Brener sequence data. To verify the applied method, several single copy genes were included in the analysis. The vast majority of the expected single copy genes resulted in a 1:1 signal, indicating that the method can be used reliably for copy number quantification.

By this classification approach, a total of 346,696 (49%, 137 Mbp) unused reads from Sylvio X10/1 were sorted into 69 different categories (Figure 3). From these unused reads, 233,574 (33%, 92 Mbp) were assigned to six categories only (sialidase, DGF, RHS, mucin, MASP and GP63). In terms of combined alignment length, these gene families were estimated to represent 7-8 Mbp of the haploid Sylvio X10/1 genome. For Sylvio X10/1 and CL Brener, the sialidase and DGF categories were the largest for each genome respectively, comprising 5.4% and 6.1% of the sequence data. According to this analysis, a smaller proportion of the sequence reads match the DGF family in Sylvio X10/1, suggesting that this family is expanded in CL Brener or contracted in Sylvio X10/1. The analysis also indicated copy number differences for the MASP, mucin, GP63 and RHS gene families between the two genomes. It should be noted that this method does not discriminate between pseudogenes and functional genes and therefore, some of the predicted genes could represent nonfunctional or non-expressed gene variants.

In addition to inter-genomic comparisons between the major gene families, a more comprehensive analysis was performed on a larger set of T. cruzi genes, which included 5874 different homologous gene clusters, including singletons. The most significant differences were found among some hypothetical genes, and in most cases there was an expansion in CL Brener.

These comparative analyses of both the non-coding and coding repetitive elements indicates significant differential expansion in sequence corresponding to surface antigen repertoires and other multicopy gene families. The CL Brener genome was estimated to have about 5.9 Mbp (11.8 Mbp diploid) of extra sequence related to multigene families than Sylvio X10/1. Therefore, we conclude that expanded gene families in CL Brener underlie most of the genome size difference between Tcl and TcVI, and this may theoretically enhance functional plasticity. CL Brener (TcVI) is the product of hybridization between TcII and TcIII [59]. We cannot determine whether the gene family expansions occurred pre- or posthybridisation (or both). However, Tcll, Tclll and TcVI strains all have similarly increased DNA contents relative to TcI [28]. This suggests the bulk of expansion occurred within ancestral TcII and TcIII.

Conclusions

This first intra-species comparative genomic analysis



Figure 2. Nucleotide differences and dN/dS estimations. Black lines (circles) represent Sylvio X10/1 compared to non-Esmeraldo, blue lines (triangles) represent Sylvio X10/1 compared to Esmeraldo and red lines (crosses) represent non-Esmeraldo compared to Esmeraldo. A) Shows the distribution of single nucleotide differences (ND) in genes, normalized to show the number of ND per 1000 bp. Sylvio X10/1-Esmeraldo show the largest number of ND, and have 25 ND/kb/gene in average. B) Shows the ratios of non-synonymous and synonymous nucleotide variation (horizontal axis shows dN/dS) between the comparisons as a fraction of the genes examined (vertical axis). All comparisons have average dN/dS around 0.40 and the shape of the curves has a similar appearance. About 95% of the examined genes have a ratio below 1, implying that the genes are under purifying selection and 336 genes show evidence of positive selection (dN/dS .1).

of T. cruzi provides several significant insights. First, it is clear that core genome synteny and gene identity are highly conserved between Tcl and TcVI, with very few unique and no major gene differences. Similarly, the overall quantity of non-coding DNA is largely unchanged between the two genomes. The most significant variation between the two genomes is in the size of several multigene families, which encode many important surface proteins. These families are



Percent of total sequence data (%)

Figure 3. Gene content comparison between Sylvio X10/1 and CL Brener. Shows estimations of gene content between Sylvio X10/1 and CL Brener as percent of the total data. Searches was performed on the read libraries of Sylvio X10/1 and CL Brener. DGF, mucin, MASP, GP63, RHS, 90 and kinesin are more expanded in CL Brener. The sialidase family is indicated to be slightly smaller in Sylvio X10/1.

significantly larger in TcVI and account for approximately 54% of the c.11 Mbp size difference between TcVI and TcI. Our findings compare well with recent comparative genomic studies of other parasitic trypanosomes at the sub-species (T. brucei, [54]) and species complex (Leishmania, [55]) level. In both cases few gene differences are apparent in the core genomes, congruent with the remarkable synteny observed at the inter-species level [31]. This apparent lack of genomic rearrangement, gene deletion and insertion between trypanosome genomes could derive from the constraints of polycistronic transcription, disruptions of these long co-transcribed gene clusters being likely to be deleterious.

Genetic recombination is a common mechanism by which structural change may be introduced between genomes, as well are providing sources of new genetic information. The excessive accumulation of nonsynonymous changes that we observe between Tcl and TcVI suggest that this recombination may be infrequent in T. cruzi at the inter-DTU level at least. However, the overall natural frequency of intraspecies and intra-genotype genetic recombination in all three major human parasitic trypanosome genera is a still a matter of some uncertainty and considerable debate [60,61,62,63,64,65]. Functional dissection of the larger surface gene families in TcVI presents an interesting problem. Both Tcl and TcVI efficiently infect humans and TcVI is found among far fewer hosts than Tcl [3]. However, TcVI may have emerged quite recently in conjunction establishment in the human host (Lewis et al, submitted). It remains to be defined how much of the differential surface gene diversity is actually expressed.

This study represents a significant advance in unraveling the diversity of T. cruzi and encourages further comparative genomics of the T. cruzi lineages and related species of the subgenus Schizotrypanum. We are currently engaged in sequencing other representatives of Tcl, and the apparently bat specific trypanosome T. cruzi marinkellei.

SUPPORTING INFORMATION

FIGURE S1 READ LENGTHS AND ASSEMBLY COVERAGE.

A) Shows the number of reads (vertical axis) with a certain read length in base pairs (horizontal axis). Shaded lines (light grey) represent 454 FLX reads and black lines represent 454 Titanium reads. One major peak at around 250 bp is distinct for FLX and another major peak at 500 bp is distinct for the 454 Titanium.

B) Shows the coverage of the assembly. Number of positions is plotted on the vertical axis with a certain level of redundancy (coverage) on the horizontal axis. The curve has a peak at 11 times coverage, which is the mean coverage.

Found at: doi:10.1371/journal.pntd.0000984.s001 (0.10 MB PDF)

TABLE S1 INCOMPLETE GENES AND INCORRECT PSEUDOGENES IN CL BRENER.

An Excel file containing three sheets: A) Genes in Esmeraldo (CL Brener) with sequence gaps and the corresponding ortholog in Sylvio X10/1. B) Genes in non-Esmeraldo (CL Brener) with sequence gaps and

the corresponding ortholog in Sylvio X10/1. C) Pseudogenes in CL Brener that is likely to contain a sequencing or assembly error in this genome.

Found at: doi:10.1371/journal.pntd.0000984.s002 (0.10 MB XLS)

TABLE S2 EVOLUTIONARY ANALYSIS AND SPECIFIC GENES.

An Excel file containing three sheets: A) Contains dN/dS estimates for Sylvio X10/1 versus Esmeraldo and Sylvio X10/1 versus nonEsmeraldo, along with product descriptions and information about signal peptides and transmembrane domains. B) Contain detailed results from the McDonald-Kreitman test, for those genes that were subject to this analysis. C) A list of CL Brener open reading frames that were not identified in Sylvio X10/1.

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AUTHOR CONTRIBUTIONS

Conceived and designed the experiments: OF MAM BA. Performed the experiments: OF SO. Analyzed the data: OF SO ES MDL MSL. Contributed reagents/materials/analysis tools: OF MDL MSL MAM BA.

Wrote the paper: OF SO MDL MSL MAM BA.

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PERSPECTIVE

The Exploded Time Bomb Examining the Ebola Tragedy and Public Health Crisis in West Africa

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A lbert Camus in The Plague wrote, "Everybody knows that pestilences have a way of recurring in the world yet somehow we find it hard to believe in ones that crash down on our heads." Since 1976, more than 20 Ebola (2,569). During the week ending outbreaks have erupted in sub-Saharan Africa, confirmed cases were reported yet the world was woefully unprepared for the from Sierra Leone, less than one current tragedy².

By nine months of the Ebola outbreak , a total of 4507 confirmed and probable cases of Ebola virus disease (EVD), as well as 2296 deaths from the virus, had been reported from five countries in West Africa -Guinea, Liberia, Nigeria, Senegal, and Sierra Leone. In terms of reported morbidity and mortality, the current epidemic of EVD was far larger than all previous epidemics combined. The true numbers of cases and deaths were certainly higher and escalating with numerous reports of symptomatic persons evading diagnosis and treatment. There were also of laboratory diagnoses that had not been included in of national databases, and persons with suspected EVD who were buried without diagnosis.

The epidemic began in Guinea during December 2013, and the World Health Organization (WHO) was officially notified of the rapidly evolving EVD outbreak on March 23, 2014. On August 8, the WHO declared1 the epidemic to be a "public health emergency of international concern." By mid-September, 9 months after the first case was reported, the numbers of reported cases and deaths increased incessantly despite multinational and multisectoral efforts to control the spread. The epidemic became so large that the three most-affected countries Guinea, Liberia, and Sierra Leone faced challenges enormous implementing control measures at the scale required to stop transmission and to provide clinical care for all persons with

According to the World Health Organization2 update on January 28, 2015, a total of 22,092 probable, confirmed, and suspected cases of Ebola and 8,810 deaths had been reported as of January 25 from the three West where African had been transmission widespread and intense. Total counts included all case suspected, probable, and confirmed cases, which are defined similarly by each country Because of improvements in diagnostics laboratory and surveillance, totals overestimated the actual number of cases in some areas. The highest reported confirmed case counts were from Sierra Leone (7,968) and Liberia (3,138), followed by Guinea

January 24, an average of 11 from Liberia, and three from Guinea each day. The areas with the highest number of confirmed cases reported during January 5-25 were the Western Area and Port Loko, Sierra Leone.

Eight cases and six deaths were previously reported from Mali. No new confirmed cases have been reported from Mali since December 5, 2014. On January 18, 2015, the World Health Organization declared Mali free of Ebola

According to WHO Situation Report (18th February), Guinea reported a decrease in cases from the previous week, the first weekto-week decline since January 25 Transmission remained widespread in Sierra Leone and was most intense in the capital, Freetown. Following the steep decline in case incidence in Sierra Leone from December until the end of January, the fire of incidence burned out slowly (see WHO Response roadmap below).

THE DISEASE

Although highly pathogenic, Ebola is not particularly contagious compared to for example, influenza viruses, which are airborne. Ebola virus disease is passed through bodily fluids (e.g., blood or saliva) and infected individuals are most contagious after their symptoms have appeared. As a result, most of the more than 20 previous Ebola epidemics died out quickly, killing relatively.

Transmission can be stopped by a combination of early diagnosis, contact tracing, patient isolation and care, infection control, and safe burial. Before the current epidemic in West Africa, outbreaks of EVD in central Africa had been limited in size and geographic spread, typically affecting one to a few hundred persons, mostly in remote forested areas.

The largest previous outbreak occurred in the districts of Gulu, Masindi, and Bundibugyo in Uganda. This outbreak, which generated 425 cases over the course of 3 months from October 2000 to January 2001, was controlled by rigorous application of interventions to minimize further transmission - delivered through the local health care with support from system, international partners and the saintly heroism and selfness of health workers.

THE RESPONSE

Speed is of the essence. The global response to Ebola was tardy, in part because 24 previous outbreaks of the virus since 1976 were contained, so it was assumed that this one would also be extinguished quickly. But when Medicines San Frontiers (MSF) began to warn in April that different something was unfolding, that Ebola was getting out of control in West Africa where it had not previously struck - the call was not heeded to.

The World Health Organization response lagged. The U.N. agency has suffered budget cuts and is poorly structured, with regional offices not easily accountable to its headquarters in Geneva. In this case, the Africa office of the WHO was slow to react, and that put the



whole organization behind the curve. Margaret Chan, the WHO director general, first learned of the urgency of the situation in June, according to a WHO timeline disclosed by the Associated Press⁵

No doubt the slow response was also a product of public health agencies that were illprepared and overwhelmed in the three hardest-hit countries: Guinea, Sierra Leone and Liberia.

The worst hit countries were recovering from civil wars and regional anarchy with miserable healthcare systems, hospitals and treatment centers tried but buckled in battling the disease. While there was no known effective cure for Ebola, the centers isolated patients from the healthy and thus prevented more infections. The lacking health education of natives made the problem bigger, ordered cremation of bodies was frustrated by traditional burial, including ritual touching and bathing of the body.

Violated guarantines escalated transmission rates of EVD, creating a dangerous cycle.

In the end, fighting an outbreak is not only battling a virus but also dealing effectively with people, modifying their behavior and taming their fears.

Such was the pathetic

environment with every healthcare stage from WHO to village health teams inadequate.

PROSPECTS

Governments have first priority to take care of their people and provide adequate health care. The countries hit as a matter of priority need to set up a decent health care system.

Public health operations such as laboratory services, disease surveillance, and maintenance of vital statistics (including cause-ofdeath data) are poor in many countries.In low-income countries, investing in such services may not be cost-effective or affordable given the limited budgets and competing demands from various burdened sectors. Public health preparedness requires greater therefore domestic and global funding for these activities. What is needed is a binding global health framework - a Framework Convention on Global Health.

This proposed framework would be based on the right to health and aimed at national and global health equity.

In September, 2014, The US global president challenged leaders to use the Global Health Agenda to spearhead global preparedness, and to put an end to repeating, unnecessary tragedies

 \triangle nd though this Ebola epidemic İS V particularly dangerous, we've seen deadly diseases cross borders before. H1N1. SARS. MERS. And each time, the world scrambles to coordinate a response. Each time, it's been harder than it should be to share information and to contain the outbreak. As a result, diseases have spread faster and farther than they should have which means lives are lost that could have been saved. With all the knowledge, all the medical talent, all the advanced technologies at our disposal, it is unacceptable if, because of lack of to control equally worse harms preparedness and planning and global coordination, people are dying when they don't have to — The US President

In such devastating times, the world looks at science to save the day. It was illogical that after several outbreaks of EVD, there was no licensed vaccine or treatment. Yet centuries ago, with barely no technology scientists battled deadlier plagues and saved the torment of mankind. The lesson is clear, the extensive scientific and health research need to be facilitated.

Ebola fundraising only began well after the outbreak had advanced. As a result, funding was

insufficient and delayed. This is not a new problem while the World Health Organization (WHO) has a contingency fund for outbreak response, the fund is structured such that money sits around unused and few donors are motivated to contribute .A more effective outbreak contingency fund would work more like callable capital at the multilateral development banks.

The Ebola epidemic has exposed a major gap in the international capacity to respond

to outbreaks, and in particular to epidemics that could pose a global threat. WHO leadership was slow to facilitate a response early in the outbreak, when containment of the disease was most important, but the role of the WHO remains critical in the midst of outbreaks that cross borders. The agency is in a unique position to initiate and coordinate disease-incidence tracking, sample sharing, standard setting, laboratory quality assurance, and epidemiological and healthsystem responses. The containment of such sets ground like Bioterrorism.

CONCLUSIONS

When the world is in the grip of a devastating health, humanitarian and security crisis, it is natural to focus on doing everything possible to curb the suffering and death. Yet, this is also a time to think creatively about the future. How did this epidemic spin out of control and what can we do to prevent the next disaster.

Planning now for a reinforced global health system, setting up an emergency fund for such outbreaks, building capacity and innovative scientific undertakings would be the greatest legacy we could offer to those who have suffered so badly and needlessly.

PERSPECTIVE

Thinking Mobile Health A Role for the Gulu University Medical Student

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The average medical student at Gulu University Faculty of Medicine (GU-FOM) assumes a critical role in the regional primary health care space by the end of his third year in medical school. During in-school rotations and holidays, students perform a wide array of procedures at local hospitals and health centers ranging from treatment of malaria to delivering babies and assisting with surgeries. Whether by choice or default, these future physicians are directly exposed to the myriad of systemic, structural and financial problems that have plagued the Ugandan, and by extension most Sub-Saharan health care systems for decades. These problems include, but are not limited to, a shortage of both private and governmental funding for health care facilities and an acute shortage of doctors, which is further compounded by severe brain-drain. The challenges are structural, systemic and financial. Thus, when viewed as a whole, these challenges seem insurmountable. Where should a medical student start? What is most critical? What meaningful contribution can he or she make, beyond doing what the senior supervisor instructs?

To objectively evaluate this assertion, one needs to consider factors, plausible limitations and dig a little deeper for the opportunities. It is true that medical students may not have direct influence in the high level policy decisions that ultimately result in acute shortages of health professionals and basic drugs in health centers. They may also perhaps not have much say in the allocation of

limited financial resources for medical care or the construction facilities. of physical The traditional option then is for students to simply wait until they have attained the 'credentials' to fill clinical positions in health centers, and many years down the road, an administrative/ policy level position. Should this really be there case? Are there avenues they through which can immediately begin to act to shape the future of health care in their communities for the better?

I contend that the 21-century Gulu University medical student is actually uniquely positioned to tackle some of the most pressing challenges in the Ugandan healthcare system and progressively shape the future. They need not wait. I will make the case for Mobile health (mhealth) as a compelling area to explore. M-Health refers to the practice of medicine and public health aided by mobile communication devices such as mobile phones, mobile tablets and personal digital assistants. Over the course of the decade the mhealth has emerged as an application amenable to healthcare systems in developing nations. This emergence comes at a time when there is a dire need to address some of the aforementioned challenges, which continue to be exacerbated by high population growth rates coupled with brain-drain of talent to neighboring countries. The drastic rise in mobile phone access in both rural and urban areas presents the potential of information reducing and transaction costs associated with healthcare delivery, in addition to

increasing access to professionals and scaling their current reach.

their Unlike experienced instructors, many of whom have 'habituated' and somewhat resigned to some of these systemic problems as a 'normal' standard, these students are new to the intricacies of the problems. Thus they approach them with a fresh perspective, and arguably, new ideas and energy, which need to be given ground to take root and thrive. It is certainly not farfetched to suggest that a lack of prior knowledge is a significant catalyst for fresh untested, but promising solutions. Second, they are the mobile-generation, so to say: many have grown up with mobile telephones on their Day to day, they fingertips. experience the role of a basic nonphones internet mobile transforming sectors such as banking via mobile-money payments used by local phone providers a potential that can be creatively leveraged to support the emerging mobile health movement. Furthermore, these students interface more with their Information Technology and Computer Science colleagues more often than their instructors and superiors who are already in medical practice. This creates a potential avenue for interdisciplinary conversations, which I believe can be a breeding ground for realistic ideas that need to be supported by institutional stakeholders and local teaching hospitals. Moving from the idea to implementation stage is undoubtedly challenging, given the financials hurdles, however, that shouldn't be a deterrent to taking the first step

forward.

Reasonably, skeptics of mhealth contend that more emphasis should be placed on training and retaining local physicians and nurses and stocking health centers with adequate drugs. I agree. However, given the current poor infrastructure and questionable economic projections, the World Health Organization notes that the healthcare workforce in sub-Saharan African countries such as Uganda would "need to be scaled up by as much as 140% to attain international health development targets such as those in the Millennium Declaration". They further clarify that "The problem" is so serious that in many

instances there is simply not enough human capacity even to absorb, deploy and efficiently use the substantial additional funds that are considered necessary to improve health in these countries." The unprecedented rise and penetration of Mobile phone technology in Uganda, and Sub-Saharan Africa presents a realistic opportunity to creatively solve some of these challenges. It can scale the impact/ reach of the current and future healthcare work force, while increasing access for the vast majority of underserved populations. If there is a position to start, it should begin from the 'mobile generation' of medical students and project outwards.

f yesterday was the best time to plant a tree, today is the second best time to do so" - Unknown

original article Prevalence and Predictors of Pulmonary Tuberculosis Amongst HIV/AIDS Patients Attending St. Mary's Hospital, Lacor, Northern Uganda

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ABSTRACT

Background

The Human Immunodeficiency Virus (HIV) epidemic has been accompanied by a severe epidemic of tuberculosis (TB). The prevalence of pulmonary tuberculosis (PTB) among HIV/AIDS patients is largely unknown in developing countries like Uganda. Uganda is ranking 16th of the 22 high TB burden countries in the world with one of the highest treatment default rates, hence the study to determine the prevalence of PTB among HIV-seropositive Ugandans.

Objective

To determine the prevalence of PTB and socio-demographic factors influencing development of PTB among HIV/AIDS patients who attended St. Mary's Hospital Lacor, Northern Uganda in July 2009-June 2010.

Methods

By use of the hospital computer data management software, files with incomplete parameters of interest and those without definitive diagnoses were excluded. Systematic sampling of every 12th file out of 8,300 files to obtain 691 case files for review was conducted. Data extracted from records department for ART clinic included age, gender, address, marital status, level of education, occupation, distance from the study area, baseline CD4 count, TB diagnostic criteria and category, ART status at diagnosis of TB. The diagnostic criteria for TB that were considered included ZN stain for sputum, sputum cultures, specimen biopsies and chest X-rays for smear negative cases but not TB suspects or PCR(not available).Radiological diagnoses were reviewed by a physician and case files were compared with the electronic patients' database. Data statistical analysis was performed using SPSS 17.0

Results

Of the 691 case files reviewed 423 (61.2%) were females and 268 (38.8%) were males, 69 (10.0%) were coinfected with TB, 58 (8.4%) were co-infected with PTB (95% CI) of which 34 (58.6%) had been diagnosed before commencing ART and 24 (41.4%) were diagnosed while on ART. 11 (15.9%) had a form of extra pulmonary TB and none had both pulmonary and extra pulmonary TB. 37 (5.4%) males had PTB as compared to 21 (3.0%) females. The highest prevalence of PTB was observed amongst patients aged between 26-35 (4.2%), and lowest between <18 (0.3%). 41(5.9%) prevalence was observed among patients with a primary level of education. Married patients had the highest prevalence 28 (4.1%), while the minority 9 (1.3%) of patients were widowed. TB/HIV co-infected patients had a median CD4 count of 350.5 cells/mm3 compared to >400cells/mm3 of those without co-infection. Patients from rural areas were more co-infected, 31(4.5%) than those in the urban areas with shorter distance from the study area, 01(0.1%).TB/HIV co-infection was significantly associated with CD4 cell count (x2=38.40, P=0.000), sex (x2=22.56, p=0.000), marital status (x2=13.99, 0.003).

Conclusions

The high prevalence of PTB/HIV co-infection requires a multi-sectoral approach and competent collaborative management strategies for prevention, early detection and treatment. Although risk of developing PTB increases with decline in CD4 count PTB/HIV co-infection can occur at any CD4 level. HIV Patients who are not yet initiated on ART are more likely to develop TB compared to those on ART. There is a significant correlation between PTB/HIV co-infection with socio-demographic characteristics.

Recommendations: There is need to extend and strengthen TB/HIV collaborative strategies to the rural communities which are most at risk. There is need to address the socio-economic burden as it is shown to be associated with higher prevalence of PTB/HIV co-infection. There is need for routine screening of HIV patients for TB at every hospital visit irrespective of CD4 count. Prospective studies with a larger sample size especially in government hospital settings where majority of our patients access services may explore other factors that may be associated with TB/HIV co-infection in this study population.

INTRODUCTION

The HIV epidemic has been accompanied by a severe epidemic of tuberculosis (TB).WHO intends to dramatically reduce the global burden of TB by 2015 in line with the Millennium Development Goal 6, target 8, Achieve universal access to high-quality care for all people with TB, Reduce the human suffering and socioeconomic burden associated with TB and Protect vulnerable populations from TB. The prevalence of pulmonary tuberculosis (PTB) among HIV/AIDS patients is largely unknown especially in developing countries like Uganda despite its ranking 16th of the 22 high TB burden countries in the world with one of the highest treatment default rates (USAID, 2009). The prevalence of PTB in the post conflict Northern Uganda where HIV prevalence is reported to be 7-12% (NUMAT, 2008) and where people had formerly been living in internally displaced camps and currently copying with the broken up health systems following resettlement is particularly unknown. This necessitated this study to determine the prevalence of PTB among HIVseropositive Ugandans who attended St. Mary's Hospital Lacor, Northern Uganda from July 2009 to June 2010 and to assess the socio-demographic factors that influence development and progression of PTB. This information may benefit health providers and policy makers in increasing vigilance towards promoting multi-sectoral collaborative strategies tailored at communities most at risk of developing the co-infection.

METHODOLOGY

Study area

The study will be carried out at St. Mary's teaching Hospital Lacor, Gulu district in northern Uganda. Lacor hospital is a complex teaching hospital, comprising of the main hospital, and three peripheral health centers at Amuru, Opit and Pabo. It's located in Gulu municipality 6km west of Gulu town, the regional capital, along the highway to Sudan. Its activities are in line with Uganda Ministry of Health Policies of Health care provision. It offers referral services, primarily serving the population of Gulu and Amuru districts but also receiving patients from other parts of Uganda and Southern Sudan. Some of the special services offered include the HIV/AIDS and TB clinics the hospital has a very busy AIDS clinic caring 9,888 HIV patients as of financial year for 2009/2010. The package of care includes voluntary counseling and testing for HIV and treatment of opportunistic infections in particular PTB, provision of ARVs with outlined clinical laboratory and community as well as prevention of mother to child transmission. The TB ward is located between the nutritional unit, surgery and medical wards and catered for over 1055 patients in the year 2009/2010. The diagnostic criteria for TB in this hospital include clinical diagnosis, sputum analysis and chest X-rays. Most of the patients attending TB clinic are from the male and female medical wards, HIV clinic and a few from nutritional unit which is part of the pediatric ward. (St. Mary's Lacor Hospital report for financial report, 2009/2010)

Study design

A retrospective review of 691 case files of

HIV/AIDS patients who attended St. Mary's Hospital, Lacor from July 2009-June 2010 was conducted, following systematic sampling of every 12th café file out of 8,333 files that had definitive diagnoses, complete parameters of interest and had not been terminated.

DATA COLLECTION

Patients' case files and records were reviewed to collect quantitative data pertaining our dependent variable (patients with PTB) and independent variables (age, sex, education level marital status, and distance from study area) using checklists. Patients' addresses were stratified into urban, periurban and rural with reference to Gulu municipality as the urban.

METHODS OF DATA ANALYSIS AND PRESENTATION

After the data was collected the quantitative data were edited, coded and analyzed using SPSS 17.0 computer Programme software. It was edited and examined for errors and omissions, and corrections were made where necessary. In coding process, data was organized into categories after which numerals were assigned to each item before entering the data in the computer.

Measures of central tendency were used, for example mean, median, mode to describe data of one variable at a time. Statically we used proportions and compared different variables using chi square tests and logistic regression.

Ethical consideration

The consent to execute the study was obtained from Research and ethical committee, Gulu University, Faculty of Medicine under approval reference number GU/IRC/01/07/11. The committee issued an introductory letter to Medical Superintendent of St. Mary's Hospital, Lacor to allow us carry out the research. Permission to access records was sought and granted by the internal research review committee of Lacor hospital. Confidentiality of the patients' records was highly observed.

RESULTS

Socio-demographic characteristics

Of the 9,888 patients seen at Lacor Hospital in a period of 1 year under review, records of 8,300 (83.9%) were complete, 888 (9%) were incomplete and 700 (7.1%) had been terminated or missing. Of the 691 case files reviewed 423 (61.2%) were females and 268 (38.8%) were males, giving a female to male ratio of 1.6:1. Patient age ranged from 2 weeks to 80 years with majority of patients 248 (35.9%) between 26 to 35 years and the least number of patients 56 (8.1%) below 18 years of age. Majority of males122 (45.5%) were above 35 years and majority of women 167 (39.5%) were between 26 to 35 years of age. A total of 44 (6.4%) patients had a tertiary education, 187 (27.1%) had a secondary education, 343 (49.6%) had a primary education and117 (16.9%) had no formal education.

A total of 398 (57.6%) were married, 83 (12.0%) were single, 128 (18.5%) were widowed and 82 (11.9%) divorced. A total of 90 (13.0%) were employed by someone or government, 224 (32.4%) were self-employed, majority, 357 (51.7%) were

unemployed including children, and20 (2.9%) were students. Majority of patients 311 (45.0%) came from within 3 to 10 kilometers from the Hospital and the least 155(22.4%) were from greater than 10km from the Hospital. A total of 327 (47.3%) were from rural areas and constituted the majority, followed by 237 (34.3%) from periurban areas and 127 (18.4%) from urban. Their social demographic characters are shown in table 1.

CLINICAL CHARACTERISTICS

At presentation, 174 (25.2%), had a baseline CD4 count of >400 cell/mm3 and the least was 0-100 cells/mm3.The median baseline CD4 cell count was 350.5 cells/mm3. Approximately, 163 (23.6%) had baseline CD4 count less than 350cells/mm3. A total of 19 (32.8%) with PTB had CD4 cell count of 201 - 300 cells/mm3 at diagnosis, 06 (10.3%) had CD4 above 400cells/mm3 and 13 (22.4%) had CD4 count <100cells/mm3.

PREVALENCE AND PATTERN OF TB/HIV CO-INFECTION

Of the 691 HIV seropositive patients, 69 (10.0%) were co-infected with TB. A one year period prevalence of 58 (8.4%) were co-infected with PTB (95% confidence interval). Among these patients 34 (58.6%) had been diagnosed before commencing ART and 24 (41.4%) were diagnosed while on ART. Among TB/HIV co-infected patients, 11 (15.9%) had a form of extra pulmonary TB and none had both pulmonary and extra pulmonary TB.

By gender, 37 (5.4%) males had PTB as compared to 21 (3. 0%) females, this finding was statistically significant (p=0.2)

The highest prevalence of PTB was observed amongst patients aged between 26-35 (4.2%), followed by ages between >35 (2.3%) and lastly between <18 (0.3%), this finding was statistically significant (p=0.2)

With reference to education attainment, the highest prevalence, 41(5.9%) was observed among patients with a primary level of education, and the least, zero prevalence was observed amongst patients with a tertiary level of education, this was a statistically significant finding, (p=0.2).

With respect to marital status, married patients had the highest prevalence 28 (4.1%), while the minority 9 (1.3%) of patients were widowed. Differences due to marital status were statistically significant (p=0.2)

TB/HIV co-infected patients had a median CD4 count of 350.5 cells/mm3 compared to >400cells/mm3 of those without co-infection, this difference was statistically significant (p=0.3)

In regards to patient's distance from the study area, patients from rural areas having to travel longer distance were more co-infected,31(4.5%) than those in the urban areas with shorter distance from the study area,01(0.1%).

Tuberculosis presentation amongst TB/HIV coinfected patients is shown in the pie chart below.

DISCUSSION

In this present study, 10.0% of the HIVseropositive patients in Lacor teaching hospital had TB, of which 8.4% had PTB. This is much lower than the 18.3% reported among HIV sero-positive patients in rural areas of Northern Uganda (Kakoraki, 2006), although their prospective study was focussing on prevalence of HIV amongst TB patients. However the prevalence of PTB in our study was much more consistent with the prevalence of 8.5% reported in a cross section study done amongst HIV seropositive patients at Haydon Lutheran Hospital in northern rural Tanzania from September 2006 to March 2007 (Benard et al, 2008). Findings were also in keeping with10.5% TB prevalence reported in a retrospective study amongst HIV-seropositive patients attending Amino Kano teaching Hospital, Nigeria (Lliyasu, A similar study done to determine the Prevalence of Clinical Tuberculosis in HIV Infected Patients from Kermanshah Province, IRAN (Mansoori, 2002) revealed a prevalence of 11.4% close to our study.

The study showed that majority, 34 (58.6%) of PTB cases were diagnosed before initiating ART as opposed to 24 (41.4%) already on ART. This is probably because ART boosts immunity and hence lowering the progression of TB.

A total of 25 (43.1%) had PTB at a higher CD4 cell count >200cells/mm3 as opposed to 13 (22.4%) with CD4 cell count of <100cells/mm3, from these study findings, PTB can occur at any level of CD4 cell count, this was much more consistent with a study done in Tanzania (Benard et al, 2008) compared to the prospective study done in the UK (Gooze, 2003).

With respect to PTB and gender, although majority of our study population were females, the highest prevalence, and 5.4% was found in males compared to 3% among female patients this is likely to be due to the poor health seeking behaviour amongst males reporting to health facility later at advanced disease stage.

The highest prevalence, 6.5% observed in patients above 18years of age as compared to 0.3% in those below 18years of age could be due to the natural history and progression of TB as the immunity lowers in HIV patients.

Patients from rural areas and longer distances from the study area had a higher prevalence of PTB,31 (4.5%) as compared to those from urban and close to the study area,01 (0.1%),this is probably due to congestion in IDP camps which were located in rural areas before 2010,poor access to health services and poor follow up.

Highest prevalence of 5.9% amongst primary level of education and amongst the self-employed, majority of which were peasant farmers could be due to their low socio-economic states, poor accommodation and inadequate knowledge about TB/HIV preventive measures as compared to those who attained tertiary education.

Married patients had the highest prevalence of PTB, 28 (4.1%) compared to the widowed 9 (1.3%) and the single, probably due to cross infection as well as direct correlation of high prevalence of HIV amongst the married.

CONCLUSIONS

The high prevalence of PTB requires a multisectoral approach and competent collaborative management strategies for prevention, early detection and treatment.

Although risk to develop TB increases as CD4

Age	Frequency	Percent
below 18	56	8.1
19-25	141	20.4
26-35	248	35.9
greater than 35	246	35.6
Total	691	100.0
Occupation		
Employed	90	13.0
Unemployed	357	51.7
selfemployed	224	32.4
Student	20	2.9
Total	691	100.0
Sex		
Male	268	38.8
Female	423	61.2
Total	691	100.0
Education level		
primary level	343	49.6
secondary level	187	27.1
tertiary level	44	6.4
None	117	16.9
Total	691	100.0
Marital status		
Married	398	57.6
Divorced	82	11.9
Single	83	12.0
Widowed	128	18.5
Total	691	100.0
Address		
Urban	127	18.4
Pe ri-urban	237	34.3
Rural	327	47.3
Total	691	100.0
Distance from hospital		
less than 3km	225	32.6
3 to 10 km	311	45.0
greater than 10 km	155	22.4
Total	691	100.0

Table 1: Demographics







Figure 2: Showing distribution of CD4 count amongst PTB/HIV co-infected patients



Figure 3: Duration of HAART among PTB/HIV co-infected patients

count decreases, PTB/HIV co-infection can occur at any level of CD4. There is a significant correlation between PTB/HIV co-infection with sociodemographic characteristics.

RECOMMENDATIONS

There is need to extend and/or strengthen TB/HIV collaborative activities to the rural communities which are most at risk.

Further studies on a larger scale need to be conducted especially in government hospitals where the PTB/HIV co-infection cases tend to be under reported.

There is need to address the socio-economic burden as it is shown to be associated with higher prevalence of PTB/HIV co-infection.

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ORIGINAL ARTICLES

Hospitalization for Paediatric AIDS in St. Mary's Hospital-Lacor 2007-2011

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Key Words: Pediatric AIDS, Epidemiology, Hospital Admissions.

ABSTRACT

The systematic reading of hospital in-patients database can prove to be an important tool to understand the natural history of diseases: this is particularly true in countries where the hospital based information system is not coordinated at national level, but limited to administrative statistical data summaries.

Signals of a decrease of HIV epidemic in children are arising from many African countries: information is often based mainly on screening activities.

In this study we had access to a 5 year hospital database from St. Mary Lacor Hospital in Gulu, northern Uganda: we found 1231 patients below 14 years of age admitted to different wards of Lacor hospital.

Analysis of time trends showed a clear decrease in time of hospital new admissions for HIV, especially in children below one year.

Hospital lethality also decreased significantly in the 5 years of study, possibly associated to improved diagnostic and treatment.

INTRODUCTION

It is already 30 years from the beginning of the Acquired Immune Deficiency Syndrome (AIDS) epidemic: Africa has been intensively affected by this epidemic and children paid the largest price (1).

Uganda as a nation, experienced one of the highest incidence of Human Immunodeficiency Virus (HIV), but also was one of the first African Countries to show evidence of effective new HIV infections decrease: prevention, diagnosis and treatment of HIV infections contributed to a substantial reduction of the HIV epidemic (2).

But pediatric HIV has been, and still is, the most suffering impact of this terrible epidemic: millions of deaths and millions of HIV orphans have jeopardized the natural evolution of a large generation (3).

Still quality information on the HIV infections is lacking in Africa: over the official epidemiological data, much more information is needed to the medical world to effectively continue the difficult battle against this devastating disease (4).

Hospital data, despite representing only the clinically severe picture of the disease, very often is the only source of constant good quality data. This is the reason why we attempted to explore the recently instituted Lacor Hospital data base.

METHODS

Lacor Hospital is a large missionary hospital established more than 50 years ago in an area close to Gulu Town it hosts more than 40 thousands patients each year in ten different medical and surgical wards more than 250 thousands patients get treatment in the Out Patient Departments.

Since the birth of Gulu University Medical School, Lacor hospital has served as a teaching hospital to the University.

A specific AIDS service is active in the hospital from 1995 and the Laboratory provides some of the modern HIV diagnostic and monitoring tests.

Lacor Hospital is not the only hospital in the district, but it constantly gets the largest proportion of inpatients.

It is well known that only a variable proportion of truly HIV infected individuals are recognized in Africa as elsewhere in the world of those who are known to be infected a large proportion get treatment in the Out Patient Department and only cases with severe clinical syndromes are admitted to the hospital wards.

Hospital admissions data, therefore, represent a proportion of true HIV infected population, but they carry constantly high quality information so that they can be considered the best available proxy to describe some aspects of the natural history of this disease

From 2007 a new Hospital information system is active in the hospital: each patient admitted is registered in a computerized form that is updated at the patient discharge. International Classification of Disease (ICD10) is being introduced (5)

The present analysis has been possible from the Hospital admission database from June 2007 to March 2012.

HIV pediatric case was defined as a patient positive for HIV antibodies and of less or equal 14 years of age, as for the WHO definition (1). In this database we have admissions in the hospital wards, but we do not select for individual patients that could have had more than one hospital admission during the study period.

Data were analyzed with Microsoft 7 excel software.

RESULTS

From July 1 2007 to March 31 2012, 1231 patients were admitted to Lacor Hospital wards: Table 1 offers the age distribution by the admitted ward is evident that in Lacor Hospital most of the patients over 5 years are admitted in the medical ward.

It is also important to stress that almost one third of the young HIV patients suffer of nutrition problems so to be admitted to the nutrition ward.

The HIV epidemic is decreasing its strength in Africa, and more, in Uganda.

In fact the admission for HIV under 14 years in Lacor hospital are constantly decreasing: Fig 1. Offers the admission trend by month from July 2007 to march 2012: it is evident that there is a decreasing trend starting from May 2008: from more than 50 new admissions to less than 5 each month. It is possible that major contributors include earlier initiation of ART for those under 5 years, and a strengthened PMTCT system which captures the HIV positive child early.

It is also evident from fig. 2 that substantially the admissions of children under 5 years are decreasing,

Table 1 : Lacor hospital admissions	2007-2011 for under
14 years HIV patients	

Ward	one year	2-5	6 to 14	Total
Medicine		6	126	
Nutrition	69	250	13	319
Paediatrics	376	334	29	710
others	5	11	18	16
Total	445	584	168	1045

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hile the number of admissions of older children is constant.

In fact most of the Hospital admissions are below 5 years : the fig 3 pie chart offers the age distribution of the admissions : more than one third is below one year and some 48% more are two up to 5 years , while only 15% are the admission from 6 to 14 years of age.

There are no statistically significant difference by gender : in the whole population the sex ratio male/female is 1.17: 1, but in the older 6 to 14 years group there are more females : sex ratio male/female being 0,79: 1. Similarly there are no significant difference in the mean length of hospital stay : overall 12 days, but 13 days for the ones who recovered and 10 days for the one who died. Of the 1231 admissions, 955 (77,6%) were sent home as recovered, 21 escaped from the ward and 255 died in the hospital : the proportions are in fig 4. Reasons for escape include desperation, lack of food or support, apparent improvement to mother, and search for alternative care.

The overall HIV under 14 years lethality of Lacor Hospital in the years 2007-12 was 20.7 %: most of the deaths occurred in small children with severe









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lications Fig 5 offers the age distribution of HIV related deaths: 42% below one year and another 48,2% from 2 to 5 years. Hospital lethality decreased





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bstantially in the 5 years considered , in fact in fig 6 the lethality is plotted by trimester to reduce variance : it went from a 27,7 of the trimester july-sept 2007 to 8,8 of the trimester Jan-march 2012 a 68,6% reduction, the trend shows how this reduction has been constant with a regression line enjoying a r^{2} = 0,297.

CONCLUSIONS

Paediatric AIDS is the main indicator of this terrible epidemic: the number of new cases in children expresses the real strength of this contagion (6).

The unbelievable enormous number of AIDS orphans estimate in millions only in Africa is the most sad result of this unprecedented health disaster: Lacor hospital, now for more than a quarter of a century, supports a dedicated orphanage for the children directly or indirectly affected by this devastating virus.

Reading the disease evolution in each location is crucial to guide and evaluate both preventive as diagnostic and treatment interventions (7). This should be done albeit the challenges of data collection in ward settings.

Uganda is among the first countries in Africa that has experienced significant success in the fight against AIDS: the preventive campaigns as well as the provision of maternal treatment and the large availability of diagnostic tests and effective anti-HIV treatment achieved a very significant reduction of HIV incidence and of HIV related mortality (4).

Lacor hospital carried a large proportion of the

HIV burden in Gulu district: constantly close to one third of all the hospital work was dedicated to HIV patients over the last 20 years.

The availability of good quality information on the evolution of this epidemic is a problem in most African countries: many patients do not get tested many others are inconstantly treated in a large number of ambulatories and outpatient services: only those with severe complications and often in a late AIDS stage go for hospital admissions. So information based on this latter group captures only a specific proportion of HIV natural history, but that information is the only one with some complete data and, most importantly, stable enough to be used to build time trends.

This is why we embarked in this study from which we found the following conclusions:

-85% of Pediatric HIV hospital admissions is below 5 years of age.

–Pediatric HIV hospital admissions are definitively decreasing in the last 5 years.

-The decrease is most marked for children below 1 and 5 years.

–Pediatric HIV hospital lethality is drastically decreasing in the last 5 years : most likely a result of improved diagnosis and early treatment.

We highly recommend the use of admission data to determine trends of HIV even in poor resource settings. This can strongly inform interventions.

In order to further decrease HIV trends in children, it is important to embrace and fully implement the elimination of Mother to child Transmission of HIV (eMTCT), with a particular recommendation of active case identification and intervention, especially for infants and children.

There is also need for strategies to test the older children, especially of HIV positive mothers, who may not have been tested before.

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ORIGINAL ARTICLES

Awareness of Dietary and Behaviour-Related Risk Factors of Cardiovascular Disease Amongst Women of Rural Northern Uganda

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ABSTRACT

Aim

To assess the awareness of dietary and behavior-related risk factors of cardiovascular diseases amongst women of rural northern Uganda.

Methods

A Cross-sectional study was conducted on 435 women (15-70 years of age) who were sampled systematically from three different districts in Northern Uganda. Semi structured self administered questionnaires were used. Data was analysed using SPSS 17.0 statistical package.

Results

94.5% of the respondents were Luo (Acholi or Langi) by tribe and of generally low socio-economic status whereby 65.7% had at least gone up to primary school level. Over half (54.1%) were neither employed nor earning a living. For dietary risk factors, the health consequences of excessive salt consumption was best understood (84.2%) and the health benefit of fruits and vegetable based diets least understood (44.7% and 62.3% respectively). For behavior related risk factors, stress or lack of social support, smoking and excessive alcohol consumption were most understood respectively with relatively less knowledge concerning the benefit of regular physical exercise. The results show a overall general knowledge on dietary and behavior related risk factors of CVD.

Conclusions

Much as there is general knowledge on diet, health education should target mainly the health benefits of fruit and vegetable based diet as well as physical exercise for behavior factors. These should be taught and emphasized alongside other diet and behavior changes as it is the more effective in the community. KEY WORDS: Cardiovascular disease (CVD), Non-Communicable disease (NCD), Dietary risk factors, Behavior risk factors, Knowledge.

INTRODUCTION

Cardiovascular Diseases (CVDs) are the number one cause of death globally and more people die annually from CVDs than from any other cause (WHO, 2011). Non communicable diseases (NCDs) such as cardiovascular diseases, hypertension, diabetes, chronic respiratory diseases, mental illness, cancer conditions and injuries kill more people globally than infectious diseases (CDC, 2012). CVDs are projected to remain the single leading cause of death (Mathers et al, 2006) and according to WHO, it is documented that over 80% of CVD deaths take place in low- and middle-income countries like Uganda (WHO, 2011).

Sub-Saharan Africa is facing an epidemiological shift from AIDS to cardiovascular diseases being the leading cause of death. Although the USA has higher rates of cardiovascular diseases now, these are declining compared to the rates of the sub-Saharan African region (Ikemi et al, 2011). Thus, this region of Africa faces not just an epidemiological transition but rather the simultaneous burden of cardiovascular diseases related to poverty and infections, emergence of risk factors and diseases of affluence, as well as new cardiovascular problems caused by HIV/AIDS epidemic and its management (Fezeu et al, 2006).

CVD is the leading killer of all NCDs in Uganda (WHO, 2011) and by 2020, studies indicate that mortality by CVD is expected to increase. Non-Communicable Diseases (NCDs) and their risk factors are now an emerging problem in Uganda although the focus has been directed to infectious diseases to a greater extent (UBOS, 2010).

Fortunate enough, most cardiovascular diseases can be prevented by addressing risk factors such as tobacco use, alcohol abuse, unhealthy diet and obesity, physical inactivity, high blood pressure, diabetes and raised lipids (Lim et al, 2012). This is important as most of the risks are diet and behavioural related and we know that behavioural risk factors are responsible for about 80% of CVDs (WHO, 2011).

Uganda National health reporting system is yet to include NCD risk factors and little is known to effect intervention and the country has no integrated or topic-specific policy/action plan which is currently

operational for cardiovascular disease (WHO, 2011). Uganda's Health Sector Strategic Plan (HSSP) also prioritizes CVD control and management (Ssebunnya, 2013). Population-based data on the burden of cardiovascular disease risk factors can aid in the planning and implementation of an effective response to the double burden of communicable diseases and non-communicable diseases in Uganda (Maher, 2010). Therefore, awareness of the population about risks of these diseases is paramount.

In this study, we aim to assess the awareness of dietary and behaviour-related risk factors of cardiovascular diseases amongst women of rural Northern Uganda.

Cardiovascular diseases are the main noncommunicable conditions, are major public health concern worldwide and account for 9.2% of total deaths in the African region (WHO, 2005) and are the number one cause of death globally. They remain the leading killer of all NCDs in Uganda (WHO, 2011). More people die annually from CVDs than from any other cause for example an estimated 17.3 million people died from CVDs in 2008, representing 30% of all global deaths (WHO, 2011).

By 2020, studies indicate that mortality by CVD is expected to increase by 120% for women and 137% for men (Yach, 2004). The number of people who die from CVDs will increase to reach 23.3 Million by 2030 and CVDs are projected to remain the single leading cause of death (Mathers, 2006). Evidence suggests that the increasing burden of chronic diseases has grave consequences (Duda et al, 2007) and the increase in NCDs in Uganda is attributed to multiple factors such as adoption of unhealthy lifestyles, increasing ageing population and metabolic side effects resulting from lifelong antiretroviral treatment (UBOS, 2010).

Research into cardiovascular disease in Sub-Saharan Africa has been hampered by lack of funding and expertise (Mocumbi, 2012) but according to World Health Organization, behavioural risk factors are responsible for about 80% of CVDs (WHO, 2011). This has also been associated with lack of national programming for NCDs (Awah, 2008) and widespread health education and awareness campaigns are needed to address these issues (Kiawi, 2006).

Therefore, Uganda is facing a mixed burden of diseases related to poverty and infections, emergence of risk factors and diseases of affluence, as well as new cardiovascular problems caused by the HIV/AIDS epidemics i.e. both communicable and non-communicable diseases.

Limited research has been done in Uganda concerning cardiovascular disease and little has been done to educate Ugandans about this preventable killer. Since we know that more than 80% of the risk factors for CVD are behavioural related, awareness of the population is therefore important.

NCDs are on the increase in Uganda and world at large and can affect anyone without regard to age, race, ethnicity, sex, or income level. CVD being the most significant NCD in Uganda is anticipated to soon eclipse communicable and poverty-related diseases as the leading cause of mortality and disability. Lack of knowledge highly affects life style and health related behavior which makes the problem worse as CVDs tend to take long in progression.

Women being at the heart of their families should be well equipped with knowledge. They are responsible for the behaviors of their children as they grow up and are most times in charge of the daily feeding habits of the whole family. Widespread health education and awareness campaigns are needed and recommendations shall be made according to the findings. It was therefore of significance to assess the knowledge of the "mothers" about the risks for CVD.

Recommendations have been made after this study and this will help stake holders like Ministry of Health (MOH) to draft policies and other service providers like Uganda Heart Institute to set up strategies to educate the entire population and CVD patients.

METHODS

This was a Cross-sectional study using qualitative and quantitative data collection methods. who presented at the study sites during the time of research were interviewed using a self-administered questionnaire. Medical students trained on data collection techniques together with few other health workers interviewed the participants.

A total of 435 women (15 to 70 years) in rural Northern Uganda were recruited for a cross sectional study. These were from three Health Centres purposively chosen from different districts around Northern Uganda i.e. Atiak HC III in Amuru, Pader HC IV in Pader and Bobi HC III in Gulu. Systematic random sampling was used to obtain the study participants.

The questionnaire was composed of 15 items. It was obtained from a previous study, remodeled and changed some questions to make it easier to understand by our target population as advised by the institutional review board. Ethical approval was obtained from the Institutional Review Board of St Mary's Hospital, Lacor. It was pretested at Gulu Regional Referral Hospital. Data was analysed using SPSS 16.0 statistical package.

There were Limited finances to fully compensate and facilitate the study participants, i.e. respondents as well as researchers for their time. Explaining some words concerning CVD into the local language was also hard as some diseases were hard to be understood by lay men in their local language.

DATA PRESENTATION, ANALYSIS AND INTERPRETATION

The overall response rate was 100% as we got 438 respondents that agreed to participate fully and their data was analyses yet we expected a minimum of 424 respondents.

CHARACTERISTICS OF THE RESPONDENTS

The characteristics of the study population are shown in Table 1.

Knowledge of dietary and behaviorrelated risk factors of CVD

Table 2 shows the results of the responses from the participants in percentages. The questions are in the order as they appeared in the questionnaire.

DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

The purpose of this study was to assess the awareness of dietary and behavior-related risk factors of CVD amongst women of rural northern Uganda. This study targeted females as only as in this cultural context, females are mainly concerned with the day to day behavior and feeding of their families. Overall, there seems adequate knowledge about these objectives except in a few fields. This has also been noted in previous studies (Holdsworth, 2005). Also, findings show that behavior related risk factors were better understood vis-à-vis dietary-related risk factors. Note that in this study, hypertension was taken as a CVD rather than risk factor.

Discussion

For objective one which was to assess the knowledge of dietary risk factors for CVD amongst women of rural Northern Uganda, questions 1-7 were used to assess the level of knowledge on dietary related risk factors. Overall, the results show awareness on the dietary –related risk factors. There is relatively adequate knowledge about high salt consumption in relation to causing CVD at 77.9% to 84.2%. This is consistent with some previous studies performed in other relatively higher income countries like England (Parmenter, Walter and Wardle, 2000).

There is also adequate knowledge on the effects on processed sugar consumption as 76% of the respondents agreed that a ot of sugar consumption can worsen heart problems. However there is inadequate knowledge on consumption of fruits and vegetables. Less than half (44.7%) of the respondents were not aware about the benefit of fruits in CVD control. This is not surprising as people in this region do not prioritize fruit diet despite the seasonal availability of fruits especially mangoes. Previous studies have showed similar results (Parmenter, Walter and Wardle, 2000 Sapp and Jensen, 1997)

A significant percentage of people (35%) was not sure and or did not know the effect of excessive consumption of red meat. This could be linked to the general consensus that a large percentage of the public cannot easily differentiate between red meat and white meat. This is important to know as annual meat production is projected to increase from 218 million tons in 1997-1999 to 376 million tons in 2030 (WHO/FAO, 2003).

The second specific objective was to assess the knowledge of behavioral risk factors for CVD amongst women of rural Northern Uganda and Questions 8 to 15 were to assess the knowledge of the behavior-related risk factors of CVD. There is generally adequate knowledge about the behavior related risk factors. Smoking, alcohol consumption, physical exercise, weight gain and stress were assessed. Smoking, alcoholism and stress or lack of social support are common amongst the people in this post conflict area and according to the research, these were best understood risk factors (85.4% to 90%).

However, these areas should not be left out during public health education as previous surveys have shown that Ugandans continue to smoke and abuse alcohol with Uganda ranking number one in Africa and Number Eight in the whole world in terms of alcohol consumption estimated at 6.14 liters of ethyl alcohol per individual per year (CNN, 2013)

Of the behavior practices assessed, exercise was

Characteristic	Percentage
Age(Years)	
15-19	5.5
20-29	54.1
30-39	28.1
40-70	11.6
Tribe	
Acholi	77.4
Lango	17.1
Others	4.6
Religion	
Catholic	66.7
Protestant	17.1
Pentecostal	8.2
Moslem	3.2
Others	2.5
Marital Status	
Never married	17.8
Monogamously Married	51.1
Polygamously Married	19.2
Divorced/Separated	6.4
Widowed	4.3
Highest Level of Education	
None	15.5
Primary	50.2
Ordinary Level	21.5
Advanced Level	4.6
Tertiary Level	6.6
Employed or Earning a living	
Yes	27.2
No	54.1
Occupation	
None	41.1
Salaried	11
Self-employed	34.2
Student	11

Table 1: Characteristics of the respondents

ORIGINAL ARTICLES

	Item	Correct (%)	Incorrect (%)	Unsure (%)
1	Eating a lot of red meat increases heart disease risk.	64.6	17.6	17.4
2	Eating a lot of sugar can contribute to heart problems.	76	13.5	10
3	Eating a lot of salt can contribute to heart problems like hypertension.	84.2	9.8	5
4	Eating raw salt is worsens heart diseases	77.9	13.9	7.1
5	Low intake of fruits can contribute to heart problems.	44.7	39.5	14.8
6	Fatty food consumption increases the risk of diseases like heart diseases and stroke.	80.1	14.4	4.6
7	Eating more vegetables increases the risk of heart diseases	62.3	30.1	6.8
8	Weight increase and obesity gradually increases risk of heart problems	84.7	11.2	2.7
9	Obesity increases risk of developing hypertension and heart problems	84	9.8	5.5
10	Regular physical exercise decreases the risk of heart diseases and high blood pressure	75.1	17.1	7.3
11	Walking long distances and gardening are considered types of exercise that can lower heart disease risk.	59.1	27.6	12.3
12	The healthiest exercise for the heart involves rapid breathing for a sustained period of time.	62.6	25.3	11.2
13	Stress or lack of social support increases the risk of heart disease and high blood pressure.	90	6.8	2.7
14	Excessive alcohol consumption increases the risk of heart diseases, stroke and high blood pressure.	85.4	8.9	5.5
15	Smoking contributes to development of heart disease	89.5	5	5

Table 2: Table showing the correct responses for individual knowledge items (n=435 women)

least understood (59.1%). This is not surprising because this community has low literacy rate and people never prioritize regular physical exercise and are of low socio-economic status with about a quarter (24.5% (CIA, 2009), 19.6% Ministry of Finance, 2013)) of the population of Uganda living below the poverty line.

Recommendation

With 82.2% of the research participants ranging in the age bracket of 20-39 years, the young adults should be targeted for nutrition education since some gaps have been identified. Education should target fruit and vegetable consumption. Since this finding is overall, even in other countries (Lock K et al, 2005), all regions should be targeted for education. Lock and colleagues (2005) also discuss the importance of fruits and vegetable based diet in NCD control and how it is lowly utilized by majority population. The public should also be educated about the difference between red and white meat and safety of consumption.

However, WHO (2004) recommends nutrition education based on a whole diet approach which can easily be understood by relatively all communities and not just targeting one food. Regular exercise should also be emphasized in the education alongside other behavior lifestyle changes. Practical teaching practices should be employed as the population tends not to embrace the knowledge without skills.

Nutrition programs need to be implemented in school curricula, university syllabi, media

establishments, community programs. These are to educate the masses on issues pertaining NCDs, good and sustainable dietary habits and on a whole reduce the further growth of nutrition transition. These messages have to be tailor-made to different population groups – including the disadvantaged population groups like these ones. These kinds of programs give people empowerment to make informed choices on healthy foods.

Future studies should study also men as they are the heads of the families in such setting and influence the diet and behavior lifestyles of their families. Also they should try to study urban setting to compare knowledge with the knowledge from rural setting.

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ABSTRACT The Challenges Of Follow-Up Of HIV Exposed Infants In A Government

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BACKGROUND

Lost to follow-up of HIV exposed infants remains a challenge at the Early Infant Diagnosis (EID) care point, Infectious Disease Clinic (IDC) Gulu Regional Referral Hospital (GRRH). Resettlement of families in post-conflict Northern Uganda continues to pose limitations to community follow-up efforts.

PROGRAM DESCRIPTION

Efforts to strengthen EID/PMTCT program, Ministry of Health (MOH) in collaboration with the Strengthening Uganda's Systems for Treating AIDS Nationally (SUSTAIN) project has completed a number of trainings for staff at GRRH in EID, PMTCT and comprehensive Paediatric HIV/AIDS care since January 2011. These have empowered routine education of the mothers at the EID care point on the revised EID/PMTCT guidelines and thus benefits of early diagnosis.

SUSTAIN facilitates the follow-up of exposed infants lost-to-follow through a community-focused coordinator who works with the hospital Community Health Department(CHD), Expert clients/volunteers through home visits within Gulu Municipality and telephone calls using a facility telephone pre-loaded with airtime.

Using the EID/Dry Blood Spot data management register, information on 277 infants who had a DNA PCR test between 4th February 2010 and 31st January 2011 was obtained. These were either a 1st or 2ndDNA PCR. 26.7% (74) did not return to pick up their results of these 13.5% (10) had positive and 86.5% (64) had negative results respectively. Of those that returned for their results, 8.9% (18) were positive, 91.1% (185) negative.

LESSONS LEARNED

Follow-up of exposed infants is mandatory for early identification, diagnosis of HIV and therefore prompt enrolment into care. Capacity building of community based providers is paramount in curbing lost-to-follow. Re-settlement of families has affected MOH/SUSTAINS follow up activities in post-conflict Northern Uganda.

CONCLUSION

There's need to strengthen hospital community departments with trained personnel in EID/PMTCT and appropriate transportation for effective EID follow-up efforts. Post-conflict regions will benefit from support that extends to an unrestricted catchment area with-in the respective district.

Utilization And Perception Of Quality Of Antenatal Care Servicesby Pregnant Mothers At The Government Health Facilities In Laroo Division, Gulu District

Mutesasira Semei, Lubega Ronald , Mahulo Nelson, Mbabazi Grace Martha, Mugerwa Moses, Mukisa Daniel, Nakabugo Katumba, Turyasiima Munanura.

BACKGROUND

Antenatal care services (ANC) are a fundamental right to mothers and their babies. Literature on their utilization and perception is scanty in Laroo division Gulu District, although abundant globally.

OBJECTIVES

The main objective was to assess utilization and perception of quality of ANC services in government health facilities in Laroo Division.

METHODOLOGY

395 mothers were recruited using consecutive sampling in this descriptive cross sectional study. Data were collected using questionnaires and analyzed using SPSS version 17.0.

RESULTS

Majority of the respondents (44.2%) were aged between 25-34 years and were mainly Acholi (79.7%) and Langi (14.7%). Voluntary Counselling and Testing (VCT) for HIV (91.4%) and folic acid / iron supplements (86.1) were the most utilized ANC services while screening for syphilis (27.6%) and urine testing for sugar and proteins (33.4%) were the least utilized. Majority of the respondents (71.4%) reported that the quality of services was good and 88.5% stated that they were satisfied with them

CONCLUSION

Most of the services offered were satisfactory and of good quality. Urinalysis and screening for syphilis were the least utilized. Laroo Division needs to improve ANC service delivery in general educate mothers on the pregnancy danger post natal care and family planning.

Prevalence And Factors Affecting Contraceptive Use Among HIV Infected Women Of Reproductive Age

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BACKGROUND

In Uganda, Mother to child transmission of HIV still remains the main route for the unborn child, and yet the contraceptive utilization still remains low at about 30% with high unmet needs of up to 41%. Under use of highly effective contraceptives and barriers leaves women with HIV at risk for unintended pregnancy and HIV transmission to their babies.

OBJECTIVES

To establish the prevalence and factors affecting contraceptive utilization among HIV infected women of reproductive age attending IDC-GRRH.

METHODOLOGY

A Hospital based analytical cross sectional study was conducted among 434 HIV infected women of reproductive age receiving care from IDC, GRRH .Simple random sampling was employed to recruit study participants. An interviewer administered semi-structured questionnaire was employed for quantitative data collection. The data was entered and analyzed using SPSS 17.0.

RESULTS

Contraceptive prevalence among the 434 respondents was at 36% (95% CI: 31 – 40, P-value 0.000). The most significant predictors of contraceptive use were: being married (aOR= 4.2, 95% CI 2.60-6.76, P-value 0.000 and monthly income between Ugx 95,918-700,000 (aOR= 3.25, 95% CI 2.16- 4.88, P-value 0.000)

CONCLUSION

The prevalence of contraceptive utilization was greater than the national average of 30% but remained generally low at only 36%.

Only a third of HIV infected women attending IDC-GRRH had utilized contraceptive which is below the MDG target of 75% contraceptive coverage among HIV infected women by the year 2015.

Therefore, MoH and other stakeholders should sensitize the community on the importance of contraceptive utilization among HIV infected women.





- Organization of education outreach visits to the under-privileged communities/ schools.
- Screening for HIV/AIDS, Hepatitis, Mal nutrition, diabetics, cervical cancer and hypertension.
- Provide family planning methods to the communities.
- Provide home to home ANC services.
- Do immunization for children and people in need.
- Educating persons about services provided at all health center levels.

REVIEW Host Genetic Diversity in Infection

Stella Carlogmano, Professor of Genetics Second Federation of the University of Naples, Italy

Host Genetic Diversity in Infection Stella Carlogmano, Professor of Genetics Second Federation of the University of Naples, Italy

A characteristic feature of many human infections is that only a proportion of exposed individuals develop clinical disease. Heritable factors were long considered to have a dominant role in explaining this inter-individual variation in susceptibility: the early observation that cases of tuberculosis clustered within households, for example, led to the impression that tuberculosis was an inherited disease. However, the subsequent discovery of bacteria such as Mycobacterium tuberculosis as agents of infectious disease — and the experimental demonstration of the communicable nature of infections — focused attention on the pathogen, somewhat neglecting the potential importance of the genetic environment of the host.

However, in the 1930s studies on the use of malaria therapy in the management of syphilis suggested the existence of some marked interindividual differences in susceptibility to malaria in nonimmunes. The subsequent identification of the major effect of sickle haemoglobin heterozygosity on malaria resistance provided the incentive for genetic investigations in a diversity of populations.

Actually, the genetic analysis in combination with an epidemiologic analysis of infections may help in pointing out the molecular pathways of some infectious diseases, trough genome-wide association studies (GWA or GWAS), which examine many common genetic variants in different individuals to see if any variant is associated with a trait. GWAS typically focus on associations between singlenucleotide polymorphisms (SNPs) at the level of specific genes and traits like resistance or ipersensitivity to major infectious diseases.

THE NATURAL RESISTANCE TO HIV/AIDS

This June marks 30 years since the first reported case of AIDS. Extensive research over the last three decades has advanced our understanding of HIV pathogenesis, as well as our ability to treat the infection. Up until a few years ago, HIV-1 infection

was regarded as an inevitably progressive and inexorably fatal disease. In recent years, advances in HIV/AIDS research have been able to somewhat modify this sombre and fatalistic outlook on HIV infection. In fact. modern antiretroviral drug



strategies have now been able to convert HIV-1 from being an inevitably lethal infection to a chronic medical condition which is controllable by long term therapy. The second important breakthrough has been the recent discovery that there are certain individuals who possess natural mechanisms to resist HIV infection, or, if they do become infected, are able to control the infection so effectively that they remain asymptomatic for long periods of time. Although these cases are still comparatively rare, the studies have provided very important insights into natural mechanisms for resistance, or for overcoming HIV infection, which could be exploited for developing new antiretroviral drugs or HIV vaccines.

The Natural resistance to HIV/AIDS can be considered at two levels:

– Resistance to becoming infected with the virus: There has been considerable interest in investigating genetic susceptibility to HIV and AIDS over the last few years. This has been encouraged by studies of cohorts in which a small proportion of individuals remain HIV seronegative despite repeated exposure to HIV from infected sexual partners, also if immunological assays have confirmed that some such resistant sex workers have been exposed to the virus. These individuals are referred to as 'Highly exposed seronegative individuals'.

– Persons who are infected but who resist progression to AIDS: They are referred to as longterm non-progressors (LTNP). These HIV-positive individuals have not been on antiviral therapy yet have remained clinically well and have reasonable immune function with high and stable CD4+ lymphocyte counts for many years without showing signs of immune compromise or evidence of progression to AIDS.

RESISTANCE TO HIV INFECTION

Transmission of HIV is very inefficient in comparison to other human viruses. It is therefore difficult to establish how often exposures to HIV in nature which fail to establish infection are due to



resistance or are merely part of the intrinsic inefficiency of HIV transmission. There are, however, a number of examples of defined instances of HIV exposure which provide opportunities for the study of resistance to HIV infection

a) Persons in "high risk" populations who are repeatedly exposed to HIV infection yet remain seronegative to HIV. These include groups of female prostitutes in Nairobi and the Gambia and male homosexuals in Los Angeles who have been subject to intense investi-gation. These individuals continue to engage in high risk, unprotected sexual activities yet remain antibody negative. Bill Paxton, a scientist of the Aaron Diamond Center for AIDS Research in New York, focused his study on Steve Crohn, a gay male who came of age in California during the 1970s (see Photo on the left). Crohn has lost more than 80 friends and lovers to AIDS, yet he repeatedly has tested HIV-negative, and has allowed researchers to study his resistance. Paxton took a sample of Crohn's immune cells, bombarded them with 3,000 times the amount of virus that typically causes infection, and found the virus still was unable to penetrate his immune cells (see picture on the right). Therefore, Crohn was the 'mutant' for resistance to HIV representing a good start point to study how the virus infects individuals

b) Seronegative infants born to HIV positive mothers. Two kinds of resistance to HIV infection have been described — that due to mutations in coreceptors used by HIV to establish infection or, if HIV infection does become established, there are some individuals who appear to be able to mount a particularly vigorous and effective immune response which is able to overcome and clear the infection.

Mutation in HIV co-receptor: The role of the chemokine receptors which may serve as co-receptors for HIV, has recently been established. Not surprisingly, therefore, individuals with mutations in the alleles coding for this receptor have been demonstrated to be resistant to HIV infection. Chemokines are chemical messengers which transmit activation signals to recipient cells. For example, the CC chemokines called RANTES, MIP-1a and MIP-1b convey chemotaxis signals to leukocytes which cause them to move towards areas of inflammation. Steps of HIV interactions with taarget cells are shown in the figure at left. Recent genetic analyses of chemokine receptors that are coreceptors with CD4 for viral entry into macrophages and lymphocytes show that individuals homozygotes for a 32 bp deletion in the gene encoding CC chemokine receptor-5 (CCR5) (phenotype 1 in fig), the coreceptor for macrophagetropic HIV, are very markedly resistant to HIV

infection and heterozygotes display lower rates of disease progression. Mutations in the CCR-5 receptor could therefore be expected to result in cells becoming resistant to HIV-1.

In the case of Steve Chron, additional testing revealed that Crohn possesses two copies of the delta-32 mutation. Apparently, the normal CCR5 gene puts receptors on immune cells that act like doors allowing HIV to enter and hijack a cell. Without that door, the virus can't get in. Whe the gene is abnormal, no door exists.

A small number of individuals who are homozygous for the allele of CCR-5 have been found amongst the highly exposed group of sero-negative individuals mentioned above. Lymphocytes from these individuals have been shown to be highly resistant to infection with HIV-1. As yet no individuals with the homozygous mutant have been found to be HIV infected. Approximately 1% of the Caucasian population are homozygous and 15 to 20% are heterozygous. To date, mutations in CCR-5 have not been found in African subjects. Heterozygosity is thought to provide partial protection, i.e. individuals with one mutant copy of the CCR-5 gene appear to progress more slowly to AIDS than individuals without this mutation. Mutations in the CCR-5 chemokine receptor have thus been shown to be a mechanism of HIV resistance in a small number of persons. Therefore, people with European ancestors would be more likely to have this gene, and vice versa. And Steve Crohn happens to be white and of European descent. A possible link between 14th-Century survivors of the bubonic plaque (or the Black Death, as it also is known) and modern-day people who engage in high-risk sexual behavior, but appear to be immune to HIV infection, is the presence of the CCR5 gene version known as CCR5-delta32. People who survived the Black Death could have passed on a mutation that prevents the human immunodeficiency virus entering cells.

Also variants of the flanking gene for the CCR2 chemokine receptor and of the stromal-derived factor (SDF-1) gene encoding the ligand for CXCR4, the coreceptor for lymphocyte-tropic strains (phenotype 2 in fig), have also been associated with some alteration in rate of disease progression. Many highly exposed sero-negative individuals, however, do not have a CCR-5 or CXCR4 mutation and the explanation for their resistance still needs to be elucidated.

However, several other resistance genes must exist as the known variants of CCR5 account for only a minority of Caucasians and none of the African individuals found to be markedly resistant to HIV







infection.

ii) Immune protection against HIV infection:

Infants: Only about 25% of infants born to HIV infected mothers are persistently infected with HIV and progress to AIDS. Of the remaining 75%, many are uninfected because an inadequate dose of virus crosses the placenta. However, investigations of foetuses from HIV positive mothers who were electively aborted in early pregnancy have shown that the majority have HIV DNA sequences in cells from various organs. From these studies it would therefore appear that the majority of infected foetuses are able to overcome and clear the infection. The mechanism, however, is still unclear as the immune system of the foetus is immature and ineffective in clearing most transplacentally transmitted viruses.

Further evidence of immune protection in the infant is the manifestations of lymphocyte reactivity to HIV which are found in seronegative infants. In one study, some 40% of uninfected infants demonstrated lympho-cyte reactivity (by IL-2 production) in their cord blood and peripheral blood lympho-cytes in response to several HIV peptides including gp160 and nef proteins. Even more convincing is the finding of HIV-specific cytotoxic T-lymphocytes imply-ing continuous antigenic stimulation and therefore viral replication in the host.

The most striking and widely publicized illustration of the ability of an infant to overcome HIV infection is that of a child in Los Angeles born to an HIV positive mother, who had negative HIV cultures of blood at birth, but then produced sub-sequent positive cultures at 19 days and 51 days. However, numerous follow-up blood cultures were negative and the child has remained seronegative and clinically well for at least 5 years afterwards. Several other cases of seroreverting infants have also been described.

Adults: Seronegative adults who have been exposed to HIV also have demonstrated an immune response to the virus as shown by lymphocyte reactivity in response to HIV antigens. These individuals include those having unprotected sexual inter-course with multiple HIV infected partners, intravenous drug abusers, prostitutes, recipients of blood or blood products contaminated with HIV and healthcare workers who have been exposed to HIV through needlestick injuries with HIV infected blood. Some of the possible mechanisms could include exposure to virus-free antigens of HIV or defective strains of HIV. However, the finding of CD8+ cytotoxic T-lymphocytes which were MHC class I restricted, would indicate at least one round of viral replication and suggest that the immune system was able to overcome and clear the infection without the production of antibodies.

Other molecules have been implicated in the resistance and susceptibility to HIV infection. They include the human leukocyte antigens (HLA), beta chemokines and defensins, polymorphism in the cytokine genes, configuration on chromosome-22, beta 2 microglobulin, HIV-2 etc.

LONG-TERM NON-PROGRESSORS

There is a wide range of clinical responses to HIV infection in humans. In about 80% of HIV infected

individuals AIDS develops within the median time of 10 years. Individuals with this clinical course are referred to as typical progressors. In 10% of HIV infected subjects AIDS develops within 2 to 3 years after infection these individuals are referred to as rapid progressors. On the other side of the spectrum, about 5 to 10% of HIV infected persons remain asymptomatic for at least 7 to 10 years and often up to 20 years after HIV infection, despite being on no antiretroviral therapy. Their immune function is relatively well maintained with CD4+ lymphocyte counts above 600/mm3 and low plasma levels of HIV-1 RNA. Biopsies of their lymph nodes confirm the non-progressive nature of their infection with little evidence of the hyperplastic and involuted changes or lymphocyte depletion seen in lymph node tissue from subjects with progressive disease. These individuals are referred to as long-term nonprogressors (LTNP), or long-term survivors. Both viral as well as host factors play a role in long-term non-progression of HIV.

Viral factors: Culture of HIV from the blood of LTNPs is difficult and often unsuccessful because of plasma viral load. Molecular the lower characterization of these isolates have revealed the presence of a number of genetic defects which could be the basis for the attenuation of the virus. Occasionally genetic defects such as in the NfkB or Sp1 site within the long terminal repeats of the virus have been demonstrated. However, the best documented and studied genetic lesions associated with virus attenuation in LTNPs are the nef deletion mutants. The nef gene is a crucial regulatory gene of HIV-1. Monkeys experimentally inoculated with simian immuno-deficiency virus (SIV) which have deletions in their nef gene, show no signs of disease and have low viral loads in the plasma and normal CD4+ lymphocyte counts. In humans, nef deleted mutants of HIV-1 have also been shown to play a role in the genesis of long-term non-progression. The most convincing demonstration came from a study published by Australian workers at the end of 1995. An HIV infected male homosexual donated blood and infected some 7 recipients over a period of 3 years (in the era before blood was routinely tested for HIV). Surprisingly, neither the donor nor any of the recipients developed any symptoms and had remained healthy (with the exception of 2 who died from unrelated causes). Molecular studies on isolates from 4 of the 8 subjects demonstrated defects in the nef gene. Although nef deletion mutants still only account for a very small number of LTNPs, they have aroused great scientific interest because of their potential usefulness in the development of an HIV vaccine.

Host factors: From studies of a number of cohorts of LTNPs, a pattern appears to be emerging characterizing these individuals as having immune responses which are quantitatively and qualitatively more potent and more effective in controlling HIV infection. Vigorous virus-specific humoral and cell mediated immune responses have been demonstrated in these subjects. High titres of potent neutralizing antibodies to a wide spectrum of HIV isolates have been shown to be present in the sera of LTNPs. In addition, there are strong CD8+ cytotoxic lymphocyte responses in these individuals, reflecting longstanding stimulation of the immune system by continuing viral replication. The resulting immune response is able to effectively suppress viral replication and thus relatively low viral loads are found in their plasma and high CD4+ lymphocyte counts are maintained in the blood. The lymph node architecture remains intact and the degree of virus trapping in the follicular dendritic network in the lymph nodes is considerably lower.

Precisely why some individuals respond with a more favourable immune response than others is still not clear. It is also uncertain whether the more effective immune response is a cause of lower viral loads or whether the more effective immune response is the con-sequence of infection with more attenuated viral variants.

Long-term non-progression as well as resistance to viral infections is apparently a relatively uncommon phenomenon. However, the importance of the phenomenon of resistance to viral infection lies in the lessons that it teaches which could be used in developing therapeutic and vaccine interventions to control and prevent infection. For the present, and for the majority of HIV infected individuals, antiretroviral therapy remains the only effective way of controlling HIV infection.

Genetic associations have already provided numerous insights into the pathogenesis of infectious disease and the relevance of particular defence mechanisms. Association of polymorphisms in cytokines and chemokines or their receptors has led to attempts to modulate the activity of these mediators in particular diseases. For example, the upregulatory variant of the polymorphism at position -308 of the TNF promoter was associated with susceptibility to severe malaria and agents that may reduce the activity of this cytokine are under Another application is in the assessment. understanding of specific immune defences used in host resistance to infection or disease. For example, enhanced susceptibility to the non-virulent mycobacteria in children with mutations in the interferon-y receptor has highlighted the importance of this pathway in controlling these mycobacteria. But the finding that these children appear to have little or no alteration in their susceptibility to other common pathogens has also been informative. Studies of mannose-binding ligand deficiency have demonstrated that this molecule plays a key role in resistance to some but not to other infectious agents.

CONCLUSIONS

A major goal in the field is the identification of genetic loci that influence the predominant type of cellular immune response to infectious pathogens and potential allergens. The vast amount of evidence suggests that there is a natural resistance to HIV infection and to progression to AIDS. However, the exact mechanisms accounting for such resistance are not yet completely elucidated. Future research may reveal the exact mechanisms by which this natural

resistance operates, with the potential of developing appropriate therapeutic interventions and vaccines. Long-term non-progression, as well as resistance to viral infections, is a relatively uncommon phenomenon. Adequately controlling factors that contribute to fast progression to AIDS can delay the onset of the symptoms and provide a better life style for those patients. At the present time, however, and for the majority of HIV infected individuals, antiretroviral therapy remains the only effective way of controlling HIV infection. Modern genetic techniques provide several completely new tools to study how the genetic diversity may influence the development of infectious diseases. Variants either the host or the infectious agent may determine different courses of the infection. As immunogenetic associations with infectious diseases may facilitate vaccine design. For example the association between the HLA class I molecule, HLA-B53, and resistance to severe malaria in African children has been analysed in detail and suggested that the association resulted from the action of HLA class I restricted T cells. A search for such cells in Africans exposed to malaria employed a new strategy, known as reverse immunogenetics. Peptides are eluted from the groove of the disease-associated HLA molecule and sequenced to identify the characteristics of peptides that bind to that HLA type. This sequence information is then used to scan protein sequences from the relevant microorganism to identify candidate epitopes for T cells restricted by that HLA molecule. Application of this approach in malaria led to the identification of an epitope restricted by HLA-B53 in the P. falciparum liver-stage antigenl. These findings provided support for efforts to develop vaccines against malaria that would induce protective CD 8+ T cells against liver-stage antigens. However, the technique may be applied to different infections, revealing important targets for future vaccine development. The use of genetic information to predict infectious disease risk in individuals is unlikely to alter clinical practice in the near future, and the predictive value of genetically based risk assessment remains poor, even in more-extensively studied, non-infectious disease phenotypes. Clinical translation is more likely to result from the characterization of the molecular pathways involved in disease and the identification of novel targets for immunomodulatory drugs or vaccines. The application of systems biology to integrate genomewide studies, including genome, transcriptome and proteome analyses, as well as small interfering RNA (siRNA) screens, may be a particularly powerful approach for identifying novel therapeutic targets. To adopt and use these techniques, a laboratory ad hoc is required. We are working at setting up such a lab in Gulu FOM, in order to start very soon genetic studies of both patients and infectious agents. The molecular microbiology laboratory will be devoted to the isolation and preliminary molecular characterization of pathogenic bacteria.

Faculty — Articles

Medical Internship crisis in Uganda Has Uganda finally lost it? Byamukama Onesmus, MBChB V

Making it through medical school is always a dream of the doctors in-training and those hoping to join medical school but guess what awaits them "NO PLACE FOR INTERNSHIP"

This raises many questions to a country whose doctor-patient ratio is 1/1298 yet the recommended by WHO is 1/439. Is it that we have many doctors in that the ministry of health can no longer afford to produce more doctors? Or is it that there is poor management and less priority is given to health?

Young doctors who have just finished medical school undergo a one year training under the supervision of specialists in the hospitals .During this period the doctors get to put the knowledge acquired into practice. It's always considered as a period where man works as hard as a donkey.

However in august 2014, it was quite a drama as the internship committee couldn't distribute all the intern doctors to different centres, with an explanation that they are many. Many hospitals too scrapped off the privileges of accommodation and feeding. The government too delayed the salaries of

Beyond the biologic basis of disease Health care worker shortage in Uganda steams from government economic policy Tayebwa Bekson MBChB V Gulu University Faculty of Medicine, Uganda Email: tayebwabekson@gmail.com

Uganda: Where are we?

With the current Life expectancy of Uganda at 57 years for both sexes (58 years for females and 56 years for males) (WHO, 2014), Ugandans are definitely living longer than before. However, Uganda still lags behind as compared to the rest of the world at 175 out of 224 countries. The current population of Uganda stands at about 37.5 million people up from 34.5 million in 2011 with a high fertility and population growth rate.

According to The United Nations Social and Economic Affairs Division in New York, Uganda will be one of the top 10 most populated countries in the whole world by the year 2100 with its population expected to increase by five-fold by then (The New Vision, June 23, 2013). Uganda also hosts an increasing number of refugees from neighboring countries like South Sudan, Rwanda and DRC. (WHO, 2014) these young doctors for four months, some interns had to actually be suspended for laying down their tools.

Speaking of that, When young doctors who have no source of income are forced to work under such hard conditions, with no time off and no feeding and accommodation privileges, yet with a delay in salaries and intimidation from the seniors who are supposed to play a mentorship role, then we as a country have finally lost it. How are these young doctors supposed to make ends meet?

The hunger, anger and depression of this young doctor is transferred to the patient who will in turn not receive quality care. We still ask the same question is the country committed to provision of quality health care to its citizens.

This call is not only to doctors but to all concerned citizens, the Abuja declaration signed among others by our president states that member countries are to allocate at least 15% of their budget to health which has never been realized. Our very own citizens don't reap the benefits of the quality doctors its produces. Intern doctors continue to work under poor conditions and yet even after this period, the pay is demotivating. Let's stand and advocate for a country that is concerned about the health of its citizens.

All this calls for a definite plan especially concerning the health system if the health indices are to improve given the exponential population growth.

Health crisis why?

The National Development Plan [2010/11 – 2014/15] highlights the shortage of health workers as a major challenge in improving the health of the Ugandan population. The health care worker to population ratio in Uganda is 1:1298 compared to the World Health Organization (WHO) guidelines of 1:439 (National Development Plan 2010/11 – 2014/15). In 2010 there was a very low doctor to patient ratio of 1:24,725 and a nurse to patient ratio of 1:11,000. WHO recommends a doctor-to-patient ratio of 2:10,000 for developing countries.

In 2006, the Global Health Workforce Alliance identified Uganda as one of 57 countries facing a crisis in its human resources for health. The country has been aggressively recruiting workers in recent years, but according to a 2013 government report, 42 per cent of Uganda's health positions were still vacant, with only one doctor for every 24,725 people.

The Ugandan health sector has experienced challenges related to recruitment and retention of qualified staff. This is mainly due to low remuneration as well as insufficient career opportunities (National Development Plan 2010/11 –

2014/15). Both at an international and regional level, remuneration of health workers in Uganda is much lower than most other countries. A doctor in Kenya for example earns approximately four times more than their counterpart in Uganda (Matsiko, 2010)

The Social Medicine (SocMed) school of thought

SocMed, is a non-profit organization which advocates for and implements global health curricula founded on the study of social medicine. By engaging health professionals through careful examination of the social and economic contexts of health and immersing them in partnership with a diverse group of students from around the world, it aims to foster innovative leaders who are ready to tackle challenging health problems in communities around the world.

SocMed utilizes a curriculum that places great importance on building personal partnerships and encouraging students to reflect upon their personal experiences with power, privilege, race, class, gender, and sexual orientation as central to effective partnership building in global health. In the spirit of praxis (a model of education that combines critical reflection with action) these components of the course give students the opportunity to discern their role in global health and social medicine through facilitated, in-depth conversations with core faculty and student colleagues.

Currently, SocMed offers annual courses in partnership with Lacor Hospital in Gulu, Uganda (January-February) and with Physicians for Haiti in Port-Au-Prince, Haiti (July and August). (http://www.socmedglobal.org/)

Government policy on Health

With Uganda currently funding over 80% of its national budget, however a big portion of the health sector funding is not from the government. According to the National Health Accounts for FY 2009/2010 the government funded only 15% with 49% from private funding and 36% from NGO's and donors towards the Total Health Expenditure (WHO, 2014).

The Government Budget allocation to health as of 2014/2015 was 8% of the national budget reducing from 8.6% in 2013. This is much lower than the Government commitment to the Abuja Declaration to provide 15% of the Government budget and the HSSP (Health Sector Strategic Plan) costing US\$28 per capita. The overall goal of the HSSP is to reduce morbidity and mortality from the major causes of ill-health in Uganda and the disparities therein, as a contribution to poverty eradication and economic and social development of the people. This is a very good strategic plan, but where are we in implementation towards this goal?!

Medical Brain drain vis-à-vis health care worker shortage

The crisis of health worker shortage affects many economies though not to the same extent. However low income countries suffer most because of outflow of many health workers to countries with better developed and facilitated health systems. This medical brain drain has further worsened the already deplorable health status of such countries which include Uganda. Recently it was reported in the media about the Uganda government exporting about 241 medical workers to Trinidad and Tobago (AFP, 2015). This raises a question of whether the government is committed to strengthening its health system or it is not bothered about the far reaching consequences of this practice.

In Uganda, 42 percent of vacancies remain unfilled, and according to a 2012 British Medical Journal study the country has fewer than 5,000 doctors for 35 million people, with 50 specialists having left in search of better pay overseas in the past decade, while the bulk of new graduates prefer to look for jobs abroad too. (AFP, 2015)

With expanding populations worldwide, the patient: health worker ratio threatens to escalate even in developed countries. The net result will be a far stronger "pull" that will draw many more of the scarce health professionals away from the world's poorest countries, many of which are located in Sub Saharan Africa. The result is the dire indices we see in Africa, with life expectancy less than in the more developed countries, infant and childhood mortality rate higher than in rich countries. Demographic trends portend a worsening crisis.

Recommendations

Steaming from the perspective, our prospects should be to reinforce our ailing health care system. Majorly, a fundamental national economic commitment to the Abuja declaration should be a priority. Progress should be made in strengthening the primary health care system and infrastructural development. There is great need to facilitate the health worker better to stop this brain drain. The inherent flaws in the ministry like dysfunctional surveillance, chain supply, downscaling and low recruitments of health workers, need to be ironed out with a supportive budget.

This can be achieved by collectively realizing that the health sector is no longer a supporting sector of national development but a major organ. Empowering the productivity of the citizen is paramount to achieving the much desired health and economic growth.

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Report For NUV-HOP 2014 Byamukama Onesmus, MBChB V

Introduction

Northern Uganda Village Health Outreach Project (NUV-HOP), is a village based health outreach project running in the districts of Gulu, Amuru and Nwoya. NUV-HOP 2014 was carried out by students of Gulu University Faculty of Medicine and Belgian Medical Students' Association (BEMSA) with an objective of providing health services to the rural poor in northern Uganda.

NUV-HOP comprises a number of activities including, outpatient consultations, family planning, cervical cancer screening, HIV testing and counselling, circumcision, health education in schools and homes. All the above activities are carried out during a one day integrated health camp by students

Partner NGO	Nature Of Support
Comboni Samaritans	HIV test kits for 6 outreaches
Reproductive Health Uganda	Cervical Cancer Screening and family planning services for 6 outreaches
Youth Alive Uganda	Counsellors for SMC and HIV testing
TASO	Circumcision kits and condoms for 6 outreaches
Straight Talk Foundation	HIV counselling & testing for 2 outreaches
NU-HITES	Tents used during the 6 outreaches
Gulu university	Bus for 6 outreaches

NGO Partnership and nature of support

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Faculty — Projects

Activity	July	August	Total
Opd Consultation	995	1656	2651
HIV/AIDS Counselling And Testing	421	950	1372
Family Planning	162	56	218
Cervical Cancer Screenin	120	230	350
Circumcision	39	25	64
Total	1737	2917	4654

Statistical summary of the records

from Gulu University Faculty of Medicine and other Medical students from Belgium. The internal students were also attached to Gulu Regional Referral Hospital to have an experience of tropical medicine. The activities were supervised by Medical Doctors and other health workers from the different health centres. The supervising medical doctors include Dr. Pebalo Francis Pebolo, Dr. Cana Kenneth, Dr. Ocitti Morris and Dr. Ojara Morris.

NUV-HOP also carried out its activities in partnership with different Non-Governmental Organizations which offer some of the above activities alongside the students and health center staff.

Report Of Activities Carried Out

A total of twelve outreaches were carried out during the months of July and august. For all the outreaches a number of patients received medical attention in the activities mentioned above and health education was given in 10 schools and about 100 homes in the districts of Gulu, Nwoya and Amuru. Below is a comprehensive list of the different outreaches and statistics from the different health activities for the months of July and August respectively.

Achievements

NUV-HOP registered a number of achievements in the three months of its implementation.

-NUV-HOP 2014 conducted 12 outreaches reaching out to a very high number of patients

-Delivery of public health services, especially in villages. These include cervical cancer screening, family planning, VCT (voluntary HIV testing and counseling), immunization and safe male medical circumcision.

-In addition, NUVHOP 2014 offered comprehensive laboratory to the clients. These include malaria testing, hepatitis B testing, HIV/AIDs testing, urinalysis etc.

-Sensitization of the community, especially primary and secondary school children, focused on sanitation and reproductive health including HIV/AIDS, sexual health etc.

The Outcome Of The Gulu Nap Italy-Uganda Collabortion Project Prof. Dr. Greco Luigi*, Dr. Dan Elly Aniku ** and Felix Bongomin***

* Associate Dean, Lacor Italian Co-operation, Gulu-Nap Project, Italy

** Interim Chairperson Gulu University Medical Graduate Alumni Association

***MBChB IV and Editor-in-Chief, Gulu University Medical Journal Concept Note October 4th 2012

Introduction

The Faculty of Medicine of the University of Gulu started on October 2004 by the GULUNAP collaboration. In January 2010 the first 46 'pioneers' graduated in Medicine out of 52 that started in 2004. In January 2011 fifty more students (of 60 who started in 2005) gained the graduation in Medicine.

In January 2012 fifty five students qualified as Medical Graduates out of 64 who entered the faculty in 2006.

By today the GULUNAP collaboration produced 151 new doctors in a region of Uganda that, when the project was conceived in 2003, had less than 30 doctors working in the whole region.

The productivity of the Faculty of Medicine has been very good since 151/176 (86%) students enrolled reached the graduation in due time. This target was not reached by reducing the quality of their accepted performance, which was controlled by a National Council of Higher Education.

The 2010 Graduation Cohort – The

Pioneers

All the 46 'Pioneers' completed the year of Internship after the Graduation, they have been scattered through the whole Uganda. The general feeling we received is that their dedication and expertise was often much appreciated.

14 of these are now attending post-graduate Master Courses in different Medical Specialties in -Good interaction and motivation for the Ugandan and Belgian students. This was manifested by different social gatherings we had

-Positive support from the community, district officials and Gulu University.

-Strong partnership with Comboni Samaritans, Youth alive, straight talk, Reproductive Health Uganda (RHU) and district authorities etc.

-Good relationship with the host families

-Both local and international students were able to carry out screening tests under supervision which is important for their skill development.

-Commitment, persistence, accountability and transparency by the organizing taskforce.

-Initiation of the Academic aspects on the NUVHOP 2015 to enable the faculty gain from the exchange program

Makerere University, Mbarara University or in Uganda martyr's University-Nsambya Hospital.

7 are engaged in Family Planning and reproductive Health services throughout the country.

5 found job opportunities in Kampala. 3 moved to Kenya, two to Sudan and one to Czech Republic for Master.

15 work in health districts all through the country with full responsibility for primary and secondary care.

Two of these started a Midwifery and Nursing School in Kitgum.



Gulu University served the whole of Uganda as a country. Map showing where the 120 graduate worked at 2012,

The 2011 Graduation Cohort: The Followers

Of the 50 graduates only 3 entered, to date, a postdoc Master program. 3 moved to Sudan and one to Rwanda. 9 are working in Kampala and surrounding and the other 35 are scattered across the country with several degrees of medical responsibilities. 7 new doctors are employed in St.Mary's Hospital Lacor of Gulu district.

The 2012 Graduation Cohort

All the 55 graduates successfully completed their internship and are scattered across the country.

Comment

The Gulu University Faculty of Medicine, started and supported by the Italy-Uganda collaboration project GULUNAP, produced, since the start in 2004, already 151 Medical Doctors. The vast majority of them are actually employed all throughout the country. Few moved to neighboring countries with a dramatic shortage of doctors. None went oversea. Twenty five are in the Kampala area, where most of them entered a post doc Master program.

Gulu University - University Of Naples Federico II

Development Of Master Program

Luigi Greco M.D. M.Sc.(MCH), PhD, Professor of Pediatrics

Associate Dean at the Faculty of Medicine of the University of Gulu

Preamble

The University of Gulu, Uganda and the University of Naples Federico II, Italy signed a MoU on September 6th 2014 in order to reinforce the long lasting cooperation between the two Universities, which led to win the prestigious prize 'Feltrinelli' from the Accademia dei Lincei in Italy (National Academy of Sciences), dedicated to the reinforcement of the cooperation. The new resources, from the prize, are dedicated to the support to academic cooperation for the Faculties of Agriculture and Sciences and to support the development of post-graduate programs in Medicine.

With the collaboration of the GULUNAP project, 275 new doctors graduated at the Faculty of Medicine of the University of Gulu since 2011.

These doctors were distributed across all districts of the country (Fig.1 shows an estimate) for their residencies and for professional engagement, after completion of the residency.

All available estimates, by independent observers, of the quality of the professional attitudes of these new doctors, agree on a very positive judgment. University and hospital institutions across the country generally appreciated the dedication, professional commitment and sensitive care of the Gulu University medical doctors.

But all these young fellows do require further qualification, in order to improve their professional

The figure gives a clear picture of where these doctors actually work. There is no need for comments.

Perspectives

There is a strong need to offer Post-Doc Master Courses in Gulu, if some of the graduates have to be retained locally.

The ONG – International Agency and private sectors offer several job opportunities which are competitive to the public sector.

The majority of doctors employed by Hospitals and Districts in the National Health System take full responsibilities for comprehensive health care.

A few doctors moved to neighboring countries, where there is gross shortage of medical personnel.

There is a commonly felt need to keep in contact with the 'mother' Faculty of Medicine of Gulu and with the fellow doctors.

Among the several doctors who will shortly acquire Masters Degree, there is ample choice to support and renovate the Faculty of Medicine of the University of Gulu.

skills and adhere to the university motto 'For Community Transformation'.

To support the development of Master Programs at the Faculty of Medicine at the University of Gulu, namely:

– Pediatrics & Child Health

– Public Health

Both University have set up a joint committee to develop a Curriculum program for both Masters. Gulu University will undergo all the required procedures for the government approval and the management of the courses.

Recruitement

Admission to the courses will follow the University and Government rules of Uganda, through transparent and shared rules at national level. Students are required to pay the required fees independently by the source of funding.

The fellowship supported through the GULUNAP project will add to the basic requirement, as a priority:

- being graduated at the University of Gulu

- being committed to at least 3 years of permanence in the region, after graduation, as estimated to a direct interview by the responsible Department staff.

The GULUNAP project aims to support :

– N.4 Fellowship for a 3 years Master in Pediatrics

 N.8 Fellowship for a 2 years Master in Public Health

For the fellow in Pediatrics the project aims to cover all University fees and a monthly salary to the fellow engaged full time in Clinical Rotations.

For the fellow in Public Health the project aims to cover all University Fees including Research Fees.

Gulu University will organize the full management of the courses and will take

responsibility for the best practice of the enrolled students. In particular for the Master in Pediatrics it has to guarantee that the student have full access to two children's wards, one at Gulu Regional referral Hospital and the other at St. Mary Hospital Lacor. The Department of Pediatrics have to organize the daily presence of supervisors to the clinical practice in both hospitals. None of the staff of the Deptm. of Pediatrics, listed in the Master Program, should omit direct surveillance to the mandatory clinical practice.

For the Master in Public Health, the staff of the Department of Public Health, listed in the Master Program, has to guarantee the direct supervision of the students' practice and outreach activities.

Gulu University will contribute financially to the development of the Master Program, according to the available budget

The University of Naples – GULUNAP - will :

- collaborate to the development of the curricula

- support the stages of experts and professors to both courses

- facilitate the development of joint research programs

- provide the starting sum to support some of the fellowships

N. 8 fellowship for the Master in Public Health – for University Fees + research Fees

N. 4 fellowship in Pediatrics – for University Fees and Monthly small stipend to the candidate engaged in full time clinical rotations The University of Gulu will contribute to all the other expenses required for the start and the running cost of the Master Programs.

UNIVERSITY OF GULU – FACULTY OF MEDICINE GLI STUDENTI VENGONO DA TUTTI I DISTRETTI DELL'UGANDA



Faculty — Scientific Trivia

Surgeons Discover A New Anatomical Structure Kantu Ronald Lawrence, MBChB II kan2ron@gmail.com Sources BBC health news, Wikipedia and The anatomy journal 2013 vol232.

As always said that its neither too late nor too early for a discovery to be made. At a Belgian University Hospital Leuven, two Orthopedic surgeons have for the first time given a full anatomical description of a new ligament that they term the anterolateral ligament (ALL) which is thought to play an important role in anterior cruciate ligament (ACL) tears.

Orthopedic surgeons Dr. Steven Claes and Prof. Johan Bellemans and colleagues, wrote about some of their findings in An Article in the Journal of Anatomy (Vol 223, Issue 4, pages 321–328, October 2013)

For the last 4 years, the two surgeons have been researching ACL tears to find out why, despite undergoing successful ACL repair surgery and rehabilitation, some patients still experience "pivot shift," where the knee sometimes gives way. Their enquiries began with an 1879 article by the French surgeon Segond who suggested the front of the human knee had an additional "pearly resistant



fibrous band. So, using macroscopic dissection techniques, they carried out in-depth examinations of 41 cadaver knees and found the new ligament in all but one of them. They write: "The ALL was found to be a distinct ligamentous structure at the anterolateral aspect of the human knee with consistent origin and insertion site features."

Researchers propose that the ALL

contributes to the control of the rotation of the tibia

They propose, given its structure and location in the knee, that the ALL controls the rotation of the tibia and that pivot shift may be caused by an injury to the ALL. They have since carried out some research that appears to confirm this. The findings question current views about serious ACL injuries and could signify a breakthrough in the treatment of patients with such injuries.

Dr. Claes and Prof. Bellemans are already working on a technique to correct ALL injuries and hope it will be ready in a few years' time. Dr Claes said: "We surgeons may need to rethink what we know about common ACL injuries. Though we have shed light on the purpose of this ligament and its role in common injuries, we now need to find out for certain when it is best to intervene surgically. Long-term studies will give us that answer and hopefully allow us to perfect a minimally invasive techniques to give our patients a better recovery."

ACL tears are common among athletes who practice pivot-heavy sports, such as basketball, skiing and football. "A recent study from the US published in the Journal of Athletic Training, found that because they are more prone to landing in a knockkneed position and women are more likely to tear the ACL than men."

This shows that its never to late for a discovery to be made. All it takes is the courage to start up the research because there's always something new that you will find out and help to broaden the knowledge of science.

Medical Picture Quiz Compiled by Kigonya Victor Martin, Intern Doctor Dr. Ambrosoli Memorial Hospital Kalongo

A 40 year old male reported to the surgical department after being attacked by robbers who attempted to kill him by twisting his neck. He was clinically stable except for severe neck pain with very limited and painful neck movements. Antero-posterior and lateral cervical vertebrae plain radiographs were taken as shown in the figure aside.

- a) What are abnormal findings in the x-ray?
- b) What is the diagnosis?
- c) What's the management?

Answers

a) Fracture line at the base of the odontoid process (Red Arrow). Odontoid process displaces anteriorly. Lamina of C2 is fractured (yellow arrow).

b) Fracture of C2 at the base of the odontoid process (Type 2 Dens Fracture) and fractured lamina. Odontoid fractures are the most common of upper cervical spine fractures with type 2 fracture (Anderson-D'Alonzo's classification) being the commonest.

c) Better fusion rate and early recovery can be got by internal fixation with screws or C1/2 fusion with posterior instrumentation. However, these are technically demanding and need various equipment. Therefore, skull traction with a hallo was applied using 4kg for 6 weeks. A neck collar was to applied until the neck is stable.







Faculty — Obituary

THE LATE MR. KISIGE MICHAEL MEMORIAL LECTURE Topic: The role of the community in injury and fracture

management.

Venue: GRRH conference Hall

Date and presenters: To be communicated

Facilitators: The RED CROSS, Department of Surgery-GRRH, GUMJ AND GUMSA

Dealing With Traditional Fracture Splint.

With the increasing number of physical body trauma due to auto mobiles, falling off heights and other forms of accidents, majority of the victims sustain broken limbs and other injuries distances away from health units.

With shortages in paramedical ambulance services, the community simply makes simple wooden splints to transport victims either to the bonesetter or to the hospital for management.

The wooden splints locally made have existed in community for now a long time. They are the oldest splints before a British bone setter Hugh Owen Thomas (1834-1891) invented the famously used hospital Thomas' splint.

The community designs local splints used to stop the injured limb from dangling during transportation or to facilitate healing. In Modern Orthopaedics, Thomas' splints, Cremer wires and other industrially made splints are used for immobilization of fractures of long bones.

Teaching the community on the basic techniques of splinting and first aid of fractures is a resourceful feat in the pre hospital management and minimizes fracture and trauma complications.

Full Article GUMJ-2009/2010 by the late Mr. Kisige Michael (Emeritus orthopedic surgeon-GRRH and honorary lecturer, Department of surgery -Gulu university).

TO OUR FALLEN COMRADE BASHIR AN ATHLETE DYING YOUNG

The time you won your town the race We chaired you through the market-place Man and boy stood cheering by, And home we brought you shoulder-high.

Today, the road all runners come, Shoulder-high we bring you home, And set you at your threshold down, Townsman of a stiller town.

Smart lad, to slip betimes away From fields where glory does not stay, And early though the laurel grows It withers quicker than the rose.

Eyes the shady night has shut Cannot see the record cut, And silence sounds no worse than cheers After earth has stopped the ears.

Now you will not swell the rout Of lads that wore their honours out, Runners whom renown outran And the name died before the man.

So set, before its echoes fade, The fleet foot on the sill of shade, And hold to the low lintel up The still-defended challenge-cup.

And round that early-laurelled head Will flock to gaze the strengthless dead, And find unwithered on its curls The garland briefer than a girl's

EUROLOGY OF DR. THOMAS OKELLO OYOK By Henry Oboke Edonga, Acting Head of Department Department of Psychiatry, Faculty of Medicine, Gulu University

I write about Dr. Thomas Okello Oyok from the point I met him and interacted with him. Anybody writing about a man who studied medicine, married, raised and educated children and went to study Master in Psychiatry while in 50s must know from onset that what he will describe is only but the tip of the iceberg. To the blind man who experienced the tail, the elephant looks like a stick. You can believe me in this feat in attempting to describe Dr. Thomas Okello-Oyok. Career

I met him as a student admitted to do Master of Medicine-psychiatry. I had seen his name from the time we discussed admission as faculty in the Department of Psychiatry, College of Health Sciences-Makerere University. The idea was to train him as a clinician to cover Mental Health services in the North of Uganda where there was increased issues of mental health due to insurgency. He qualified as a psychiatrist and returned to work in Gulu Regional Referral Hospital (GRRH) as head of department and doubled as mental health focal person in Gulu District. He participated in training doctors, clinical officers, nurses and any other allied health workers who rotated in Mental Health Unit. He retired from Ministry of Health and was appointed a senior lecturer in the Faculty of Medicine, Gulu University and later Head of Department, Department of Mental Health and Psychiatry. He served in this position until his death from complications of diabetes from Lacor Hospital.

The Holistic Life And Persona

Dr. Thomas Okello Oyok will be remembered not only from his contributions in the many roles he carried but also from his influence within Watoto Church and in social circles.

This person was warm and entertaining. Life for him was about being happy. He encouraged everybody to know Christ as a source of strength.

He would tell stories to everybody including students and patients and later would go home and tell more stories to his wife who passed on one year before him.

Here I am telling his story: a story of a man who was full of life and was an inspiration to all he interacted with. We miss him and pray that may the risen Lord whom he dearly served rest him in peace. Amen. Doctor Oyok was a contributor to the journal in areas of psychiatry. The GUMJ remembers him on paper and persona covered is one of the articles.

Acute dystonia and other neuroleptic side effects in a clinical setting

Neuroleptic side effects are numerous and are mainly due to the anti-dopaminergic effects. It is often difficult to achieve the therapeutic effects dose if the side effects are not known.

Acute dystonia is induced by drug treatment with antipsychotic, antiemetic and antidepressant drugs. Acute dystonia caused by drug treatment can seriously disturb the relationship between the doctor and patient and should be prevented.

It usually manifests as torticollis, oculogyric crisis, increased muscle tone and Parkinsonism. Parkinsonian effect may be controlled by antiparkinisonian drugs. Other side effects include Akathisia and tardive dyskinesia

Akathisia is not easily controlled by antiparkinisonian drugs but disappear if the antipsychotic drug dosage is reduced.

Tardive Dyskinesia may be caused by long term antipsychotics due to dopamine receptor super sensitivity. Reduction in antipsychotic dosage and tranquilizers may reduce the movements.

Logical use and knowledge of drug profile is therefore very essential in clinical psychotherapy.

Full article GUMJ VOL.2 ISSUE 1 By DR Thomas Oyok (Emeritus psychiatrist and Head of Department, Mental health Gulu University)

PREVENTION AND EARLY DIAGNOSIS OF NON COMMUNICABLE DISEASES PROJECT

Focusing on diabetic and hypertension screening, community NCD awareness campaigns and improving NCD research among medical students.

FUMSA

For more information contact:

Projec

Tumwine Conrad +256704976874 npo.uganda@gmail.com

www.fumsa.net

www.imcc.dk

Information for contributors

The Gulu University Medical students Journal (GUMJ) aims to improve the practice of all aspects of medicine and health care in general. To achieve these objectives, the journal publishes original scientific articles, reviews, clinical case reports and letters dealing with any factor impacting on health from Gulu university Medical students and staff. Gulu University Medical students Journal is published annually. Communications should be addressed to the Editor-in-Chief, Faculty of Medicine Gulu University, P.O. Box 166 Gulu.

The articles submitted to (GUMJ) are review by people experts in the areas. A primary reason for rejection of most articles is lack of originality, lack of significant scientific message important to a general medical readership. Such a decision is normally reached within a short time.

A title page should be provided to contain the title of the paper, author(s) name(s) and signature(s), degrees, designation, name of institution where the work was carried out, present address, telephone and facsimile or telex numbers and e-mail address, if available, and name and address of the author to whom all communications should be addressed.

General instructions

All materials submitted to be considered for publication must be submitted exclusively to (GUMJ). It is a condition that all authors must give signed consent to publication. For original scientific articles and clinical case reports, written permission must be obtained from the Director/Superintendent of the hospital where the work was done or the case was managed. All manuscripts should be typed in double line spacing on numbered pages and conform to the uniform requirements for manuscripts submitted to biomedical journals. Authors should provide their names, addresses and appointment/designation at the time they undertook the study. They should also provide a current address (including telephone, facsimile and E-mail) for purposes of correspondence.

Original articles and reviews: Please send three copies. You are advised to keep a further copy for your own reference. Articles should be between two and four thousand words with a maximum of eight tables or other illustrations. Original articles should report data from original research which is relevant to the practice of medicine especially in Gulu and other parts of Uganda. The message carried in the article should be clear and having the potential of improving the practice of medicine upon implementation.

Reviews must be critical analyses of the subjects reviewed, giving a state-of-the art and a balanced view of all the issues, for instance, controversies. Reviews should preferably be contributed by authorities and experts in the respective field. Similar to the case for original articles, the message of the review must be clear and of significance.

A structured abstract of no more than 250 words must be included. For original articles, the abstract should have the following headings objective(s), design, setting, subjects or participants, interventions, main outcome measures/ results conclusion.

For reviews the headings should be objectives(s), data sources, study selection, data extraction, data synthesis and conclusions. Copies of related papers already published should be submitted. This requirement is important where details of study methods are published elsewhere or when the manuscript is part of a series, say, part II of a series where part I has been published elsewhere. Copies of any non-standard questionnaires should also be submitted for consideration of publication as indexes, if deemed necessary. Statistical methods should be defined and the level of significance used stated.

Other submissions

(i) Case reports are welcome, however, the reason for presenting them must be clearly stated, particularly their critical significance in clinical practice. Case reports must be authentic, adequately and appropriately illustrated and the identity of any individual concealed according to ethical requirements. They must not be more than one thousand five hundred words which includes a succinct, informative prose summary of no more than one hundred words.

(ii) Letters to the Editor are welcome but must not be more than eight hundred words contain only one illustration (table or figure) with less than five references. Priority will be accorded to letters responding to articles published in the journal within four months. Letters to the Editor will be edited and may be drastically shortened without losing the gist of the message, but proofs will not be sent to authors.

Ethical issues

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One of the highlights of medical school is definetly the Medical dinner ...Among the many couples thatgraced the carpet!
 Finalists dinner is certainly the best place to give speeches-these finalists listened through!
 End of rotation picnic:The department of internal medicine was in the spotlight-The physians turned up too
 Rare sights and sounds: The only moment when the clerks SMILED IN DR.Kansiime's presence and he returned the smile.
 Dr Mathew joined in the pose for the clerks.















6 - In one of The GUMSA screening campaigns: This time the sun didn't scorch thanks to th many participants that turned up to give the shade!
7 - This time it was -THE RUN AGAINST CERVICAL CANCER- and these two visibly won the race.
8 - One of the NUVHOP participants at the supported child clinics
9 - After a long day of work they had to settle for A Doctor- Patient Snapshot: NUVHOP COMMUNITY OUTREACHES!
10 - You have to the see the cysts or you come back next semester :Microbiology never got easy!
11 -The BEMSA was fully represented in NUVHOP! : girls on the Job or Job's girls!

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