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EDITORIAL

KIDNEY TRANSPLANTATION IN ETHIOPIA: THE DAWN OF A NEW ERA IN RENAL CARE

Yewondwossen Tadesse, MD*¹, Sileshi Lulseged, M.D, MMed²

Kidney disease is a global public health problem that affects more than 750 million people globally. (1). Both Acute Kidney Injury (AKI) and Chronic Kidney Disease (CKD) impose significant burden on health care systems but receive less attention than other noncommunicable diseases on the global policy agenda (2).

Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for > 3 months, with implications for health (2). Glomerular filtration rate (GFR) <60 ml/min/1.73m² is the cutoff point used to define decreased GFR that represents decreased kidney function. The global incidence and prevalence of CKD have been observed to have increased by 87% and 89%, respectively from 1990 to 2016(3). Although accurate data on the prevalence of CKD in Africa are lacking, a recent meta-analysis of 98 studies involving 98,432 individuals showed that the overall prevalence of CKD was 15.8% (95% CI 12.1–19.9) for CKD stages 1–5 and 4.6% (3.3–6.1) for CKD stages 3–5 in the general population.(4)

There are no data on the incidence and prevalence of CKD in Ethiopia but there is evidence to show that risk factors for CKD like diabetes and hypertension are quite prevalent. In a national survey for noncommunicable diseases(NCDs) using the World Health Organization (WHO) STEPS in which a total of 10,260 people aged 15- 49 years participated, the prevalence of hypertension was 15.8% while the prevalence of diabetes was 3.2% (5). It will, hence, be logical to infer that CKD may be as common in Ethiopia as elsewhere in Africa.

While many patients with CKD die from cardiovascular disease before they reach end stage kidney disease (ESKD) for those who reach end stage kidney disease, transplantation offers the best prospects for improved survival and quality of life. The first successful kidney transplantation was done at the Brigham Hospital in Boston, USA in 1954 by a team led by Joseph Murray (6). In the six decades since the first successful kidney transplant was done, transplant activities have increased and spread across the globe. In 2017, the last year from which data are available from the Global Observatory of Donation and Transplantation a total of 90,306 kidney transplants were done in 81 countries (7). Ethiopia's kidney transplant program did its first transplant in September 2015 allowing Ethiopia to join the list of countries with solid organ transplantation programs (8).

In view of the presumed rise in the prevalence of CKD and ESKD, the establishment of a kidney transplant program in Ethiopia by the Federal Ministry of Health is quite a laudable achievement. All those involved in establishing the program and seeing it through, including the Federal Ministry of Health, the management and transplant team at the Saint Paul Millennium Medical College (SPMMC) and the University of Michigan deserve to be congratulated. The success of the program, in terms of clinical outcome, is on a par with outcomes in the developed world (8).

In this special issue of the Ethiopian Medical Journal (EMJ), several papers related to the new transplant program are presented. The topics covered range from history of the development of renal replacement therapy in Ethiopia to the outcome of the first 52 patients that had kidney transplant in the SPMMC. Surgical complications among the transplanted patients, follow up results of the donors and the surgeries done on animals in preparation for the program are among the topics addressed. Although the numbers are quite small and the period of follow-up rather short, the EMJ believes that recognizing this milestone in the development of advanced medical care in Ethiopia would encourage individual professionals and health care institutions to drive towards higher goals.

It is important to emphasize at this point that renal care in Ethiopia must be planned beyond the care of the few who reach end stage kidney disease. Renal care must encompass the promotion of kidney health, the detection and prevention of risk factors for kidney disease, slowing the progression of kidney disease as well as the provision of

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renal replacement therapy for patients with acute kidney injury (AKI) and end-stage kidney disease (ESKD). We would, therefore, like to make an appeal to all stakeholders to work on a Comprehensive National Policy for Renal Care as a matter of urgency.

Once a policy framework is agreed on, concrete strategies and plans for renal care at all levels of the health care system can be drawn and implemented. Renal care must be part of Universal Health Coverage (UHC), the ambitious guiding policy of the global community led by the World Health Organization (WHO) (9). UHC is aimed at improving the health of the global population and at stopping hundreds of millions of people from falling into poverty as a result of health care costs. Health care costs are quite high in renal care and the increasing burden of kidney disease has been raised as one of the most significant barriers to the achievement of UHC (11).

Improving focus on early intervention through the identification of risk factors and treatment, innovations in later stage care by way of developing low cost dialysis technology and removing barriers to transplantation are some of the proposed means to achieve UHC in renal care in low- and middle-income countries (10). In this regard the need for generating local data on the burden of kidney diseases to improve the evidence base to guide policy cannot be overemphasized. The EMJ is pleased to serve as the scientific forum for sharing the results of new program as done through the articles in this Special Issue as well as epidemiological evidence generated through penetrating and comprehensive research in the future.

Renal registries provide critical information to support the planning, delivery and evaluation of renal services particularly dialysis and transplantation. Most African countries do not have renal registries but recently an initiative to establish a continental Africa Renal Registry has taken off the ground (11). If renal care in Ethiopia is to grow to meet the public needs, it is imperative to establish a renal registry and it is incumbent upon the Federal Ministry of Health to take the necessary steps towards this goal with the advice and support of renal care professionals.

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OVERVIEW

KIDNEY TRANSPLANT IN ETHIOPIA: WHAT IS IN THIS ISSUE?

Jeffrey D. Punch, MD^{1*}

In this issue of the Ethiopian Medical Journal (EMJ), a series of eight reports describe the development of a renal transplant program at St. Paul's Millennium Medical College (SPMMC). A team of surgeons and nephrologists from SPHMMC were assisted in this endeavor by a team of surgeons and nephrologists from the United States of America (U.S.A). The articles review the historical milestones of renal replacement therapy in Ethiopia beginning in 1970. They highlight the unsustainable efforts to offer dialysis in different settings until 2004 and 2013, when effective dialysis was made available in the private and public sectors, , respectively. Followed by initiation of a live donor kidney transplant program in Addis Ababa in 2016 (1). The Ethiopian Federal Ministry of Health did a commendable work in playing the lead role in initiating and supporting the program.

Two and a half years of planning was necessary before the first live donor kidney transplant was accomplished. In this series of articles, the team reports on a novel approach used during the development of the program (2). Swine transplants were done to test the readiness of facilities, the staff and the medical team at the Hospital. This effort turned out to be highly successful allowing the team to overcome many potential challenges prior to undertaking the first nephrectomy and kidney transplant in September 2016.

In this Issue of EMJ, three reports on the outcome of patients who had kidney transplantation are presented. Overall, graft and patient survival was highly successful (3). This can largely be ascribed to the meticulous planning that that was effectively executed by the team. In addition, an article in this Issue reviews the surgical complications of the first 52 live donor kidney transplants (4). Although the patients were followed up for short period, the proportion of patients with immediate surgical complications was comparable to what one would expect of programs in well-developed settings. The team also reviewed Kidney donor outcome, which was found to be acceptable (5).

The team at SPHMMC has begun advancing the field by analyzing and reporting various aspects of its experience, including the report in this Issue on the prevalence of metabolic syndrome in the patient population at the facility (6), and a case report on BK viral nephropathy (7). Another important report in the series looks at pre-existing knowledge and attitudes of medical students at SPMMC. Knowledge among students was good, but many negative attitudes were documented (8). A case has thus been made for the importance of educational efforts and future research in this area, since future physicians will play an important role in the development of ongoing organ donation efforts in Ethiopia.

The success of this program suggests that highly sophisticated medical care can be provided in a developing setting and can be sustained without ongoing external assistance. Previously, complex medical procedures of this nature were usually performed by short-term medical/surgical missions, which bring with them the supplies and auxiliary staff. While these efforts benefited a small group of patients, they were not sustainable and as they were not coupled with local capacity building. In fact, it can be argued that such efforts could even undermine local efforts to develop local capacity to perform such procedures.

In the live donor kidney transplant program described above, the efforts put in place a program that can function independently in a completely sustainable way. This can serve as a model on how future efforts need to support local partners develops capacity to sustain programs. Such short-term support initiatives should also focus on training physicians, surgeons, nurses, and other staff to ensure continuity of services. Our experience at the SPHMMC has demonstrated that through a steadfast support from leadership, a dedicated team of local physicians can establish effective, quality and sustainable programs if assisted as deemed necessary by visiting professionals who guide programmatic development in a careful and deliberate manner.

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ORIGINAL ARTICLE

MILESTONES OF RENAL REPLACEMENT THERAPY IN ETHIOPIA

Mahteme Bekele Muleta, MD^{1*}, Engida Abebe, MD¹, Mekdim Tadesse, MD, MHE¹, Tekleberhan Berhae, MD¹, Momina Muhammed Ahmed, MD¹, Kenneth woodside, MD², Leja Hamza, MD¹, Berhanu Worku, MD¹, Seifemichael Getachew, MD¹, Hamelemal Gebeyehu, MD¹, Berahne Redae, MD¹, Balkachew Nigatu, MD¹, Wondemagegn Gezhegn, MD, MHE¹, Zerihun Abebe, MD¹, Mersema Abate, MD, MPH³, Fasika Tedla, MD, Msc⁴, Aklilu Getachew, MD, MPH, FASN⁵, Senait Fisha, MD, JD², Alan Lechieman, MD², Jeffery D Punch, MD²

ABSTRACT

Introduction: End-stage kidney disease is a growing and leading cause of morbidity and mortality worldwide, thus the need of renal replacement therapy, defined as dialysis or kidney transplantation, is expected to rise. In Africa, renal replacement therapy was available as early as 1957, but initiation and maintenance of the service remains a major challenge for many parts of the continent.

Objectives: This study aimed to document the major historical milestones that were achieved to successfully establish renal replacement therapy in Ethiopia and the lesson learned from a historical point of view.

Methods: This study utilized mixed method of quantitative and qualitative study. Data was collected from June 1, 2018 – July 30, 2018. Data about the hemodialysis service in all parts of the country was collected by structured questionnaire, and a descriptive analysis was performed. The data about kidney transplant service was collected from the only transplant center in the country, St Paul's Hospital Millennium Medical College. The data was collected through in-depth interviews of key informants who have participated in the program any time from the inception of the transplant program until the successful establishment of the kidney transplant program.

Results: The first dialysis service started in 1980 at Tikur Anbessa Specialized Hospital but a maintenance dialysis service started in 2001 at St Gabriel Hospital. The expansion of the service was restricted to Addis Ababa until recently, and majority of the dialysis service was provided by the private sector. The first successful human kidney transplant happened in September 2015 at St Paul Hospital's Millennium Medical College. Four critical factors for the development successful and sustainable renal transplantation program at College were identified: commitment at individual professional level, careful comprehensive planning, supportive leadership, and strong collaborative relationships with foreign universities and institutions.

Conclusion: As the expansion of hemodialysis service is currently limited to the major cities, kidney transplantation offers an alternative for patients with chronic kidney disease. Even with limited economic resources, with committed physician and supportive leadership, transplant can be achievable in developing countries. Furthermore, the practice organ transplantation addresses some of the fundamental challenges of advanced healthcare delivery and can positively impact the entire health care system by advancing other hospital services.

Key words: Renal Replacement therapy, Dialysis, Kidney Transplant, Ethiopia, Historical milestone

INTRODUCTION

The burden of chronic kidney disease and end stage renal failure is becoming a major problem worldwide (1). In sub-Saharan Africa, 12-23% of adults are estimated to have chronic kidney disease (CKD), with the associated risk of developing end-stage renal disease (ESRD) and requiring renal replacement therapy (RRT) to live.

Several studies have shown that lack of access to dialysis results in the death of 2·3 million to 3·2 million people yearly (2). The history of dialysis dates back 1884 but successful dialysis achieved in 1940s when Dr. Willem Kolff invented the 1st hemodialysis machine in the Netherlands. Soon after it started the service reached Africa; South Africa and Egypt, in 1957 and 1958 respectively (3).

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However, as support was limited elsewhere, maintenance dialysis remained a challenge in most countries of the continent (2, 3). The history of organ transplantation began in the medicine of mythology. Chimeric gods and heroes appear in a number of cultures. Probably the first and most famous amongst them is Ganesha, a child upon whom the Hindu god Shiva xenografted an elephant head (4,5). Well known to theologians and historians is the legend of Saint Cosmas and Saint Damian. Their most famous miraculous exploit was the grafting of a leg from a recently deceased Ethiopian to replace a patient's ulcerated or cancerous leg, which was the subject of many paintings and illuminations (6,7).

The first successful experimental kidney transplant was carried out by Emerich Ullman on March 7, 1902, in Vienna, where he auto-transplanted a dog kidney from its normal position to the vessels of the neck; which resulted in some urine flow.(4) After several years of experimentation, Ukrainian surgeon Yurii Voronoy performed the first human deceased kidney transplant in 1933 by anastomosing the renal vessels to the right femoral vessels in a young woman who had acute renal failure due to mercury poisoning. However, as the donor's blood group was B and the recipient's blood group was O, the kidney never functioned and the recipient died after 2 days (4)

In 1954 at the Peter Bent Brigham Hospital in Boston, a special kidney transplant case would succeed and teach medicine a great deal. One of the lead surgeons, Dr. Joseph Murray, was awarded the Nobel Prize for his work in organ transplantation (2). The first organ transplant at our collaborating center, the University of Michigan (UM), was a kidney donated from one identical twin to the other, which was performed in 1964. In Africa, the first kidney transplant was performed in South Africa by Dr. Chris Barnard in October 1967. Later, the procedure was introduced and performed in different African countries such as Sudan, Egypt, Nigeria, Tunisia, Kenya, and Ghana. (7,8).

In Ethiopia, dialysis service started in 1980 (3) but there is no formal documentation of how and where the dialysis service started and the progress to date. Regarding the transplant, there was no solid organ transplant happened until St. Paul started it in 2015. This study is aimed to document the development of dialysis service in Ethiopia and to describe the major historical events that took place to come up with a successful kidney transplant program in the country.

METHODS

This study was conducted in Ethiopia, data collected from June 1, 2018 – July 30, 2018. Ethiopia is the 14th most populous countries in the world and the second most populous country in Africa, second only to Nigeria.

Ethiopia is a Federal Democratic Republic composed of nine national regional states: Tigray, Afar, Amhara, Oromia, Somali, Benishangul-Gumuz, Southern Nations Nationalities and People Region (SNNPR), Gambella and Harari, as well as two administrative states (Addis Ababa City Administration and Dire Dawa City Council).

The study design was a mixed type of quantitative and qualitative research. The quantitative study focused on the development and expansion of hemodialysis service in the country. The study included all dialysis centers in the country that have started providing dialysis service, irrespective of their patient load. The Data about dialysis service was collected with structured questionnaire, it included the name of the center, region where it is found, ownership (private, Government) how many dialysis machine it owns and type of service it provides (acute or maintenance hemodialysis), what are the common challenge they are facing. The data were collected by nephrology fellows and crosschecked by the Principal Investigator (PI). Additional in-depth interview was done; on how Ethiopia started dialysis service and progress to date, by the Principal investigator with Dr. Yewondwosen Tadesse a senior consultant nephrologist and ISN fellow, renal unit head at the Department of Internal Medicine, Addis Ababa University (AAU), College of Health Science, School of Medicine.

The data regarding kidney transplant services was collected from the only transplant center in the country, At the FDRE National Kidney transplant center which is under the auspices of St. Paul's Hospital Millennium Medical College. The data was collected by in depth interviews of key informants who have participated in the program any time from the inception of the transplant program until the successful establishment and progress of the kidney transplant program.

All interviews done by the PI. The study focused on the factors resulting in the establishment of sustainable kidney transplant services in Ethiopia. A thematic approach used for data analysis. Ethical clearance to conduct the study was received from the SPHMMC Institution Review Board (IRB). After describing the aim of the study and the possible risks and benefits, informed consent was obtained from the participants to collect data and to conduct the interviews.

Key informants were: Dr. Senait Fisseha, Professor of Obstetrics and Gynecology at the University of Michigan, leader of the University of Michigan - Ethiopia collaboration. Dr. Jeffery D Punch, Professor of Surgery and a lead transplant surgeon at the University of Michigan.

Dr. Fasika Mesfin, Associate Professor of Medicine and Medical Director of Kidney Transplantation, SUNY Downstate Medical Center, Brooklyn, Dr. Zerihun Abebe, Provost of SPHMMC during the transplant happened in Ethiopia, Dr. Berhane Redae, the Medical Service vice Provost of SPHMMC. Dr. Momina Muhammed, Nephrologist, founding director of the Ethiopian National kidney transplant center, Dr. Engida Abebe, Associate Professor and transplant fellow, SPHMMC. Dr. Tekleberhan Berhae, Assistant professor, General and Urology Surgeon, transplant fellow, SPHMMC, Dr. Mekdim Tadesse, Assistant professor, Transplant fellow, SPHMMC. Dr. Berhanu Worku, Assistant Professor, nephrology fellow, SPHMMC, Dr. Seifmichael Getachew, Assistant Professor and nephrology fellow, SPHMMC, and Leja Hamza, Associate professor, nephrology fellow, SPHMMC.

RESULTS

Historical Milestones of Dialysis Service in Ethiopia

Tikure Anbessa Specialized Hospital (TASH), the oldest but often pioneering medical institute in the country started providing hemodialysis in 1980.

Dr. Yewondwosen Tadesse, stated that “The late Professor Edemariam Tsega must be given credit for starting the first residency program in Ethiopia, organizing internal medicine into subspecialties and starting subspecialty services in many areas including nephrology.” In his statement he recalled that “The first dialysis, both hemodialysis and peritoneal dialysis, in Ethiopia were done in 1980 by the Cuban team led by Professor Alfonso Guerra from the Institute of Nephrology, Havana, Cuba.” Dr. Yewondwosen explained that the service continued since then even if there were interruptions for some time “The Renal Unit of the TASH continued to perform hemodialysis (HD) and peritoneal Dialysis (PD) whenever supplies were available from the time of its first procedures in 1980 to the present date. There were interruptions in the HD services from 1990 to 1999 as consumables could not be found for the first HD machines the unit owned, NIKKISO HD machines. In 1999 the hospital bought 2 B. Braun machines and over the years donations from various sources have kept the acute dialysis service the unit provides going.”

Table 1: Historical development of Hemodialysis service In Ethiopia, July 2018

No	Name of the center	Owner	Type of BD service (acute or Chronic BDD)	Year service started	Name of the center	Owner	Type of BD service (acute or chronic BD)	Year service started
Region :- Addis Ababa City Administration								
1	Tikur Anbessa specialized hospital	government	acute	1980	Tsigereda Dialysis Specialty Clinic	private	chronic	2014
2	St. Gabriel Hospital	private	both	2001	St. Yared Hospital	private	both**	2010
3	Bethel Teaching Hospital	private	both	2006	Zewditu Memorial Hospital	government	chronic	2016
4	St. Paul hospital's Millennium Medical College	government	Both	2013	Girum Hospital	private	both	2017
5	MABD Dialysis Specialty clinic	private	both	2013	St. Peter's TB Specialized Hospital	government	acute	2017
6	Sante Medical Center	private	both	2011	Addis Hiwot Hospital	private	both	2014
7	Tom Advanced Renal Care	private	chronic	2013	Mimlik Specialized Hospital	government	chronic	2017
8	Bethzatha General Hospital	private	both	2013	Aynalem Primary Hospital	private	both	2017
9	MCM Korean Hospital	private	both	2013	hallelujah general hospital	private	both	2017
10	Hayat hospital Tigray Region	private	both	2014	Dire Dawa City Administration Council Ddel Chora General Hospital	Private	both	2016
1	Ayder Specialized Hospital/Mekele	government	both	2013	Oromia Region			
	Amhara Region			1	Adama General Hospital	private	both	2013
1	Gambi Hospital	private	both	2014	Jimma University Hospital	government*	both	2016
2	Gondar University Hospital	government*	both	2017	Sothern Natrions nationalities and Peoples Region			
3	Felegehiwot Referral Hospital	government*	both	2015	Yanet Specialized Medical	Private	both	2014
4	Woldiya General Hospital	government	acute	2018	Hawassa University College	government*	both	2017

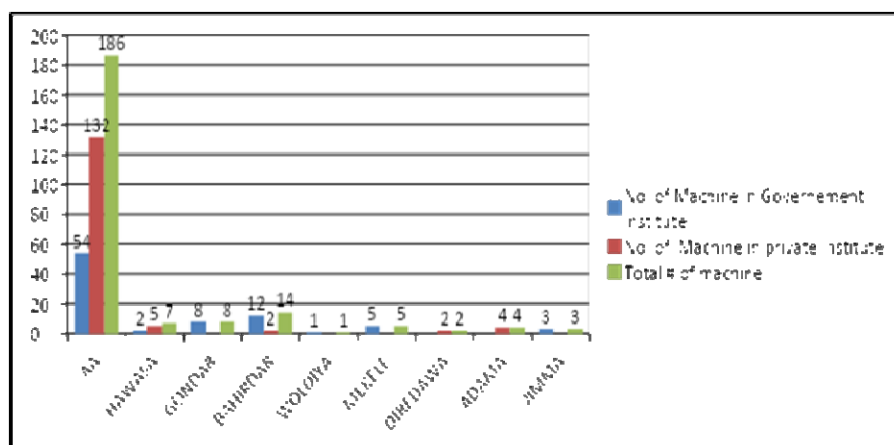
*public private partnership in government hospital

In Ethiopia maintenance dialysis started in a private center in 2001, St. Gabriel Hospital was the pioneers in the country to start providing maintenance dialysis. However no successful maintenance dialysis service was initiated at any government institute to date. The maintenance service provided in some of the government institute is through private public partnership (Table 1).

SPHMMC renal unit established by ISN fellow Dr. Momina Muhammed Ahmed in 2012. A year later, the unit started dialysis service limited to acute

kidney injury in collaboration with the Egyptian Government. The Egyptian Government provided six machines, consumables for certain period and supportive staffs at SPHMMC started providing acute dialysis officially in August 2013, and later the unit expanded its capacity and started maintenance dialysis as a bridge to kidney transplantation in early 2015.

Dialysis service growth was initially somewhat slow, but later erupted after the year 2013, when most of the dialysis center opened in the capital city Addis Ababa and few regional cities (Table 1).



The number of dialysis machines in government and private hospitals by city, Ethiopia , July 2018

Unfortunately, the growth was not evenly distributed throughout the country. As dialysis started at committed teaching institutes and private sectors, expansion initially remain in the capital city (Table 1). All service providers -be they government-supported or private owned - faced challenges, with the first and most important challenge shared by both the ability to obtain consumables for the dialysis. The private sector has the challenge of not making a profit from the service, which resulted in declining or closing services in some centers. The biggest challenge faced by the government is to pledge and convey the maintenance dialysis service at subsidized dialysis cost.

Historical milestones of Kidney Transplant

The first solid organ transplant occurred in September 2015, where the first three patients transplanted at the National Kidney Transplant Center. The surgery was led by renowned and highly respected transplant surgeon from the University of Michigan, Jeffery D Punch, working closely with four Ethiopian transplant fellows; Engida Abebe, Mahteme Bekele, Mekdim Tadesse, Teklebrehan Berhae, to establish local surgical expertise. Since then, 86 transplants have been performed, and the center has also expanded dialysis service from acute to maintenance dialysis as bridge to kidney transplant, from 6 to 32 hemodialysis chairs over the years (Table2).

The National Kidney Transplant Center was established and led by an Ethiopian nephrologist, Momina Muhammed , with the assistance of an experienced nephrologist from the USA.

The successful kidney transplant in 2015 is one of the major milestones in Ethiopia's medical history. The burden of chronic kidney disease is estimated to be huge in Africa in general, and in Ethiopia in particular. Thus, the need to for transplant service was undisputed.

These historical events happened at the country's young institution (SPHMMC), organized by several committed individuals, the Ministry of Health, the college management, and the University of Michigan collaborators. The interview of key informants at different level has revealed factors for the success of this huge mile stone of kidney transplant in the country.

These key factors are divided into four main themes, commitment at every level, bold leadership, Taking adequate time for planning or creating a sustainable system and strong collaboration with foreign university.

Table 2: Historical achievements of renal replacement therapy in St. Paul’s Hospital Millennium Medical College, July 2018

Year	Activity	Developments by July 2018
April 2013	Dialysis service Started with 6 machines, offering hemodialysis service for patients with acute kidney	32 dialysis Chairs (18 in the main hospital and 14 in the national kidney transplant center) Service expanded for Maintenance dialysis as a
April 2015	Simulation (three rounds laparoscopic donor nephrectomy and transplantation in a pig model)	Effectively used to test the center readiness for transplantation by September 2015
September 2015,	Kidney transplant the 1st 3 patients transplanted in September 2015, then 3 to 4 patients transplanted at roughly monthly intervals	- 86 live related kidney transplant has been performed Additionally, the center is now becoming the main hub for long-term care of patients transplanted else where
April 2014	Training of transplant fellows 4 transplant fellows enrolled in the training	All fellows completed their training in July 2018
April 2016	Nephrology fellowship started	Plan to enroll new fellows The first 3 senior fellows completed their training in July 2018 and 5 junior fellows are in their training

The choice to make St. Paul’s hospital a center of excellence in renal care made earlier in 2010. The Ethiopian diaspora, Dr. Fasika Mesfin Tedla, Medical Director of Kidney Transplantation, SUNY Downstate Medical Center, Brooklyn, stated that “*I began my involvement in the establishment of nephrology programs in May 2010 when the Ministry of Health requested the assistance of the Ethiopian North American Health Professionals Association (ENAHPA) with establishing a renal center. At that times the Ministry of Health had already identified St. Paul’s Hospital as the site of the future renal center.*”

The medical service vice provost Dr. Berhane Redae stated the reason why SPHMMC become transplant center “*The main reason that we were chosen to be a transplant center is the capacity we had in dialysis service and the committed staff in nephrology unit, surgical department, and the strong leadership that execute things on time.*”

Individual Commitment

The commitments of individuals are the driving force to start anything. It is well known that changes are the results of these driving forces.

It was no different when it came to transplant. When one see the level of commitment and eagerness to see the transplant happen, from the Provost and specialists, to the cleaners, one can make sure that the program will be a success. Everybody has been engaged in the design, re-innovation of the center, protocol development, procurements of supply and equipment to cleaning of the surface in preparation for the first transplant.

The lead transplant surgeon, prof. Jeffery D Punch, who has an impeccable input in the transplant program, expressed how he was impressed by the commitment of the Ethiopian physicians “*When I came to Ethiopia I found a group of young and enthusiastic surgeons and an expertly trained nephrologist. When I realized the quality of the physicians and how dedicated they were to the patients and their country, I thought that I can teach transplant to them and we can bring transplant to St. Paul, Ethiopia.*” The leader of the University of Michigan collaboration, Dr. Senait Fisseha, expressed the need of believing in a vision and committed to it.

“It is really very difficult to believe in a vision when you don’t have so many things, so it really took resilient and committed people with vision to make it happen. You cannot say we are in a poor country we don’t have the resource; when people are committed, set a goal and put a real achievable plan around it, anything is possible” Dr. Momina Muhammed Ahmed, who attended ISN fellowship in South Africa, returned to her home country to serve those who need her expertise. Her dedication and commitment was instrumental for the realization of transplant in Ethiopia. *She said that “The road was so bumpy but I never lost hope and never had a doubt on its realization because to achieve something requires faith, hard work, determination and dedication. All stakeholders, including our collaborators from University of Michigan, St. Paul Hospital Management team, MOH and local transplant team have all those qualities.”*

Dr Mekdim Tadesse, a transplant fellow expressed his commitment briefly *“transplant is my passion and I am committed to it , whatever it takes”* and Dr. Engida Abebe, the other transplant fellow said his commitment came from his motivation deep seated inside. *“I have been always thinking to contribute something to the advancement in medical practice in the country, I was very happy and committed to give whatever I can when the college offered me the chance to be part of transplant team.”*

Adequate time for preparation

This includes developing guideline, suitable infrastructure, defining work flow, training the staffs, making sure the availability of equipment, medications and functional laboratory. At the start, the lead transplant surgeon from the UM discussed with the Health Minister, he stated that the possibility of stating transplant in 3 to 6 months. But the preparation of this huge undertaking took around 30 months.

Dr. Zerihun Abebe ,who took over the responsibility of leading the college as provost after few months of planning to start the transplant said that *“Part of the reason why it took so long is, by the time we introduce that we are going to kick off kidney transplant very soon we have undermined or probably don’t understood the kind of facility, infrastructure, the medical equipment ,the enumerable supplies and most important of all the team of trained work force that kidney transplant required”*. The main reasons identified from the interviews were the program was new to the country; the procurement process was very much protracted, as it had been developed for other needs, and the infrastructure was somewhat limited.

The Medical service vice provost (MSVP), the director of the transplant center, the program manager, and all the surgical fellows expressed their serious engagement in the process of creating a sustainable system. At times, different leaders would go in person to see the construction of the building, the laboratory, the OR, and the dialysis ward, as well as lobbying the country Pharmaceuticals Fund and Supply Agency (PFSA), to obtain the needed immunosuppression or to appropriately expedite the procurement of medication and equipment.

Dr. Momina Muhammed, the founding director of the national kidney transplant center expressed her view why it took so long saying *“ Establishment of the program has taken around two and half years which were much more than we all expected. But it is for a great cause, our mission was to lay a good strong foundation, in every necessary segment the program required to make it sustainable. The major challenge was procuring items, and still remained unresolved challenge!”*

Prof. Senait said *“For me the fact that the transplant program is successfully continuing is not surprising at all--that is why it took more than 30 months to plan. If it was just to do the transplant only, we could have been doing the 1st month, the first year or so but it wasn’t to do one and stop, it was about developing a sustainable program.”*

The led transplant surgeon Dr. Jeffery said that, *“No one seems surprised it took so long, everyone seems committed. Everyone was working hard toward the goal; it was naivety from my part to think that this entire thing can happen in such a short time.”* Dr. Punch went on to say *“I was new to trying to do things in Africa and I didn’t understand African systems -- for example in purchasing they have to do a tender; if they didn’t get multiple suppliers at first they have to do retender--and these things took long times.”*

“The main challenge was to start from the scratch, there was no guideline, no trained professional (transplant surgeons, scrubs, ICU nurses, social workers), we had to purchase all equipment and consumables, we had to establish a laboratory of higher capacity”(Dr. Berhane Redae, Medical Service Vice Provost)

The planning of doing hand assisted laparoscopic donor nephrectomy partly contributed for delay to the start of the transplant. As it is technically very demanding, in a country where minimal invasive surgery is not a routine practice, getting suppliers of the equipment that enabled doing the procedure is challenging.

“As our main collaborator was the University of Michigan, we planned to start with the American standard of hand assisted laparoscopic procedures; the procurement of the complete set of this special equipment took several months. Later we shifted to an open donor nephrectomy, as the former was very expensive and less sustainable.” Dr. Tekleberhan Berhae

Supportive leadership

Huge projects like kidney transplant need unique requirements to start, so one of these key requirements is support from the highest level of health system. The experienced lead transplant surgeon who has been involved in the transplant from the inception capitalizes the need of involving high officials:

Prof. Jeffery expressed it “The only way you can safely start transplant is if you have support from the highest level, which is very critical. The transplant happened due to strong desire of the health minister for giving care to the people of Ethiopia”

Prof. Senait on her part acknowledged the role of the provost Dr. Zerihun Abebe “We had a lot of committed people who have the vision, but it just needed courageous leaders to take bold steps and take a risk, that leadership was there in St Paul and helped the transplant to happen.”

The fellows expressed the need of strong and bold leadership at St. Paul and Ministry of health as the second key factor for the success of a transplant program

Dr. Tekleberhan Berhae expressed the role of the management “The bold management and extraordinary leadership were instrumental for the transplant to happen in SPHMMC, the management especially the provost was exceptional in providing a support and delivering assistance, it was a kind of management which goes extra miles to achieve this historical milestone in the country. The Health Minister contribution was the most remarkable, he was following the condition very closely assigning a special representative, who came and attend every week meeting and extend his unreserved support.”

Dr. Engida Abebe said “We were blessed to have a committed hospital management and consistent support from Ministry of Health”

Dr. Zerihun Abebe, a kind of transformational leader and has brought a lot of changes in the institute almost changing the college into future medical city doesn't agree to be acknowledged or congratulated for what the management deed.

He stated “with army of surgeons and nephrologist ready on the ground ,huge number of patients waiting for the service ,with the support we had from Professor Senait and her army from University Of Michigan, the unreserved support from Ministry of health. It would have been surprising if we failed to do it .We should not be congratulated we should have to be questioned if we failed.

Strong Collaboration with foreign universities

Strong collaboration with foreign university who has people well experienced at international teaching was another key factor identified from the interview. The University of Michigan - Ethiopia collaboration is an example of a strong collaboration in terms of bringing sustainable change. This collaboration was started by an Ethiopian Diaspora, who living in Michigan, working as the leader of the Global women health. The collaboration started with women health, and later expanded to other areas. The leader of this strong collaboration, Dr. Senait Fiseeha emphasized that the collaboration should not be resource intensive or is not all about primarily financial support; it should be about continuous human engagement over a long period of time. That is why she has to travel every month from USA to Ethiopia to see how things were progressing. She described her experience of the collaboration:

“When the opportunity came to explore possibility of renal transplantation in Ethiopia; I reached out to the Minister and said I can reach out to my colleagues at the university of Michigan and at that time the role I saw was that; I can help in training the surgeons doing the donor nephrectomy through minimal invasive techniques, because I didn't want donor nephrectomy to be a deterring factor for the program” Dr. Senait emphasized on human engagement as main factor of strong collaboration “I think for me engagement of committed people is critical, I know resources, especially financial resource is essentials but not critical, it is really the human engagement over a long time and making a time for that face to face dialogue or conversation to make sure that people are staying within the vision or reminding we have a bigger vision.”

Dr. Fasika is the other diaspora who was actively engaged coming at least 3 times a year and supports the nephrology unit staying for one week. Besides that he used his professional network to bring other nephrologists to support the program at St. Paul, he stated that “I and Dr. Alan Leitchman contacted nephrologist colleagues who we know through our professional networks or had trained in the past.

Four other nephrologists volunteered to participate in the rotations to travel to St. Paul's. Since June 2015, I have been traveling to Ethiopia on 3-4 one-week trips per year. The main challenge of supporting programs through frequent trips overseas is reconciling the demands of your job with the time requirements of the project. In my own situation, my Department was willing to free a limited of my time for my work at St. Paul's. The remainder of my efforts came from my personal time and at my own expense. This could be sustainable only if the project's eventual goal is self-sufficiency, as was the case with St. Paul's. In addition, the availability of other volunteer nephrologists who could share the work was extremely helpful."

Prof. Jeffery also believed that a onetime mission, coming and doing surgery in group, doesn't work to transfer skills and develop a sustainable program. He was traveling almost every month to perform 3 to 4 transplant in a week. His commitment did not change, even after having a heart attack in the middle of the 5th mission. After recovering for a few months, he resumed travel every month to train the transplant fellows. He expressed the need of such collaboration:

"In the past medical mission or the so called medical partnership ,the people from the USA, Europe and Asia come to Africa they do the operation for period of time and go back; while that is good for the patients it doesn't help the country in developing its capacity and creating a sustainable system "

DISCUSSION

In 2010, 2.618 million people received RRT worldwide. The estimated number of patients needing RRT to be between 4.902 million in conservative model and 9.701 million in high-estimate model, suggesting that at least 2.284 million people might have died prematurely because RRT could not be accessed. The largest treatment gaps noted in low-income countries, particularly Africa (1). The opening of dialysis centers and their expansion in countries like Ethiopia will definitely narrow the gap observed in RRT. The expansion of the dialysis service remained in Addis Ababa, the capital of Ethiopia until recently showing serious issue of accessibility reflected in many African countries (9-11)

Marked improvements in early graft survival and long-term graft function have made kidney transplantation a more cost-effective alternative to dialysis. Thus renal transplantation has become the treatment of choice for most patients with end stage renal disease (ESRD) (9,10).

The barrier to universal transplantation includes economic limitation in resource poor country (10, 11, and 12). The practice of organ transplantation has now diffused across all income strata and has reached the populations of low-income Member States (12). Ethiopia is now one of those low income countries where transplantation is being performed.

Realistically, there is no question on the importance of resource but the experience from Ethiopian and other resource limited country proved that when people are committed set a goal and put a real achievable plan around it, anything is possible (11).

There is an important role for higher level management to play in terms of commitment to allocation of resources, proper oversight, and the creation of an appropriate normative and legislative environment in which transplantation can operate. Our study acknowledged this critical role of higher level leaders and organizational culture in the success of the transplant program (11,12).

Ethiopia in general, and SPHMMC in particular, are the proof of the benefit of long term medical training-based missions (13) The UM-SPMMC-Ethiopian Ministry of Health collaboration is a very good model of a long term relationship resulting in significant societal impact--where the continuous engagement of the volunteer transplant surgeons and nephrologists resulted in sustainable renal replacement program. The advantage of such model includes avoiding challenges of hands on training and brain-drain from Africa (13-15).

Conclusion: As the expansion of hemodialysis service is currently limited to the major cities, kidney transplantation offers an alternative for patients with CKD. Even with limited economic resources, with committed physician and hospital leadership, transplant can be achievable in developing countries. Furthermore, the practice organ transplantation addresses some of the fundamental challenges of advanced healthcare delivery and can positively impact the entire health care system by advancing other hospital services.

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Competing Interest:

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

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ORIGINAL ARTICLE

ON SITE PORCINE KIDNEY TRANSPLANT SIMULATION TO PREPARE A NOVICE TRANSPLANT CENTER FOR HUMAN LIVING KIDNEY TRANSPLANT

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ABSTRACT

Introduction: *The Ethiopian kidney transplantation program was recently established. Except for the transplant surgeon most professionals involved had little experience on kidney transplantation.*

Objectives: *To evaluate if simulation with a porcine helped develop the ability of the new kidney transplant center for human living donor nephrectomy and recipient kidney transplantation.*

Methods: *A review of the reports of the transplant surgeon, nursing and anesthesia team and in-depth interviews of all involved in the swine simulation was performed at St. Paul's Hospital Millennium Medical College in Addis Ababa. Additionally, a self-administered questionnaire was used to collect data on individuals' perception of the simulation*

Results: *Four simulation sessions were performed on five pigs in three months. There was a month gap between each session. In the first three sessions one swine was utilized for each encounter, while in the last session, two swine were used. With each session, new issues or problems were identified, but the skill and understanding of the team improved steadily. Successful nephrectomy, back table perfusion, and successful allotransplant was achieved by the fourth session. At the end of the fourth simulation, many gaps and areas were identified for focus prior to initiation of human transplant. Everyone involved perceived simulation as important and recommended such an approach in similar settings.*

Conclusions. *The experience, the knowledge and skills gained from porcine living donor and recipient transplant simulations were significant. We recommend using such simulation to test a new service in a new center. Simulation sessions need to be performed until the team gets comfortable and all gaps are identified.*

Key words: *swine, simulation, surgical skill, test, Ethiopia*

INTRODUCTION

End stage renal disease (ESRD) is considered as Africa's forgotten disease (1). This is because, despite an increase in the incidence and prevalence of the condition, the attention given by health authorities is limited (2). Kidney transplantation is the preferred treatment option for ESRD patients in terms long term survival and quality of life (3). But due to the nature of the disease, complex immunological interactions, and the patients' condition, transplantation demands highly trained professionals.

The list of professional needed for successful transplant, includes surgeons, competent anesthetists, operating theater nurses, ICU nurses, etc....

It also demands special surgical and non surgical supplies, which must be in place before the living donor can be placed at risk and the kidney transplanted (4). Due to these requirements, all forms of renal replacement therapy in most part of Africa, including Ethiopia, often have been inadequate, and are largely centered in the big cities (1,5). In 2013, St. Paul's Hospital Millennium Medical College (SPHMMC) located in Addis Ababa, Ethiopia began collaboration with University of Michigan with the goal of establishing kidney transplant services in Ethiopia. With the support of the Ethiopian Federal Ministry of Health, specialists from the University of Michigan began regularly traveling to Ethiopia to identify services and supplies that would be required and to advise on the development of a kidney transplant program at the hospital.

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In order to provide an optimal environment for kidney transplant care, a hotel building was renovated specifically for transplant care to include all the basic services a transplant center would need. These needs were determined to include operating rooms for the donor and recipient near each other, a four bed ICU, wards for donors and recipients, etc ... Additionally, other preparations were also made: designing the transplant program and protocol, training transplant operating theater nurses (on basics of laparoscopic surgery equipments and living kidney transplantation theater nursing), basic exposure on kidney transplantation to the fellows abroad (assisted few open donor nephrectomy and transplantation and observed laparoscopic donor nephrectomy), short term training to a transplant nephrologist, a pathologist and a radiologist. Materials and instruments for performing donor nephrectomy and transplant were also secured.

Despite the exhaustive preparations, it was still unclear if the team was up to the challenges of removing a kidney from a healthy human being, and successfully transplanting it to their loved one. It was therefore decided that trials utilizing a porcine model would be undertaken to test if the center was ready for human patients. The objective of this study was to evaluate if testing the ability of the new kidney transplant center to transplant a porcine kidney can help in preparation for beginning human living laparoscopic donor nephrectomy and transplantation.

MATERIALS AND METHODS

A mixed qualitative and quantitative study was done from April to July 2018 of the original participants in the porcine simulations to evaluate if testing a new transplant center's capacity with swine kidney transplant simulation helps in identifying and filling gaps for beginning human living donor nephrectomy and transplantation. The transplant center is located at SPHMMC in Addis Ababa. Preparations for first kidney transplant took almost three years. In the last few months (April to June 2015), four sessions of swine transplant simulation were done on five pigs.

Review of reports of the transplant surgeon (mentor) which he wrote at the end of each simulation session was used as source of data. Each simulation session was also evaluated critically by in-depth interview of key informants (the transplant surgeon, the four transplant fellows, two anesthesiologists, five operating theater nurses). The process of evaluation of performance was done by interviewing the lead transplant surgeon who was in practice for more than 25 years in kidney transplant surgery. Performance and achievements at each session was described in a narrative and with pictures. Additionally, a self-administered questionnaire was used to collect data on each individual's perception of the simulation sessions.

Ethical clearance was obtained from SPHMMC IRB.

RESULTS

A total of four simulation sessions were done on five pigs under a senior transplant surgeon from University of Michigan leadership. After each session, debriefing was held with all team members and a list of things learned was drafted. A total of 12 individuals were interviewed and completed the questionnaire. Below are findings of the reports and interviews.

Achievements and Decisions at Each Simulation Simulation: – I (Swine #1)

The swine was obtained from a local farm and transported to the transplant center after sedation. The animal was not weighed formally, but the estimated weight exceeded 80 kg (Figure 1). Intravenous access was obtained by insertion of a venous cannula in a superficial vein that was visible after shaving the animal's ear. Anesthesia was given by a veterinary surgeon and anesthesiologists. As the swine upper airway anatomy can be difficult for endotracheal intubation, tracheostomy was performed while the pig was supine under ketamin sedation. An endotracheal tube was used for the tracheostomy to align with the swine airway anatomy and sutured in position for airway control.



Figure 1: Swine #1 positioned for hand assisted laparoscopic nephrectomy. Notice the size of the pig.

The animal was put on its right side for left nephrectomy. It was noted that the animal was too large for the instruments, which simply would not reach the kidney through the laparoscopic ports. The operation was terminated without completing the nephrectomy. The team nevertheless gained significant and valuable experience because it allowed us to check all the devices necessary, including laparoscopic suction, harmonic scalpel, laparoscopic ports, CO2 insufflators, and instruments. It was also learned that the ambient light in the operating room was too bright for the images on the monitor to be seen clearly.

The hand port came from a different supplier compared to what the experienced faculty had used in the past. Unfortunately, the port did not function as expected, resulting in significant CO₂ leakage and poor intra-abdominal visualization. It was also noted that the ports that were available would not admit the laparoscopic stapler that would be used to divide the renal vasculature. After completion of the procedure we did a debriefing.

Lesson learnt

The natural room light was too bright, and a plan was developed to address that issue. The weight of the pig was too much, so the need to have a swine weighing 30-40kg was established. The purchased hand port needed to be changed or additional information was needed to be obtained from the supplier on its use. Everyone felt the lesson learnt in the process was enormous in terms of operating room management, surgeons, anesthesia and nurses understanding regarding what is needed and what needs to improve. A decision was made to repeat the simulation with a smaller animal.

Simulation session II (Swine #2)

Nephrectomy:

This time, the swine procured was a more appropriate size (approximately 35-40kg). The veterinary care and process of placing the pig under anesthesia was smooth, and similar to that described in simulation session I. Technical issues with the hand port were overcome after consultation with the supplier's representative. Laparoscopic ports were checked and their size was correct for instrument passage. Pneumoperitoneum was established uneventfully. The operation initially went reasonably smooth, but eventually required conversion to open due to bleeding from the liver. Appropriate laparoscopic packs were noted missing, which could have improved the outcome, as control of blood loss would have been easier. Though converted to open, both the artery and vein were divided using GIA staplers, and kidney was recovered successfully. The lack of TA stapler shortened the artery to half its normal length. The bleeding was likely related to a combination of laparoscopic inexperience and the fragile nature of the porcine liver.

Perfusion

Sterile normal saline kept in a deep freezer was carefully slashed, opened sterilely and manually for use as sterile ice slush. The kidney was perfused with cold normal saline. Appropriate vascular cannulae were noted lacking. Perfusion was done through regular IV cannula. Thought it was very slow cooling of the kidney on the back table, perfusion was successfully performed (Figure 2).



Figure 2: Perfusion of the Swine Kidney at the back table

Attempted Transplant

Transplantation of the kidney was attempted into the right lower quadrant of the same pig. A Bookwalter fixed retractor was used, but it was discovered that some critical components of the retractor were either not available, or were not compatible with the model purchased, and this made exposure challenging. During the transplantation, the pig was hemodynamically unstable due to the blood loss from the nephrectomy and the consequence of supine ventilation, which swine tolerate poorly as the time period of ventilation extended. The operation was terminated after the venous anastomosis, without completing the transplant as the pig no longer had a palpable blood pressure in the iliac artery. It was also noted that many of the instruments that had been obtained specifically for vascular anastomotic work were of inadequate quality. In contrast to the donor operation, the operating lights were not bright enough, and adjustability was limited due to the ceiling height of the operating room. During the attempted implantation of the kidney the electric power failed. It was restored after approximately 3-5 minutes.

Lesson learnt

The swine size was appropriate for the intended purpose. The need for right stapler for the artery, laparoscopic packs, and gentle manipulation of the swine was better understood during the nephrectomy. It was realized that better vascular cannulae were needed to perfuse the kidneys. In the attempted transplantations we learnt the appropriateness of the Bookwalter retractor and its elements, the quality of the vascular instruments bought assessed (we need better quality and finer forceps, scissors, and needle drives).

In addition, the need to have a backup generator and headlights was emphasized, as the donor laparoscopic surgery portion was completely dependent on adequate electricity. We also learned doing the nephrectomy and transplant in the same pig may not be ideal, although it was more economical.

Simulation Session III (Swine #3)

Nephrectomy

The nephrectomy on swine #3 demonstrated integration of the previous sessions' lessons and went well. Blood loss was minimal. We found that the lack of an endo-TA meant the artery was shorter than it could have been. This time, the major issue was the backup generator, which cycled off and on once activated as that it was providing too much power, causing the safety features of some of the equipment to shut itself down.

Perfusion

Perfusion of the kidney was successful, but as in simulation session II, the lack of appropriate cannulae was a problem that limited the ability to cool the organ in a timely fashion.

Transplant

Transplant was again attempted on the same pig. Despite minimal blood loss, the pig was again in extremis at this point. It was realized that the problem was the physiology of the animal model which does not support prolonged anesthesia and ventilation in a supine position. Similar problems noted with swine #2 due to the instruments and the retractors were also present. It was also problematic that there was bleeding in the pelvis. This would have been a minor problem, except that adequate suction was not available. The venous anastomosis was again performed successfully, but the operation was again terminated afterwards without completing the transplant due to the lack of blood pressure in the pig.

Lesson learnt

At this level, we felt nephrectomy can be done with confidence and many of the gaps were addressed. Perfusion cannulae needed to be available for faster cooling of the kidney. New sets of vascular surgery instrument and Bookwalter retractor parts needed to be made available. The new problem identified was the suction machine, which was not good enough for vascular surgery. As significant bleeding can occur, adequate suction was deemed a requirement to allow the best opportunity for surgical rescue. The need to do nephrectomy and transplantation in different pigs was apparent.

Simulation Session IV (Swine #4 and #5) ***Nephrectomy and Perfusion (swine #4)***

Overall the nephrectomy was very smooth and the kidney was recovered successfully, although the artery was again unacceptably short due to the lack of appropriate stapler. Perfusion was improved by the use of a larger cannula, but was still not ideal.

Transplant (Swine #5)

A different pig was anesthetized put in supine position in the adjacent operating theater (recipient OR) and for kidney engraftment (Figure-3). This worked well, as the pig's blood pressure was good throughout the procedure. An extra-peritoneal approach (analogous to that used in humans) was used, which allowed good exposure of the iliac vessels. The problems with instruments and the retractor were addressed. Both venous and arterial anastomoses were completed. The arterial anastomosis was compromised by the lack of an aortic punch. The clamps were released, and the kidney graft was re-perfused successfully (Figure 4). The kidney achieved the appropriate color immediately, the texture and turgidity were appropriate and urine production began immediately.



Figure 3: The swine is positioned for transplant in supine position. Note how the legs are fixed and supine position maintained.

Lessons learnt –The collective lessons from all the sessions were summarized and considered. While new challenges were anticipated in humans, the porcine experiences demonstrated possible critical failure points and allowed staff experience with the complex skills and logistics, prior to putting human life at risk.

NB:- After completion of each simulation session, the pigs expired, and bodies discarded according to the veterinary surgeon's protocol.

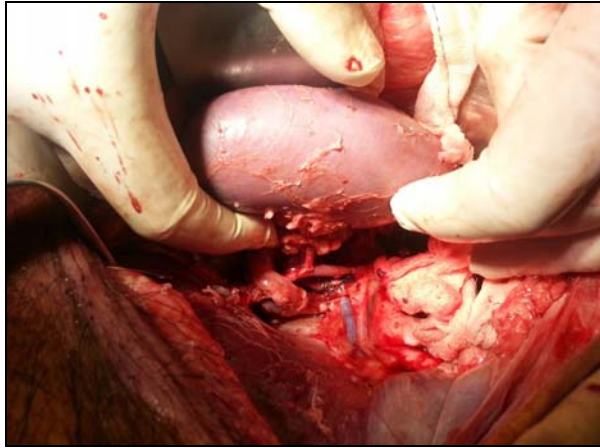


Figure 4: At the end of successful swine Kidney Transplant. Kidney color and turgidity looks great. The venous and arterial anastomosis can be seen inferior to the kidney.

Perceptions of the team members

Perception interviews were assessed in both in-depth interviews and five scale 10 Likert's item questionnaires. The targets were to interview the four surgeons, five nurses, and three anesthetists. But due to information saturation only three surgeons, three nurses, and two anesthetists were interviewed.

Everyone agreed on the need of doing swine simulation and considered it was worth doing. The surgeons and anesthetists emphasized doing both nephrectomy and transplants are equally important, but the nurses thought the donor nephrectomy simulation was more useful, as laparoscopy was a completely new encounter to them. The nurses felt the process helped them in not only understand the process of donor nephrectomy and transplant, but also identifying and understanding the special surgical instruments used in the surgeries. In addition, they felt that these sessions better pre-

All of them reported the process increased their confidence in handling humans.

The anesthesia team reported, though the pigs were normal they followed anesthesia protocol for ESRD which gave them a close to normal transplant scenario. It helped them in understanding what donor and transplant fluid management requirements could be, and at which points in the operation communication with surgeons were vital (e.g. diuretics, immunosuppressant, and relaxation).

Though anesthetists were comfortable after the first simulation, all the interviewees agreed in the need to do the simulation until all the team members are comfortable. At each session, they reported different lessons were learnt and issues not seen in the previous sessions were seen. The team felt more comfortable with each simulation as their understanding, coordination and communication improved from one simulation to the other. The nurses and surgeons reported after the fourth session they felt very comfortable, and doing more session was considered unnecessary and they felt they were ready for human surgeries.

The surgeons and the anesthetists (the nurses were indifferent) insisted in doing nephrectomy and transplant in different pigs. This is because keeping the animal in supine and alive with good blood pressure was difficult as seen in the first three sessions.

When asked if a predetermined minimum number of simulation necessary, none of the agreed, rather recommended to continue doing the simulation until everyone is satisfied. All the interviewees

Table 1: Mean, Mode and Median Scores of a 5 scale Likert's Item on Perception of individuals involved in Swine simulation

		Mean	Mode	Median
1	Swine simulation helped you understand better what donor nephrectomy details are	4.6	5	5
2	Swine simulation helped you in understanding what transplant details are	4.7	5	5
3	Set number of simulations should be done before starting	3.5	5	4
4	Simulation need to continue until everyone is comfortable and all gaps are identified	4.3	5	5
5	Swine simulation is not expensive compared to its benefits	3.2	5	4
6	The swine simulation helped you to work in less stressful situation to understand kidney transplant	4.3	5	4
7	The swine simulation was close to human transplant in most of it	4.4	4	4
8	The simulation was interesting and enjoyable exercise	4.5	5	5
9	Simulation was worth doing	4.4	5	5
10	I recommend similar simulation in other new centers	4.9	5	5

DISCUSSION

It is well established practice to use simulation to teach surgical skills and other interventions for medical students, residents, physicians and surgeons at all level (5,6). This has been done using synthetic materials, animal products, human cadavers, and living animals(5,7). Pigs or its body parts are frequently used for the purpose(8). The aim of surgical simulation is to give trainees a close to real experience under the possible lowest stress, improve patient safety, etc... without putting human life at risk (5). The process can be monitored and progress of trainee can be assessed and feedback given according to performance of the individual (5,7). By using these experiences as a background, the current study added one level or designed a different model to the practice, which is, using swine (animal) simulation to assess if a new center is ready for human care.

Training surgical specialists to perform complex and sophisticated surgical procedures such as laparoscopic donor nephrectomy and kidney transplantation poses a major challenge for any region (3,5). Such endeavors are even tougher in the developing world, due to lack of resource and expertise(1,2). Such high-end training is lengthy, and hands on experience is a must. Simply observing others perform a surgical procedure with the technical complexity of laparoscopic donor nephrectomy or kidney transplantation is insufficient to provide the observer with sufficient skill to perform the procedures independently(3). Even though the objective of the swine simulation was not primarily to teach the transplant fellows how to do donor nephrectomy or transplant, it had a huge contribution in developing their skills as witnessed by the transplant surgeon and fellows in the process.

As the goal of the simulation was to evaluate as many processes of laparoscopic donor nephrectomy and transplantation as possible (for all aspects of the transplant center and all members of the transplant team) prior to initiating the program on human patients, a set number of simulations were not planned from the outset. The number of simulation session needed can vary by specific role and prior complementary experience. After completion of the swine simulation sessions, the team emphasized performance level, rather than the number of sessions, for determination of the need for additional sessions. This is reasonable consideration, as the level of exposure of the team member for the different steps of transplant surgeries were different.

The anesthesia team didn't need much more than one such session for a reasonable understanding of the process. This was because the swine simulation required understanding the special aspect of donors' and recipient's anesthesia, more than actual new skill. After the first session, the anesthesia team understood that they cannot keep the pig alive for a time longer than two hours with good blood pressure that is adequate for doing nephrectomy and transplants on the same pig. It was shown that pigs tolerate supine position poorly (10). When possible and the right instruments and expertise are available, the pig can be intubated through oro-tracheal route, but if that is not the case, as shown in this study, tracheostomy (done by the surgeon) can be used as a safe alternative for airway control (11).

Though it was not a big problem for the anesthesia or nursing team, the surgical team recognized the size of the pig matters a lot right from the first simulation. The difficulty related to the size of the pig was improved with appropriate size, which was between 25-35kgs, and was chosen for the last three sessions. Such size of a pig is not only easier to handle, but also easy to manage the anesthesia and final disposal of the body of the animal (11). Because we didn't have the experience how to do the nephrectomy and the transplant, we were thinking to do both procedures on the same pig in the first three sessions--which didn't work, as the pig cannot tolerate long hours in the supine position (10). Another issue learnt was tissue handling in swine surgery need to be more gentle than typical. Our experience in a few of the sessions was interrupted or required conversion to open due to bleeding resulted from rough tissue handling. This a common reason for conversion of laparoscopy to open in swine and human surgeries (4).

Though doing nephrectomy and transplant on the same animal might save some money, it doesn't closely simulate the actual human surgery and logistics, which was the main goal of the simulation process. A second pig in a second room for the transplant surgery was a better option, as affords the opportunity to also see what logistical needs are required for optimal timing of engraftment. Our experience showed that longer surgeries resulted in low blood pressure for swine, despite adequate fluid administration and minimal bleeding during the surgery, which means we couldn't complete the surgeries. This in turn can reduced our learning opportunities for these sessions.

The perception of the team towards simulation was largely positive. Doing a simulation once or many times was not the factor in testing a new center. Rather, doing the simulation as many times as required in a reasonably short interval (we would say one month) is an important consideration. This could allow for team/institutional memory to develop the lessons learnt. If the time is shorter than that, there will be not enough time to fill the gaps identified, and if it is too long, the experience might fade away. Progress of performance is largely dependent on the pre-simulation paper-based preparations, and level of exposure of the team members to the intended procedure. Debriefing at the end of each simulation, along with adequate note taking and planning together for the next session, as well as guidance by an experienced mentor, cannot be overemphasized.

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Conclusions: The experience, knowledge, and skills gained were monumental that we recommend using such a simulation approach to test new complex services in a new center. Simulation sessions should be performed until the team is comfortable and all gaps are identified.

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Competing Interest:

The authors declare that this manuscript was approved by all authors in its current form and that no

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ORIGINAL ARTICLE

SURGICAL COMPLICATIONS AND OUTCOMES OF LIVING KIDNEY RECIPIENTS IN A NOVICE TRANSPLANT CENTER IN ETHIOPIA

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ABSTRACT

Introduction: End stage renal disease is emerging as a major public health problem worldwide. Kidney transplantation is the treatment of choice for patients with ESRD, but its attendant surgical complications pose significant concern to the outcome of kidney transplantation surgery.

Objective: To review surgical complications and outcomes of live donor kidney transplant recipients in a novice transplant centre.

Methods: We analyzed a retrospectively collected data on all surgical complications among kidney transplant recipients performed from September 2015 to August 2017.

Results: A total of 52 live related kidney transplant surgeries were performed during the study period. The male to female ratio was 3.3:1. Patients' age ranged from 16 to 60 years with mean (SD) age of 34.5 (± 10.4) years. The Body Mass Index of patients ranged from 15.3 to 30.6 kg/m² with mean (SD) of 20.1 (± 3.5). Nearly one-half (24 (46.2%)) of the patients received kidney from their siblings. The etiology of end stage renal disease was unknown in 33 (63.5%) of the cases, whereas chronic glomerulonephritis, diabetes mellitus and hypertension accounted for 13.5%, 7.7% and 3.8%, respectively. Post-surgical complications occurred in eight (15.3%) of the patients and most (9.6) of complications were related to surgical wound. There was one (1.9%) urologic complication due to ureteric kink. Lymphocele occurred in one (1.9%) of the patients.

Conclusion: With proper planning and support, kidney transplant surgery can be a safe treatment modality for patients with end stage renal disease even in a resource limited facility. Our rates of surgical complications were within those reported by other series.

Key words: End stage renal disease, kidney transplantation, surgical complications

INTRODUCTION

End stage renal disease (ESRD) is one of the most common causes of death among non-communicable disease. It is increasing to epidemic proportions worldwide, including in sub-Saharan region. In this region, the cause of ESRD is unknown in majority of patients due to late presentation and lack of diagnostics like renal biopsy. Among patients whose cause of ESRD is known, hypertension and glomerular disease tops the table, while DM and hypertension are the main causes in the developed world (1).

Chronic renal failure is a devastating medical, social, and economic problem for patients and their families. Its effect is worse in economically underprivileged African societies, where renal replacement therapy is not available, scarce, or unaffordable for most patients and families.

Provision of renal replacement therapy is very challenging in sub-Saharan Africa because of high cost and lack of human and material resources and only few countries run kidney transplantation program in the region. Moreover, the rate of transplantation is quite low, necessitating referral abroad for transplantation.

In Ethiopia, the management of chronic kidney disease is still evolving. A successful kidney transplantation service was started in Ethiopia, at St. Paul's Hospital Millennium Medical College (SPHMMC) in September 2015 and a regular service is being provided at the center. Kidney transplantation has become the treatment of choice for most patients with end stage renal disease and is accepted as conferring a durable survival benefit

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and improved quality of life over dialysis (2,3). Kidney transplantation is also considered the most cost-effective therapy for end-stage renal disease (4-8).

Sixty years after the first human kidney transplantation by Joseph Murray in 1954 (9), refinements in surgical technique, peri-operative management, and immunosuppressive regimens have made kidney transplantation a safe surgery with improvements in morbidity and mortality. Nevertheless, surgical complications still pose significant challenge that may increase morbidity and hospitalization costs (10).

Surgical complications following renal transplantation can occur at any time, and may affect the transplant wound, vascular anastomoses, or related to urologic problems. Surgical complications continue to occur in about 10–20% of transplant recipients.

Vascular complications account for 3%–15% of all cases and are usually associated with graft loss (11). These include thrombosis or stenosis of the renal artery or vein. Some risk factors include poor surgical technique, torsion or compression of vessels, the presence of multiple renal vessels or a renal artery atheroma. The most common variant, which is found in 8%–30% of all potential kidney donors, is the presence of multiple renal arteries (12). Urological complications are the most common complications in the late period after kidney transplantation, presenting an incidence ranging from 2.5% to 12.5% (13). These complications include urinary leak, ureteric stenosis, ureteric kink and vesicouretric reflux.

Transplant wound complications are commonly seen in patients with diabetes and obesity and most important risk factor is the use of immunosuppressant medications. Meticulous attention to the recipient operation, anticipation of these problems and prompt treatment when they occur reduces morbidity.

Lymphatic collections usually occur 4-8 weeks after surgery and affect up to 15% of patients (14). The lymphatic collection arises from the lymphatics surrounding the iliac vessels that are divided during mobilization. The incidence of lymphoceles can be reduced by minimizing the pelvic dissection and ligating lymphatics. Definitive repair involves the creation of a window in the peritoneum. The purpose of our study was to review and present our experience of surgical complications of live related donor kidney transplantations performed during the first 2 years of service.

PATIENTS AND METHODS

Across-sectional descriptive study was conducted for patients who underwent live related kidney transplant surgery from September 2015 to August 2017 at national kidney transplant center. The center is located at SPHMMC in Addis Ababa.

Ethiopian organ donation law restricts living organ donation to happen only between blood or marriage related individuals, hence all donors were related to recipients. Transplant surgeons from University of Michigan and four transplant fellows (01 urologist and 03 general surgeons) from SPHMCC were involved in the surgery.

Individual patients' medical records from outpatient department (OPD), ward registration books and the Operation Theater logbook were used as sources of data. Data was collected in a pretested data collection format by trained final year surgical residents. The data was checked for completeness, and then coded, entered and analyzed with SPSS version 20. A written ethical clearance was obtained from SPHMMC Institution Review Board (IRB) and data obtained is used only for research purpose.

Regarding the transplant procedure, all kidneys were transplanted extraperitoneally in the left or right iliac fossa. The renal vessels were anastomosed using end to side anastomoses of the renal vein and artery to external iliac vessels. Lich - Gregoir anti-reflux ureteroneocystostomy technique was used in all cases with a temporary double J stenting, which is removed after four weeks. We avoided placing drains in all cases. Surgical complications were divided into vascular, urologic, lymphatic, wound related or other types. Tacrolimus, mycophenolate and prednisolone were most frequently used immunosuppressive combination.

RESULTS

During the two years, 52 living related kidney transplants were done. Males constituted 40 (76.9%) of the patients making a male to female ratio 3.3:1. Patients' age range from 16 to 60 years with mean (SD) age of 34.5 years (± 10.4). As shown in Table 1 most 33 (63%) of the patients were in their third and fourth decades of life. Patients came from all corners of the country, but a majority 37 (71.2%) of them were from the capital city, Addis Ababa. Patients had various levels of education with those who completed high school and college education constituting 21 (40%) and 14 (27%) of them, respectively.

The weight of patients ranged from 39 to 92kg with a mean (SD) of 57kg (± 12.8), while BMI of patients ranged from 15.3 to 30.6kg/m² with mean (SD) of 20.1(± 3.5)kg/m².

The cause of ESRD was unknown in most of the cases 33 (63.5%). Among those who have known cause chronic glomerulonephritis, diabetes and hypertension were common in decreasing order (Table 2).

Nearly one-half, 24 (46.2%) of the patients received kidneys from their siblings, while six patients each received kidneys from parents or off springs (Figure 1).

Table 1: Socio-demographic characteristics of living kidney recipient patients, St. Paul's Hospital Millennium Medical College, Addis Ababa, Sept. 2015 – Aug. 2017.

Variable		Number	Percent
Sex	Female	12	23.1
	Male	40	76.9
	Total	52	100.0
Age group (years)	<20	5	9.6
	21-30	16	30.8
	31-40	17	32.7
	41-50	9	17.3
	51-60	5	9.6
	Total	52	100.0
BMI	<18	12	23.1
	18.1-25	35	67.3
	>25	5	9.6
	Total	52	100
Residence	Addis Ababa	40	76.9
	Oromia	6	11.5
	Amhara	2	3.8
	SNNPR*	2	3.8
	Tigray	1	1.9
	Dire Dawa	1	1.9
Marital status	Total	52	100.0
	Married	27	51.9
	Single	22	42.3
	Divorced	3	5.8
Occupation	Total	52	100.0
	Government employee	16	30.8
	owns small business	22	42.3
	housewife	2	3.8
	None	4	7.7
	Student	8	15.4
Literacy status	Total	52	100.0
	Illiterate	1	1.9
	Read and write elementary completed	3	5.7
	high school completed	13	25
	college graduate	21	40.4
Religion	Total	52	100
	orthodox Christian	14	27
	Muslim	36	69.2
	Protestant	9	17.3
	Total	7	13.5
	Total	52	100

Table 2: Causes of end stage renal disease, St. Paul's Hospital Millennium Medical College, Addis Ababa, Sept. 2015 – Aug. 2017

	Number	%
Unknown	33	63.5
Chronic glomerulonephritis	7	13.5
Diabetes mellitus	4	7.7
Hypertension	2	3.8
Adult polycystic kidney disease	1	1.9
Urinary stone disease	1	1.9
Vesic-uretral reflux	1	1.9
interstitial nephritis	1	1.9
Genitourinary TB (chronic interstitial nephritis)	1	1.9
Nonsteroidal anti-inflammatory drugs	1	1.9

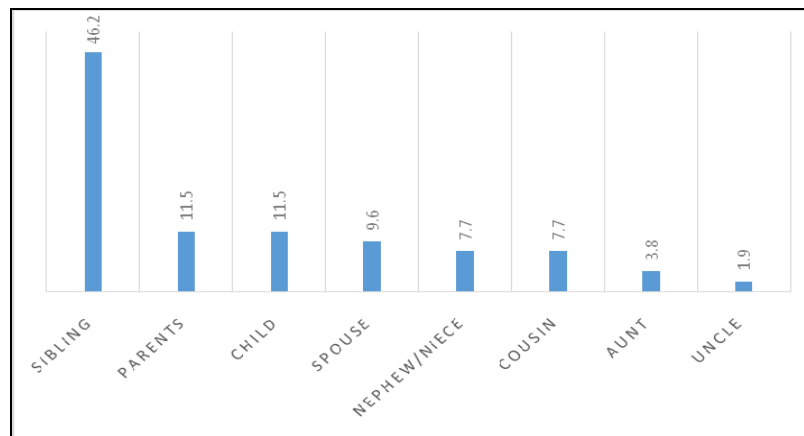


Figure 1: Kidney donation, St. Paul's Hospital Millennium Medical College, Addis Ababa, Sept. 2015 – Aug. 2017

Kidneys were transplanted on the left side in 46 (88.5%) of patients with the remaining transplanted on the right side. Forty eight (92.3%) of the patients received kidneys with single arteries, while four (7.7%) had two arteries. Operation time ranged from 110-220 minutes, with mean (SD) of 148 (\pm 25.9) minutes. Operative blood lost ranged from 100 to 350 ml, with a mean of 120ml.

Post-operative hospital stay ranged four to 20 days with a mean (SD) of 8.1 (\pm 4.1) days. There was a total of eight surgical complications (six early and two late) documented. Most (9.6%) surgical complications in our series were related to surgical wound.

Three patients developed superficial site infection; one patient had deep surgical site infection and one patient with surgical site hematoma. The infections were conservatively managed whereas the hematoma needed immediate evacuation. The source of surgical hematoma was not identified as the bleeding had stopped at the time of exploration. No patient died due to surgical complications. There was one early graft loss from unknown cause. The kidney was lost on postop day two and may have been due to hyper acute rejection, disease recurrence, or technical error.

Table 3: Surgical complications, St. Paul's Hospital Millennium Medical College, Addis Ababa, Sept. 2015 – Aug. 2017

Type of post op complications	Frequency	%
Early		
Superficial surgical site infection	3	5.7
Deep surgical site infection	1	1.9
Surgical site hematoma	1	1.9
Early graft loss due to unknown cause	1	1.9
Late		
Lymphocele	1	1.9
Ureteral kink	1	1.9

DISCUSSION

In our study, we found that male patients dominated as kidney transplant recipients (76.9%). This trend was observed in many other studies as well. A study from Nigeria showed 76.6% of their patients were males. The reason why this happened needs to be investigated but the Nigerian study attributed to the various socio-cultural peculiarities of the Nigerian population where the male sex is socially dominant. (15).

Most of our patients were also in their third and fourth decade of life, which is again consistent with other studies from developing world (1, 15-17).

The cause of ESRD in our series was unknown for most of the patients. Most of our patients presented for the first time with complication of ESRD at which time biopsy diagnosis would be inaccurate. Additionally, the biopsy service is also very limited in our set up.

Chronic glomerulonephritis, diabetes and hypertension were the major causes among those with known cause of ESRD. Studies from the region showed essential hypertension and chronic glomerulonephritis (CGN) as the predominant causes of ESRD in Africa (1, 16, 17).

Regarding surgical complications we have reported an incidence of 15.3% comparable to the 12.7% and 15.9% reported in the literature (18-20). The overall rate of surgical complications reported ranges widely. Surgical site infection (SSI) can be as low as 3% and as high as 15%. An SSI rate of 15% is reported by Anthony, who also identified higher BMI as a risk factor (21).

As the follow up of our patients ranged only 9- 33 months, late vascular complication was not documented. One of our patients had no urine following uneventful transplant surgery and color Doppler study reported as arterial thrombosis and immediate exploration carried out which revealed no thrombosis, but the kidney was completely dark, and nephrectomy performed. Biopsy result done at three institutions abroad was conflicting. The kidney was lost on postop day 2 and may have been due to hyper acute rejection, disease recurrence, or technical error.

Urological complications are the most common complications in the late period after kidney transplantation, with an incidence ranging from 2.5% to 12.5% (13) and may be responsible for poor graft outcome. Poor surgical technique and ischemia of the donor ureter are the most common causes of ureteric complications. Early recognition and effective management are critical for kidney transplant surgeons to effectively reduce their deleterious effect on long term graft survival.

We had one patient who developed severe hydronephrosis about 2 years after surgery. He had gradually rising creatinine level. Percutaneous Nephrostomy followed by antegrade pyelography study showed distal Ureteric stricture. Balloon dilation performed and showed no stricture but Ureteric kink. Double JJ stent was placed and exchanged regularly, and he is alive with functioning kidney.

A lymphocele is caused by lymphatic leakage from the perihilar renal lymphatics or the allograft bed and may occur in up to 15% of cases (14). Care in recipient lymphatics during preparation of the iliac fossa is important in minimizing such fluid collections. In our series we had one patient who presented with worsening of abdominal pain and swelling around 3 months after kidney transplantation.

Her kidney was functioning and abdominal sonography showed big lymphocele with minimal hydronephrosis. Although most lymphocele are too small to require treatment, we resorted to peritoneal window creation and patient improved remarkably.

Surgical complications of kidney transplantation can occur at any time and can be source of significant morbidity. Strict adherence to standard surgical techniques, early recognition and prompt treatment of surgical complications reduce morbidity of transplant patients.

Conclusion

The cause of ESRD in our series is unknown in most cases. Most of our recipients were in their third and fourth decades of life. Our rates of surgical complications were within those reported by other series. Kidney transplantation (KT) should be promoted and there is a need for concerted effort to expand and establish sustainable KT service in the country.

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Competing Interest:

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

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ORIGINAL ARTICLE

OUTCOME OF RENAL ALLOGRAFT RECIPIENTS AT SAINT PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE KIDNEY TRANSPLANT CENTER, ADDIS ABABA

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ABSTRACT

Introduction: *Kidney transplant is the current modality of choice as a renal replacement therapy due to superior patient survival and quality of life than both peritoneal and hemodialysis. The service is limited outside of developed countries due to the requirement for structured organization, extended expertise, and qualified supportive laboratory, as well as extensive health system service support in general.*

Objective: *The aim of the study is to describe renal allograft recipient outcomes during the first two years following establishment of the national kidney transplant center in Addis Ababa, Ethiopia.*

Methods: *A review of the case records of all recipients of renal allografts at Saint Paul's Hospital Millennium Medical College between September 2015 and August 2017 was done.*

Results: *Fifty two live donor kidney transplants were performed over two years. The cause of native kidney diseases was unknown in majority (32.6%), while chronic glomerulonephritis accounted for 30.8%. One fourth of recipients were transfused at least once before transplant. There was no biopsy proven rejection episode. There was one early graft loss from unknown cause. At least one organ system was affected with drug side effects in nearly in all (96%), leucopenia occurring in one fourth (22%) was very serious. Death censored graft survival at one year is 97.5% while mean GFR at one week, three month, six month and one year was 73.1, 93.6, 95.6, and 96ml/min, respectively. After successful kidney transplant pre-transplant hypertension subsided in 46.5% of patients.*

Conclusion: *Graft survival and graft function at one year were excellent, and comparable to well reputed centers worldwide.*

Key words: *Ethiopia, kidney, transplant, outcome*

INTRODUCTION

For those patients with ESRD, dialysis is often the only option, although renal transplantation is the treatment of choice, with better long-term survival and quality of life.

The introduction of calcineurin inhibitors has significantly reduced first year graft loss, while improvements in optimal use of immunosuppressants has improved patient survival (1).

The first-year graft and patient survival is best with a living-related fully matched DSA negative and ABO compatible young allograft recipient from a young male in a good outcome center.

Outcomes are somewhat lower for the recipient of a deceased renal allograft recipient. A report from WHO in 2018 outcome of organ transplant on one year graft survival across the world is depicted Figure 1 below (2,3).

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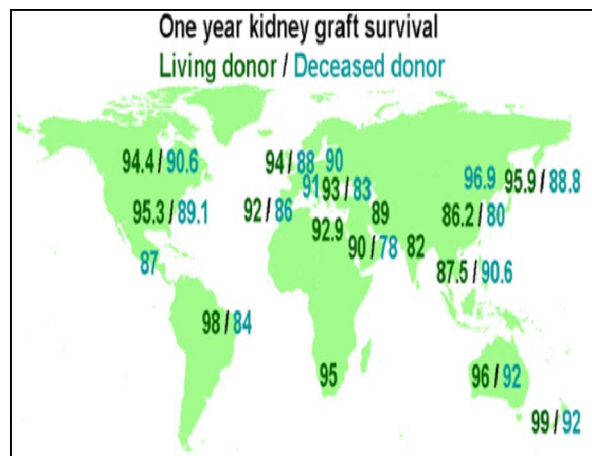


Figure 1: WHO 2018 outcome of organ transplant

The average graft function six months post-transplant from a report of the United States (US) Kidney Transplant Database in 2010 was 58.0 (47.0,70.7), mL/min/1.73 m² while percent of acute rejection in the first six months and percent of patients requiring dialysis during the first week was 8.5% and 3.2%, respectively. These outcomes were worse for black Americans (4,5).

Recipients of ABO compatible living-related kidney transplants are more likely to receive a less intense induction and maintenance immunosuppression. This practice decreases the frequency of infectious, cardiovascular, malignant, and other complications. In addition to the common bacterial infections, cytomegalovirus, and BK virus, fungal infections and post-transplant tuberculosis is common and a challenge in developing countries. Tharayil GJ reported the three-year post-transplant tuberculosis in 1,414 renal allograft recipients to be 13.3%. Of 166 patients who developed post-transplant tuberculosis 53 died (6-8).

Renal transplant services have largely been limited to developed countries, due to requirement for structured organization, extensive expertise, and qualified supportive laboratory services. Because of these requirements, only a few African countries have initiated transplant services. Ethiopia started a renal transplant service in 2015 at the national kidney transplant center (9).

This study was performed with intent of describing outcome of renal transplant recipients of the first two years at St. Paul Hospital's Millennium Medical Colleges (SPHMMC) National Kidney Transplant Center of Ethiopia to create understanding of how acceptable outcomes are and depict peculiar features of the center.

PATIENTS AND METHODS

The study was conducted in SPHMMC National Kidney Transplant Centre, Addis Ababa, Ethiopia. The transplant center was established in 2013 under the Federal Ministry of Health in collaboration with University of Michigan. A multidisciplinary team of specialists was developed that included surgery, nephrology, cardiology, radiology, pulmonology, endocrinology and others. Fifty two end stage kidney disease (ESRD) patients selected with prespecified selection criteria in intermediate risk of rejection got a renal transplant in the first two years of transplant service.

All patients received an induction therapy of basiliximab 20mg intravenous (IV) on days one and four. Methylprednisolone 500mg iv in the operation theater followed by 250mg iv, 80mg iv, 60mg per os (po), and 40mg po on post op day1,2,3 and 4, respectively, was given to all. Maintenance therapy included Tacrolimus (Pangraf), mycophenolate (CellCept) and prednisolone. Prednisolone was tapered to 5mg by the end of first month, while tacrolimus was maintained 8-12ng/lit in the first two months, 5-10ng/dl two to three month and 5-8ng/dl after wards. CellCept was initiated 2 days before transplant and maintained as 1gm twice a day.

Prophylaxis for bacterial, viral, fungal and tuberculous infections were given to all as cotrimoxazole 960mg po/d for a year, valgancyclovir of 900mg po/d for three months, nystatin oral gel four times a day for one month and isoniazid 300mg for six months. Dose and duration of prophylaxis medications were modified as necessary. The mean follow-up was 22months (11 to 36 months) with 92% followed for more than a year excluding patients who died. No patient was lost from follow up.

RESULTS

The first recipient was an elderly male. Since then, a total of 52 transplants were performed over two years; 41 (78.8%) of the recipients were male and given care mainly by the spouse (38%) during transplant (Table 1). All kidneys were collected from live donors, mostly blood related (89%) to the recipients, with 46% being sibling donors. Most donors were below the age of 45(75%); 23% were below the age of 25. HLA typing and CDC cross match was done for all patients. CDC was negative for all recipients, and DSA was either negative or not performed. HLA typing revealed the following: three zero mismatch, 10 (20.4%) halo match, and 10 three mismatch. Only three were six mismatch. No patient had a prior organ transplant, while 25 (48%) have received blood transfusions, and three of the 11 female recipients had at least one pregnancy.

Table 1: Socio-demographic characteristics of live donor kidney transplant recipients, SPHMMC*, Addis Ababa, Ethiopia. September 2015 to August 2017.

Variable		Number	Percent
Sex	Male	41	78.8
	Female	11	11.2
	Total	52	100
Age group (years)	18-25	8	15.4
	25-45	36	69.2
	45-65	8	15.4
	>65	0	0
	Total	52	100
	AA	37	71.2
Residence	Outside Addis	15	28.8
	Single	19	36.5
	Married	28	53.9
Marital status	Divorced	4	5.8
	Widowed	2	3.9
	Total	52	100.0
	Employee	20	40.0
Occupation	Personal business	11	22.0
	Jobless	7	14.0
	Other	12	24.0
	Total	50	100.0
	Cannot read and write	2	4.0
Literacy status	Read and write	2	4.0
	Primary complete	13	26.0
	High school complete	20	40.0
	College graduate	13	26.0
	Total	50	100
Care Giver	Mother and father	14	29.8
	Spouse	18	38.3
	Lives alone	1	2.1
	Other	14	29.8
	Total	47	100

Very few patients had clear cause for native kidney dysfunction, although the following causes were noted: lupus nephritis (2%), diabetic nephropathy (5.8%), hypertensive nephrosclerosis (7.7%), and ADPKD (2%). The most common cause was unknown (32.6%) or probable chronic glomerulonephritis (30.8%). Five percent of patients had a pre-emptive transplant (5.8%), while 10% had more than two years of hemodialysis.

Of note, while 35% of patients have BMI of less than 18.5% at the time of transplant, only 7.7% have BMI below 18.5 at one year of transplant. No single patient had a biopsy proven rejection episode; all renal biopsies with suspected rejection turned out to be ATN.

Four patients were empirically treated for a possible rejection, all with pulse dose methyl prednisolone with graft function returning to baseline.

Nineteen patients had at least one episode of infection requiring antibiotic use. GI and urinary tract were the most frequently affected organ systems. There were nine severe bacterial infections (pneumonia, sepsis, etc...) for which patients required hospital re-admission after transplant. Three patients were treated for CMV infection, while one for BKV nephropathy. Only one recipient developed tuberculosis after transplant. He successfully completed a six-month course of treatment. The patient's requirement for tacrolimus increased during treatment with INH, rifampicin, ethambutol and pyrazinamide.

New onset diabetes after transplant developed in 7.69%, while 36.5% developed post-transplant erythrocytosis. Hypertension was present in (86.5%) of recipients prior to transplant, with resolution in (46.7%) after kidney transplant. Only one patient developed a new onset hypertension after transplant. No patient required transfusion after transplant.

Nearly all patients reported (96.2%) at least one drug related side effect. GI upset was the most common (47%), followed by dermatologic complications (32.7%), hematologic complications including leukopenia (22%), transaminitis (16%), and nephrotoxicity (10%). One patient discontinued cotrimoxazole early for allergy, while three patients discontinued INH for severe transaminitis.

Only one patient reported failing to take medications at a prescribed dose and schedule for at least six days a week.

One-year death censored graft survival was 97.9%, with only one recipient losing the allograft early. The mean graft function at one week, three months, six months, and one year following transplant was 73.1, 93.6, 95.6, 96 and 83.3ml/min, respectively. Only 12% of patients had stage 3 CKD the one-year post-transplant. The following bar graph shows proportion of patients with specific stages of graft function at different time from transplant. (Figure 2).

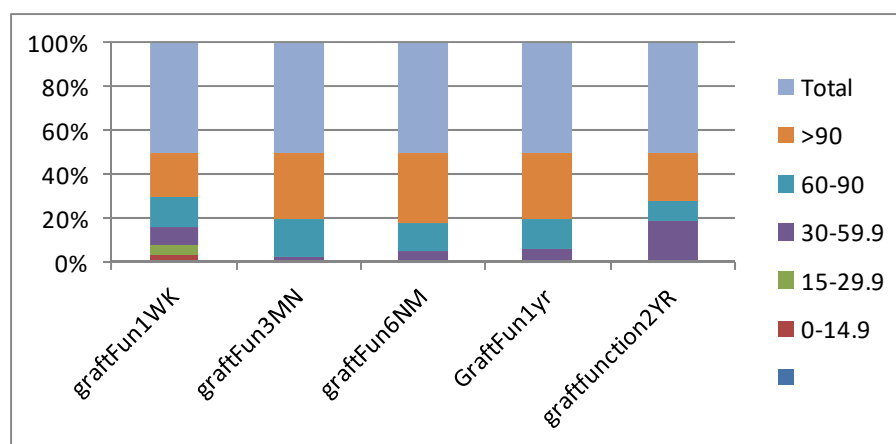


Figure 2: Graft function at different time from kidney transplant of live donor kidney

There were four deaths in the first-year post-transplant with serious infections being the cause for all. Two had CMV infection, while the third had infective endocarditis and the fourth patient had uncontrolled graft pyelonephritis. One-year patient survival is 92.3%. On logistic regression, 3 HLA mismatch [AOR=27(95% CI: 1.26- 578.354)] and pre-transplant transfusion [AOR=23(95%CI: 1.396-378.898)] were independent predictors of worse outcome.

DISCUSSION

Transplant has succeeded as the prime choice for ESRD care in Africa. Ethiopia has joined as the fifteenth country to successfully establish a kidney transplant service. A large proportion of our patients had unclear cause of the native kidney disease, a result of limited renal service in general.

The proportion of patients with diabetic nephropathy and hypertensive nephrosclerosis was low, due to a selection bias for younger patients with less comorbidities. As the center is new, the first patients were intentionally closer to ideal candidates.

We reported a very low number of preemptive transplants compared to a report made by Colleen et al. This may be attribute to the fact that our center is new, and patient backlog was significant. The long waiting time for transplant service once having a designated kidney donor, as well as late presentation to the health care system, are designated targets of intervention once service expansion is realized (10).

No single patient experienced biopsy proven rejection episode, although we treated four patients empirically. This was amazingly low especially compared with other center experience, although may have results from a conservative approach to histocompatibility. In a Nigerian report of 47 patients followed for three years with same maintenance immunosuppression regimen as recipients in our center, the reported incidence of rejection was 29.8%. Though the two populations are similar in terms of native kidney disease, triple immunosuppression and relatively young recipients the difference in rate of rejection is significant. Differences between these two studies, particularly as a possible reason for differing rejection rates, includes a higher rate of unrelated donors and lower rates of drug level monitoring in the Nigerian study, particularly as our center utilized mostly related donors with good matching, regularly monitored tacrolimus level, had aggressive approach to adherence monitoring and follow (11).

The susceptibility for infections due to active immunosuppression from tacrolimus MMF and prednisolone couple with drug related leucopenia/neutropenia predisposes these patients for serious infections. The usual sanitary parameters including food hygiene, waste disposal and clean and safe water are limitations that place special risk for these patients, although the physicians and transplant team have risen to challenge. These problems, coupled with the lagging microbiology and infectious disease specialty services in the country in general and our hospital, pose serious challenges to patient survival.

Post-transplant CMV infection was very serious, as two out of three of the patients with CMV disease died despite a preserved graft function. All CMV disease occurred after recipients completed a three-month valgancyclovir prophylaxis. The rate was higher than reported from USA for late onset CMV disease (4%). It is possible that the low rejection rate is the counterbalance to the infection and CMV rate. Regular monitoring can reduce these serious infections (12).

The prevalence of tuberculosis was 2%, which is very low for tuberculosis given the higher burden expected, since many report incidences as high as 15%. The use of INH preventive therapy for all recipients tolerating it helps to explain these outcomes (13).

The incidence of NODAT was similar with worldwide estimate, but it is low as compared to a report from Cape Town of 18%. Early tapering of steroid to maintenance dose, regular monitoring of CNI's and relatively younger recipient age may have contributed to our rate (14).

Almost all patients have hemoglobin values more than 11gm/dl and post-transplant erythrocytosis was present in 36.5%. Addis Ababa lies 3000meters above sea level, and is known for champion athletes, which can be a major factor for this finding.

When compared with a rate of less than 5% normotensives in an Italian report, post-transplant hypertension was very low, and with resolution in 46.7%, representing a secondary hypertension that subsided in correcting renal function (15). Despite these findings, and as tacrolimus can cause hypertension long term, we continue to monitor these patients.

Leucopenia is a common and frustrating complication of valgancyclovir and mycophenolate. The prevalence was marginally higher than reported figures of 10-15%. In a 64 individual report who received MMF and valgancyclovir, the rate was 20%. These complications have been major reason to discontinue valgancyclovir prophylaxis and hold MMF for a while until recovery (16).

Of all outcome measures that one looks at after kidney transplant, graft function is of paramount importance. Since kidney transplant first developed, first year graft survival has reached its peak. Many experienced centers enjoy a graft survival of 98% or more for live donor ABO compatible kidney transplant. According to the 2017 WHO report, across the globe the best 1year graft survival for live donor kidney transplant was 99% while the worst 82%, and most countries had between 90 and 94%. Our center has enjoyed a death censored graft survival rate of 97.5%, which compares favorably with the best. Average graft function was also good with a glomerular filtration rate (GFR) of 96ml/min. Proper patient selection, protocol-based immunosuppression and prophylaxis, and a motivated home team working in harmony with experts from the University of Michigan and frequent mentoring of Ethiopian nephrologists by US nephrologists has contributed to this outcome (3).

Conclusion

Ethiopia's first transplant center has demonstrated excellent graft and patient survival, with good graft function for those ESRD patients, who were transplanted. Rejection rates were low, although this may have been at the expense of increased CMV infections. As the nascent transplant center further develops, we will continue to analyze our results to optimize care of the expanding post-transplant patient population.

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Competing Interest:

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

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ORIGINAL ARTICLE

CLINICAL OUTCOME OF RENAL ALLOGRAFT DONORS AT NATIONAL KIDNEY TRANSPLANT CENTER IN ADDIS ABABA, ETHIOPIA

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ABSTRACT

Introduction: Chronic kidney disease is defined as the presence of one or more markers of kidney damage for greater than three months. The global burden of chronic kidney disease is increasing accompanied by increase in need of kidney transplantation and the number of living donors. Studies show that kidney donation has a medical risk to the donor with differences based on varying demographics. In Ethiopia, there is no report on the risk to the donors associated with possible medical complications.

Objectives: To assess medical outcome of renal allograft donors at the national kidney transplant center.

Methods: A cross-section chart review study was conducted at St. Paul Hospital's Millennium Medical College in Addis Ababa among 43 kidney donors who were on follow up from September 2015 to August 2018. Data was collected using pretested data abstraction tool. Epi-Info version 7.2.1.0 was used for data entry and SPSS version 23.0 and STATA version 14.1 were used for analysis.

Results: Median duration of follow up was 12 months. Majority of the donors were young less than 40 years, with mean pre-donation glomerular filtration rate 125ml/min and more than half were females. No cardiovascular event occurred during the follow up and 4(20.7%) of the females had post donation successful pregnancy without pregnancy related complications. Post donation hypertension and Chronic Kidney Disease were detected in 9.3 and 4.7 % of the donors.

Conclusions: The development of post donation hypertension and chronic kidney disease indicates the need for regular follow up of donors group. This study also recommend further study with a relatively longer duration of follow up to reach at a better conclusion.

Key words: Renal allograft donor, medical outcome, retrospective chart review, survival analysis, Ethiopia

INTRODUCTION

Chronic kidney disease (CKD) is defined as the presence of kidney damage (urinary albumin excretion of 30 mg/day or more, or equivalent) or decreased kidney function (glomerular filtration rate (GFR) less than 60 mL/min/1.73m²) for three or more months, irrespective of the underlying cause. Available evidence suggests that CKD is a risk factor for cardiovascular disease, premature mortality, and decreased quality of life. Among patients with CKD, the risk of death, particularly due to cardiovascular disease, is much higher than the risk of eventually requiring dialysis. Once the patient has reached GFR of less than 15 mL/min we call it end-stage renal disease (ESRD) (1,2).

The overall global burden of CKD is showing an increase. According to the U.S Centers for Disease Control and Prevention (CDC) report, the prevalence of ESRD increased by more than double between 1990 and 2015 (3). The Global Burden of Disease Study shows that kidney disease was 18th global leading cause of death, accounting for 1.1 million deaths worldwide and the 17th leading cause of global years of life lost in 2015. This rising burden of CKD disproportionately impacts low- and middle-income countries, where growth in obesity and diabetes is showing an increase (3-5). A systematic review of literatures among African countries shows that in the community-level the prevalence of CKD ranged from 2% to 41% and in

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high-risk groups it ranged from 1% to 46% in patients with HIV, 11%–90% in patients with diabetes and 13%–51% in patients with hypertension and in sub-Saharan African countries the overall prevalence of CKD was 13.9% (6, 7). A study conducted in Butajira hospital, southern Ethiopia shows that 18.2% and 23.8% of the study participants were found to have CKD, as defined by eGFR < 60 ml/min/1.73 m², according to the MDRD and Cockcroft-Gault equations, respectively (8). The increase in CKD burden is accompanied by increase in need of renal replacement therapy particularly kidney transplantation increasing the number of living donors in parallel. Since the first kidney transplantation done over 60 years ago, living kidney donation is the gold standard among renal replacement therapy for ESRD (9). Studies show that rates of living donor kidney transplant have steadily risen in most regions of the world, increasing its global significance as a treatment option for kidney failure (10-12).

Studies conducted around the world regarding long term outcome of kidney donors shows different type and degree of complication based on difference in population characteristics, genetic make-up and other factors. Some studies show no increased risk or even lower risk of mortality, ESRD, hypertension, proteinuria, pregnancy complications, cardiovascular disease, quality of life, life expectancy and others as compared to the general population (13-15). Other studies show increased risk of complications with major associated factors being black race, male sex, old age in non black donors, higher Body Mass Index (BMI) and a close biological relationship to the recipient (13,14,16-24).

In Ethiopia, since the establishment of the National Kidney Transplantation Center at St. Paul's Hospital Millennium Medical College (SPHMMC) on 2015 a total of 52 living kidney transplantations have been done. Studies regarding medical risk of kidney donation have not been conducted at the center. Donors are individuals who volunteer to save others' lives with no known benefits but accepting the risks the donation may carry. Therefore, it is important to identify potential complications so that donors make a choice with the knowledge of potential risks that are associated with kidney donation.

Knowing the occurrence of post donation complications among donors will help to identify prospective donors with long term risk of ESRD, for planning medical follow up and treatment to minimize complications and their effects and for counseling and providing informed consent. There is also a need for data that can be used as baseline for further studies in the field.

The aim of this study was to fill this gap by analyzing data on the medical outcome of renal allograft donors at the national kidney transplant center-SPHMMC from September 2015 to August 2018.

PATIENTS AND METHODS

The study was conducted in Addis Ababa, the capital city of Ethiopia, which has ten sub-cities and a total population of 3,273,001 (25). During the study period, there were 12 governmental hospitals in Addis Ababa. The study was conducted from April to July 2018 at one of the governmental hospitals, SPHMMC national transplant center. The transplant center has three nephrologists, four transplant surgeons, 20 nurses, and other supportive staffs with a functioning 15-bed dialysis unit, a four-bed Intensive Care Unit (ICU), ward, 24 hour working pharmacy and laboratory. The study design was hospital based retrospective chart review. Medical records of renal allograft donors who donated kidney since the opening of the transplant center were reviewed. The dependent variable is donor incidence of: CKD, Hypertension, Proteinuria, Pregnancy related complications, Diabetes mellitus and Cardiovascular event. The independent variables are classified into three categories: socio-demographic, pre donation medical status and post donation medical status related variables. The data collection was carried out by donor chart review, clinical evaluation and relevant laboratory data using pre-tested data abstraction tool that consists of questions to assess all the variables. The data was collected by trained professionals from April to July 2017.

The collected data was coded and entered into Epi-Info version 7.2.1.0, cleaned and stored and exported into SPSS version 23 for analysis. Descriptive statistics is presented with frequency tables, line graphs, Kaplan Meier (KM) plots and incidence density. Kaplan-Meier plots were used to compare survival experience of different groups of patients by using survival curves. Log-rank test was used to assess significant difference among survival distributions of groups for equality.

The study was conducted after ethical clearance was obtained from SPHMMC Institution Review Board (IRB) and written informed consent was obtained from the participants. The study had no risk/negative consequence for the participants. Medical record numbers were used for data collection and personal identifiers were not used in the research report. Access to the collected information was limited to the principal investigator and confidentiality was maintained throughout the project.

RESULTS

Socio-demographic related variables

From the 52 donors, information was collected from 43. The rest were unavailable at the time of the study due to different reasons. Majority of the donors (51.2%) were in the age range of 23-29 years, 55.8% were females and more than half of the donors were married (58.1%).

Regarding educational status and occupation, majorities were College/University complete (44.2%) and were self employed (51.2%). Thirty-seven (86.0%) of them donated kidney to blood related (first degree) family members and the rest (14%) donated their kidney to their spouse (**Table 1**).

Table 1: Socio-demographic related variables among renal allograft donors at St. Paul Hospital's Millennium Mesial Center, Addis Ababa, 2018 (n=43)

Variable	Frequency	Percent (%)
Age		
23-29	22	51.2
30-39	13	30.2
40-49	4	9.3
>= 50	4	9.3
Sex		
Female	24	55.8
Male	19	44.2
Marital status		
Married	25	58.1
Single	18	41.9
Education		
Cannot read and write	6	14.0
Primary school	4	9.3
High school	14	32.6
College/University	19	44.2
Occupation		
Government employee	12	27.9
Self-employee	22	51.2
No job	6	14.0
Student	3	7.0
Relationship with the recipient		
Blood related	37	86.0
Spouse	6	14.0

Pre donation medical status related variables

The mean glomerular filtration rate (GFR) measured before donation among the donors were 125.1 +/- 21.3 SD.

Regarding blood pressure measured before donation, the mean systolic and diastolic pressure among the donors were 112.8 +/- 9.7 SD and 74.7 +/- 7.4 SD respectively (**Table 2**).

Table 2: Pre donation medical status related variables among renal allograft donors at SPHMMC, Addis Ababa, 2018 (n=43)

Variable	Mean	Standard deviation
Pre-GFR	125.1	21.3
Systolic blood pressure	112.8	9.7
Diastolic blood pressure	74.7	7.4

Post donation medical status related variables

Regarding post donation health status, none of the donors developed diabetes mellitus or cardiovascular event. Only one sixth (16.7%) of the female donors got pregnant post donation but none of them developed pregnancy related complications.

Among the 43 donors, two (4.7%) of them has developed CKD after one year of donation while 41 (95.3%) did not develop CKD during the three years observation period. Only four (9.3%) of the donors developed post donation hypertension and the rest (90.7%) had normal post donation blood pressure and none of the donors had post donation dipstick proteinuria (Table 3).

Table 3: Post donation medical status related variables among renal allograft donors at SPHMMC, Addis Ababa, 2018 (n=43).

Variable	Frequency	Percent (%)
Diabetes mellitus		
Yes	0	0
No	43	100.0
Cardiovascular events		
Yes	0	0
No	43	100.0
Pregnancy		
Yes	4	16.7
No	20	83.3
Pregnancy related complications		
Yes	0	0
No	4	100.0
Post donation BP		
Normal	39	90.7
Hypertensive	4	9.3
Post donation dipstick proteinuria		
Yes	0	0
No	43	100.0
CKD		
Yes	2	4.7
No	41	95.3

The change in post donation blood pressure over time shows that, the systolic blood pressure shows a highest and lowest peak at the 12 month and 24 month of follow up respectively. The curve indicates a smooth flow till 12 months and then a relatively sharp decline till 24 months of follow up.

The DBP curve shows that there were sharp increase and decrease except between the 1st and 6th months of follow up where it remained relatively constant (**Figure 1**).

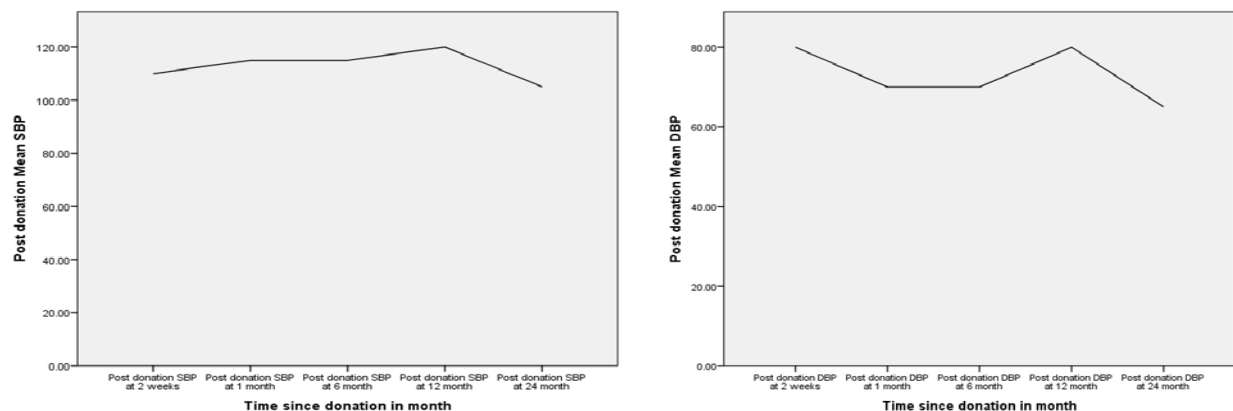


Figure 1: Liner graph of post donation mean SBP and DBP by time, Addis Ababa, 2018

The BMI curve shows a less steep increase throughout the time. The GFR curve shows that the mean GFR of the donors showed a relatively sharp decline

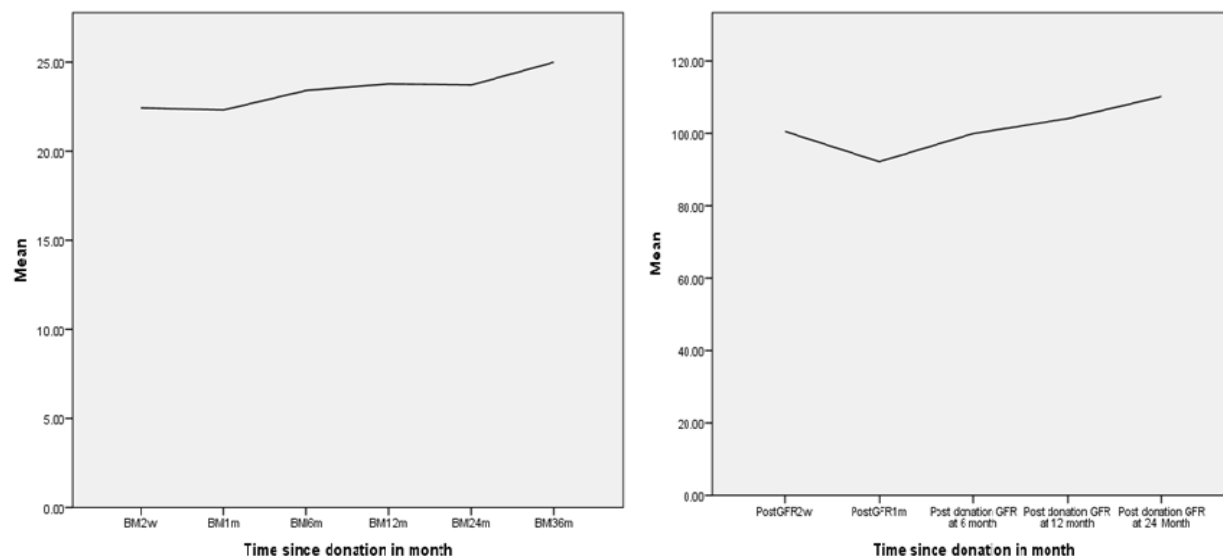


Figure 2: Line graph of post donation mean body mass index and glomerular Filtration Rate by time, Addis Ababa, 2018.

Censoring status

Among the 43 donors, two (4.7%) of them has developed CKD after one year of donation while 41 (95.3%) did not develop CKD during the two years observation period. Only four (9.3%) of the donors developed post donation hypertension and the rest 39 (90.7%) had normal post donation blood pressure and none of the donors had post donation dipstick proteinuria or pregnancy related complications.

On the other hand, during the two years observation period, any of the donors did not develop proteinuria (dipstick) and pregnancy related complications. The incidence rate ratio among the groups classified by the above independent variables did not show significant difference (P values >0.05).

Comparison of survival experience

KM plot and log rank test were used to assess the difference in the survival distribution among groups. It doesn't show statistically significant difference among the groups.

DISCUSSION

The main purpose of this study was to assess clinical outcome of renal allograft donors at the national kidney transplant center-SPHMMC. The study revealed that two (4.7%) of the donors has developed CKD after 1 year of donation while 41 (95.3%) did not develop CKD during the three years observation period.

from the 1st to 6th month of follow up and then it shows a progressive increase till the end of the follow up period (**Figure 2**).

Only four (9.3%) of the donors developed post donation hypertension and the rest (90.7%) had normal post donation blood pressure. This is in contrast to other studies conducted in the US which reported a median risk of kidney failure of 34/100,000 donors and risk of 0.24% among black men, 0.15% among black women (19, 24). This difference could be due to the difference in the duration of follow up among the studies and also could be because of the varying socio demographic and population characteristics. On the other hand, it is comparable with another study showing a prevalence of hypertension to be 7% (17,22).

The post donation CKD and hypertension among the donors during the three years observation period was on average 4.1 per 100 person years of observation (95% CI=1.0194, 16.2969) and 8.2 per 100 person years of observation (95% CI= 3.0594, 21.7192), respectively. This is less than findings in a study done with long term follow up resulting higher level of donors with CKD up to 14.5% and hypertension of 32.2 %(10).

On the other hand, during the three years observation period, any of the donors did not develop proteinuria (dipstick), diabetes mellitus, cardiovascular events and pregnancy related complications. This is in line with the above systematic review and meta analysis study showing no such complications across countries (13).

Conclusion

Majority of our donors were young with normal mean pre donation GFR. No post donation cardiovascular event happened to all donors and no pregnancy related complication happened among the pregnant donors.

The development of post donation hypertension and chronic kidney disease indicates the need for regular follow up of donors group. This study also recommend further study with a relatively longer duration of follow up to reach at a better conclusion.

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Conflict of Interest

Authors have no conflict of interest to declare.

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ORIGINAL ARTICLE

MAGNITUDE OF METABOLIC SYNDROME AND ASSOCIATED FACTORS AMONG RENAL TRANSPLANT RECIPIENTS: EXPERIENCE FROM A NEW CENTER, ADDIS ABABA

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ABSTRACT

Introduction: *Metabolic syndrome is a cluster of risk factors for cardiovascular diseases. It is also common in renal transplant recipients and is associated with increased risk of graft dysfunction and cardiovascular mortality. Its magnitude is not known in our Ethiopian patients.*

Objective: *The study is conducted to determine the magnitude of metabolic syndrome and associated factors among renal transplant recipients.*

Methods: *Analytical cross-sectional design was used. Eighty-seven Ethiopian renal transplant recipients having follow-up at St. Paul Hospital's Millennium Medical College Kidney Transplant Centre were studied from May to July 2018. A structured data collection format was used to collect data. Contextualized "WHO STEPS Instrument for Non-communicable Diseases Risk Factor Surveillance" was utilized for collecting data on behavioral risk factors, biophysical measurements and laboratory tests. The diagnosis of metabolic syndrome was made according to the revised National Cholesterol Education Program-Adult Treatment Panel III criteria. Data were described by frequencies, percentage and mean (\pm SD). Comparative analysis between variables was done using bivariate and multivariate logistic regression. Statistical significance of the prediction was declared at p -value < 0.05 with 95% confidence interval.*

Results: *Majority 64 (73.6%) of the cases were male patients. Most of them were young with mean (\pm SD) age of 35.8 (\pm 11.9) years. Hypertension was the commonest component of metabolic syndrome accounting for 49 (56.3%) of cases. The magnitude of metabolic syndrome was 34.5%. Only central obesity (P value = 0.046; AOR 39.1 (95% CI 1.1, 141) and hyperglycemia ($P=0.031$; AOR 25.1 (95%CI 1.3, 467.8) were significantly associated with metabolic syndrome.*

Conclusion: *The magnitude of metabolic syndrome was high in our kidney transplant recipients. However, only waist circumference and hyperglycemia were found to have significant association with metabolic syndrome. Comprehensive preventive strategies should be implemented for management of metabolic syndrome to minimize its impact.*

Key Words: *Metabolic syndrome, renal transplant, Diabetes Mellitus, Hypertension, Dyslipidemia, Central Obesity.*

INTRODUCTION

Metabolic syndrome (MS) is a cluster of risk factors for cardiovascular disease (CVD) that has drawn more clinical attention. It comprises multiple risk factors including abdominal obesity, hypertension, hyperglycemia and dyslipidemia that can occur in different combinations. Different expert panels have provided various definitions for MS to enable a clinical

diagnosis and treatment of patients at risk of associated complications (1-3). Metabolic syndrome is one of the major public health issues globally. World-wide, the prevalence of MS ranges from 10% to 50%. The International Diabetes Federation (IDF) believes that this cluster of factors is driving the twin global epidemics of type 2 diabetes and cardiovascular diseases (4-6).

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Lifestyle changes such as dietary habits, sedentary life and consumption of energy-dense foods that have occurred over the years has led to an epidemic of abdominal obesity, which in turn resulted in dramatic increase in the prevalence of metabolic syndrome. Obesity and obesity mediated MS has been paralleled by escalation in the incidence of chronic kidney disease (CKD) (7, 8). MS is also common in renal transplant recipients. MS has been shown to be an independent risk factor for chronic allograft dysfunction, graft failure, new-onset diabetes, and cardiovascular disease. The development or worsening of obesity plays a central role in the development of metabolic syndrome after kidney transplantation. Risk factors specific to transplant recipients include the duration of pre-transplant dialysis and post-transplant immunosuppression and weight gain. Immunosuppression also plays an important role in the pathogenesis of the individual components of the metabolic syndrome. They should be designed to limit exacerbation of components of the metabolic syndrome (9-15).

The metabolic syndrome is emerging as a significant surveillance target following kidney transplantation. Control of body mass index (BMI), blood glucose and lipid levels, as well as blood pressure, is required to prevent the consequences of the metabolic syndrome. Patients with metabolic syndrome or components of metabolic syndrome need to have complete clinical evaluation and optimal management including screening and treatment of risk factors, comorbidities and expected complications. There are internationally accepted standards of clinical care for such patients. Efforts toward promoting lifestyle modification including healthy diets, physical activity, and blood pressure control must be undertaken (8, 10, 16-21).

Since renal transplantation service was established only two and half years ago, the magnitude of MS in transplant patients in Ethiopia is not known. A better understanding of the magnitude and impact of metabolic syndrome in our transplant patients would help in prevention, early detection, and management of the syndrome as well as its detrimental sequelae of cardiovascular morbidity and mortality.

PATIENTS AND METHODS

A cross-sectional study was conducted from April 15 to July 15, 2018 at St. Paul's Hospital Millennium Medical College (SPHMMC) Kidney Transplant Centre, in Addis Ababa, Ethiopia. The transplant center was established in September 2015, under the Federal Ministry of Health, in collaboration with University of Michigan. The transplant center has a multidisciplinary team involving nephrologists, transplant surgeons, nephrology fellows, a vascular access surgeon, interventional radiologists, psychiatrists, nurses, and other supportive staffs.

A total of 83 patients have been transplanted. Additional 37 patients who were transplanted abroad are also having post-transplant care and follow up in our transplant outpatient clinics. Out of the total (N= 120) patients currently having regular post-transplant treatment and follow in our transplant center, 87 sampled adult (age \geq 18 years) patients who came for their regular follow-up during the study period were included in the study whether they were transplanted in our center or abroad. Those who were transplanted within three months before the study period were excluded.

Variables of interest for data collection were patients' socio-demographic characteristics, behavioral risk factors; clinical characteristics including BP, weight, height, waist circumference; and laboratory tests including FBS, lipid profile and serum creatinine. A structured data collection format was used to collect data. For collecting data on behavioral risk factors for metabolic syndrome, we used the "WHO STEPS Instrument for Non-communicable Diseases Risk Factor Surveillance" with modification and contextualization (22). Data were collected using patient interview, clinical evaluation, and laboratory tests. Data collection tools were standardized and pretested. Data collectors were nephrology fellows and transplant nurses. They were trained by the principal investigator on the objective of the study, the instruments of data collection, and the process of data collection. Laboratory tests were performed by a trained laboratory technologist.

To ensure data quality, the questionnaire, prepared in English, was translated into Amharic and back to English for checking language consistency. Pre-testing was conducted on four patients. Accordingly, gaps and ambiguity were clarified by further discussion, including demonstration and practical session on patient interviewing and anthropometric measurements. Weighing scales and BP measurement apparatus were used for biophysical measurements. They were checked and calibrated every morning and after each measurement for functionality and consistency. Standard laboratory procedures were implemented. The principal investigator assisted and supervised the data collection process.

The collected data was checked for completeness and consistency by crosschecking with the source documents when it was needed. Then it was coded and entered in to study database using EPI Info Data software version 3.1. Then, the data was exported to Statistical Package for Social Science (SPSS) version 21 program for analysis. Continuous observations were expressed as means while categorical observations were described by frequencies and percentages.

Bivariate analysis was done first to select candidate independent variables for the multiple logistic regressions. For those variables whose p-value were > 0.25 on bivariate analysis, multiple logistic regression analysis was done to identify independent predictors of MS. Statistical significance of the prediction was declared at p-value < 0.05 with 95% confidence interval.

Ethical clearance was obtained from SPHMMC ethical review committee. Objectives of the study and procedures of data collection were explained to the study subjects and they gave informed written consent. During the interview, all patients were given a brief description about MS components. They were also advised on preventive strategies.

Patients were diagnosed to have MS if they fulfilled the updated NCEP-ATPIII criteria; i.e. if they have any three of the following five criteria (1-3):

- Waist circumference ≥ 94 cm for male; and ≥ 80 cm for female;
- Systolic BP > 130 mmHg or diastolic BP > 85 mmHg or being on treatment for HPN;
- FBS ≥ 100 mg/dl or being on treatment for DM;
- Fasting HDL ≤ 40 mg/dl for male or ≤ 50 mg/dl for female or being on treatment for dyslipidemias;
- Fasting Triglyceride level ≥ 150 mg/dl or being on treatment for dyslipidemias.

Healthy lifestyle was defined as fulfilling all the following criteria (17-20):

Healthy Diet:

- Regular consumption of fruits and vegetables (daily consumption of at least three servings of vegetables and fruits);
- High intake of cereals, whole grains, poultry, fish, low-fat dairy foods, and vegetable oil;
- Low intake of high calorie foods and fats (butter, fatty meat, honey, sweets, and saturated fat); and
- Low sodium intake (i.e., ≤ 2.4 gm per day);

Healthy physical activity:

- A minimum of 150 min per week of moderate-intensity physical activity continuously done at least for 10 minutes; AND

No habit of cigarette smoking or alcohol drinking.

Graft dysfunction: was defined as stable creatinine level ≥ 1.5 mg/dl at three months or more after transplantation.

RESULTS

Among 120 post renal transplant patients having regular follow up and treatment in our transplant center, 87 were sampled and involved in the study.

Sociodemographic characteristics: Men accounted for 64 (73.6%) of the study sample. The mean age was 35.8 (+/-11.9) years, with 78.2% of patients under the age of 45 years (Table 1 and Figure 1).

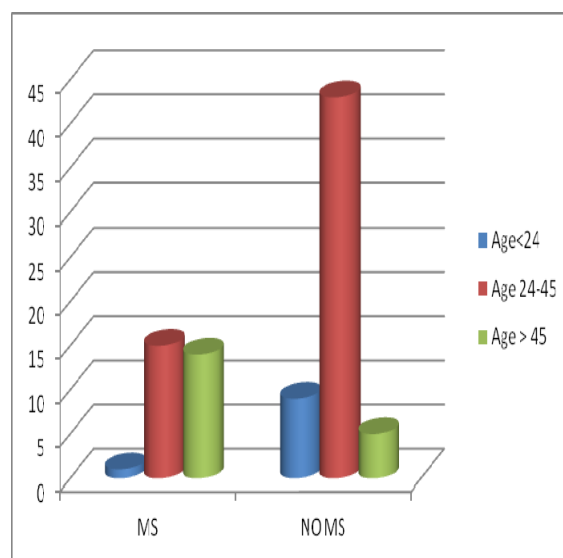


Figure 1: Distribution of metabolic syndrome by age, among transplant recipients at St. Paul's Hospital's Millennium Medical College Transplant Center, July 2018.

Table 1: Socio-demographic characteristics of renal transplant recipients, on follow up at SPHMMC* national transplant center, July 2018.

Sociodemographic Characteristics	Category	Frequency	Percentage (%)
Age	<24 years	10	11.5
	24-45	58	66.7
	>45	19	21.8
Sex	Male	64	73.6
	Female	23	26.4
Educational status	Illiterate	1	1.1
	Can read and write	3	3.4
	Primary Education	10	11.5
	Secondary Education	29	33.3
	Tertiary Education	44	50.6
Occupation	Non-government employee	8	9.2
	Self employed	34	39.1
	Student	6	12.6
	unemployed	30	14.9
Marital status	Single	37	32.5
	Married	46	52.9
	Divorced	3	3.4
	Widowed	1	1.1
Residence	Addis Ababa	63	72.4
	Elsewhere in Ethiopia	24	27.6

Behavioral risk Factors

Diet: Fifty four (62.1%) patients eat three times servings of fruits at least three days a week. The majority, 83 (95.4%), eat 3 times servings of vegetables at least three days a week. All of the patients knew that salt is harmful for health; and 70 (80.5%) of patients consume too little amount of salt in their diet occasionally. Similarly, 72 (82.7%) patients don't use high caloric or fatty diet like fatty meat, butter or sweets. Most, 67 (77%), patients use vegetable oil for cooking while only 18 (20.7%) patients use small amount of butter occasionally. Thirty six (41.4%) patients always consume home prepared meals. Only 14 patients consume more than three meals per week prepared outside home.

Smoking and alcohol: None of the patients currently smoke cigarettes nor drink alcohol. Only 9 (10.3%) patients have past history of smoking. The mean number of cigarettes they used to smoke was 12 per day for a mean duration of 132 (+/- 5.4) months.

Similarly, only 33 (37.9%) have past history of alcohol drinking for a mean duration of 118.6 (+/- 4.7) months.

Mostly they used to drink beer; on average 3-4 bottles of beer per day three days a week. All of them quit smoking and drinking while diagnosed with CKD.

Exercise: Most, 85 (97.7%), of the patients do moderate intensity exercise like walking for at least 150 minutes per week. The mean duration of exercise was 48.6 (+/- 15.7) minutes at least three days a week. Most, 48 (55.2%) of them, do exercise on daily basis. The mean duration spent by patients while sitting or reclining was 5 (+/- 1.6) hours a day with only 8 patients sitting or reclining for ≥ 8 hours (Table 2).

Table 2: Frequency of behavioral risk factors for MS among transplant recipients having treatment follows up at SPHMMC national transplant center, July 2018.

Behavioral Risk Factors	Category	Frequency (N)	Percentage (%)
Current smoking	Yes	0	0.0%
	No	87	100.0%
Currently alcohol drinking	Yes	0	0.0%
	No	87	100.0%
Past history of smoking	Yes	9	10.3%
	No	78	89.7%
Past history of alcohol drinking	Yes	33	37.9%
	No	54	49.1%
Doing moderate intensity exercise like walking for at least 150minutes per week	Yes	85	97.7%
	No	2	2.3%
Consumption of Fruits*	Yes	54	62.1%
	No	33	37.1%
Consumption of Vegetables**	Yes	83	95.4%
	No	4	4.6%
Consumption of fatty foods or high calorie diets	Yes	15	17.3%
	No	72	82.7%

*Patients eat 1-3 times servings of fruits at least 3days a week.

**Patients eat 1-3 times servings of vegetables at least 3 days a week.

Transplant characteristics: Most patients, 64 (73.6%), were transplanted at our transplant center. The rest were transplanted abroad. The underlying cause of the renal failure was not known for a larger proportion of patients, 37 (42.5%). Of the known causes, HPN and DM accounted for 24 (27.6%) and 14 (16%), respectively. Five of the patients were transplanted before starting dialysis. For the rest the mean (\pm SD) duration of dialysis was 12.6 (\pm 11.0) months. The mean (\pm SD) duration since transplantation was 16.6 (\pm 15.5) months.

All of the patients were on maintenance doses of triple immunosuppressive therapy comprising of tacrolimus, mycophenylate mofetil (MMF) and prednisolone except two who were taking cyclosporine instead of tacrolimus and another two taking azatioprin instead of MMF. Only 11 (12.6%) of the patients had graft dysfunction.

Magnitude of Metabolic Syndrome and its Components

Hypertension (HPN): HPN was the commonest component of metabolic syndrome. Forty nine (56.3%) patients were on treatment for HPN of which 33 (67.3%) have good control of their HPN. Eight of the patients became hypertensive after transplantation.

Hyperglycemia: A total of 23 (26.4%) patients have hyperglycemia of which 19 (82.6%) are already diagnosed with DM and on treatment. At base line, only 14 patients had DM as an underlying cause of the renal failure.

Central Obesity: Most, 69 (79.3%) of the patients had normal BMI while only 15 (17.2%) were overweight. Twenty five (28.7%) patients were found to have central obesity with a mean waist circumference of 96cm.

Dyslipidemia: The commonest form of dyslipidemia was low high density lipoprotein (HDL) level occurring in 29 (33.3%) patients followed by high triglyceride, high low density lipoprotein (LDL), and high total cholesterol level each accounting for 25 (28.7%), 21 (24.1%), and 20 (23%) respectively. However, only 3 patients were on lipid lowering treatment.

Magnitude of metabolic syndrome and its components is shown in Figure 2.

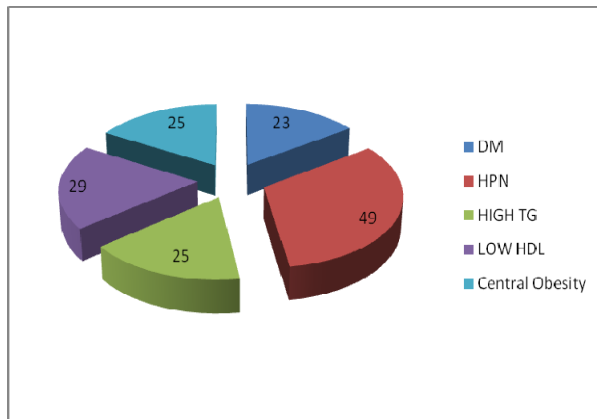


Figure 2: Frequency of Components of metabolic syndrome among transplant recipients having treatment follow up at SPHMMC national transplant center, July 2018.

Magnitude of Metabolic syndrome: According to revised NCEP-ATP III criteria 30 out of 87 patients were found to have metabolic syndrome making the prevalence 34.5%.

Factors associated with MS: Age, past history of smoking, BMI, waist circumference, HPN, DM, dyslipidemia, and creatinine level showed statistically significant association with MS when analyzed with binary logistic regression (P value <0.05).

However, with multiple logistic regression analysis only central obesity (P value=0.046; AOR 39.1 (95%CI 1.1, 141) and hyperglycemia/DM (P=0.031; AOR 25.1(95%CI 1.3, 467.8) were significantly associated with Metabolic syndrome (Table 3).

Table 3: Multivariate logistic regression of components of metabolic syndrome among transplant recipients on follows up at SPHMMC* Transplant Center, July 2018.

Category of Independent Variables		With Outcome Variable (MS)		Without Outcome Variable (No MS)		COR (95% CI)	AOR (95% CI)	P Value
		No	(%)	No.	%			
Waist Circumference	Normal	8	9.2%	54	62.1%	1.0	1.0	0.046
	Above normal	22	25.3%	3	3.4%	49.5 (12.0,204.0)	39.1 (1.1, 141)	
HPN	Yes	4	8.7%	19	41.3%	4.63 (0.48, 45.1)	0.26 (0.012,5.66)	0.391
	No	1	2.2%	22	47.8%	1.0	1.0	
DM	Yes	11	12.6%	53	60.9%	22.9 (6.5, 80.6)	25.1 (1.3, 467.8)	0.031
	NO	19	21.8%	4	4.6%	1.0	1.0	
Low HDL	Yes	10	11.5%	48	55.2%	10.67 (3.8, 30.2)	15.4 (0.867, 273)	0.62
	NO	20	23.0%	9	10.3%	1.0	1.0	
High Triglycerides	Yes	11	12.6%	51	58.6%	14.7(4.8,45.3)	1.47 (0.007, 290.7)	0.886
	NO	19	21.8%	6	6.9%	1.0	1.0	

DISCUSSION

Consistent with other literatures, a majority of our patients (73.6%) were males (23-26). Our patients were younger, with the mean age of 35.8(\pm 11.9) years compared to findings of other similar studies. This can be explained by relatively younger age of our CKD patients and by our transplant center's highly selective criteria.

Even though, most of the patients eat fruits (62.1%) and vegetables (83%) with their diet, the frequency of consumption and the variety are below what is recommended by literature (7, 10, 22, 26). As patients were advised to avoid certain fruits and raw vegetables, particularly during the early months following transplantation, for fear of contamination and food- drug interaction, they tended to continue avoiding fruits and vegetables for several months. Unavailability of a dietician or nutritionist in the center might have contributed to this over-precaution.

Most of our patients restrict or avoid salt (80.5%) and fatty foods or high caloric diets (82.7%), matching recommendations from other studies and WHO for risk reduction for chronic non communicable diseases (7, 10, 12, 22). None of the patients currently smoke cigarettes or drink alcohol. Most (97.7%) of the patients do moderate intensity exercise like walking for a mean duration of 48.6 minutes. The mean duration spent by patients while sitting or reclining was 5hours a day with only eight patients sitting or reclining for \geq 8hrs. These risk reduction behaviors are also in line with literature and WHO recommendations (7, 10, 12, 22).

Of the known underlying causes, HPN and DM accounted for larger proportion of cases consistent with findings worldwide. HPN was the most common component of MS accounting for 56.3% of cases. This finding is comparable with the findings of other similar studies done on MS elsewhere (9, 14, 23-29). Most, 69 (79.3%), of the patients had normal BMI. However, 25 (28.7%), of the study subjects had central obesity. MS was diagnosed in 21(84%) of them. This was expected as central obesity is considered to play a major role in the development of MS. This finding is comparable with the findings of other similar studies (9, 12, 14, 30).

Twenty three (26.4%) patients had hyperglycemia, of which 19 (21.8%) were already diagnosed with DM and were on treatment. At base line, only 14 patients had DM as an underlying cause of the renal failure.

This means nine (10.3%) patients have developed hyperglycemia after transplantation five of which had already started treatment for new onset diabetes after transplantation (NODAT). This can be as a result of the immunosuppressive regimens. This finding is comparable with the findings of other similar studies done on MS elsewhere (9, 14, 15, 23-29).

The frequency of dyslipidemia ranged from 33.3% for low HDL to 23% for total cholesterol level. As expected, the dyslipidemia mostly overlapped with central obesity. This is also in line with other similar studies (9, 14, 15, 23-29). Only 11 (12.6%) of the patients had graft dysfunction. The mean duration of stay since transplantation was 16.6 months. This is a shorter duration when compared to other studies (10, 25, 28). These can be justified by our center being established only two and half years back.

The magnitude of metabolic syndrome in our patients was found to be 34.5%, similar to the findings of other studies from Europe (34.2%) (9, 28); Iraq (32.5%) (24) ; and Iran (32%) (9). However, the prevalence of MS in our patients was higher compared to finding of other similar studies from Japan (28.8%) and China (25.3%) (25, 31). This might be because these studies used NCEP-ATP III criteria modified for Asians who are known to have lesser obesity. On the other hand, the prevalence of MS was higher than ours in some other similar studies from Pakistan (43.5%) (26); Brazil (44.8%) (27); and Saudi Arabia (52.8%) (24). This can be justified by our patients being younger compared with relatively older patients in the other studies which is known to increase the risk of MS. It can also be as a result of different study populations of the other studies with higher prevalence of obesity.

Among the independent variables, age, past history of smoking, BMI, waist circumference, HPN, DM, dyslipidemia, and creatinine level showed statistically significant association with MS when analyzed with binary logistic regression [$P < 0.05$]. However, with multiple logistic regression analysis only waist circumference (P. value = 0.046; AOR 39.1 (95%CI 1.1, 141.8) and hyperglycemia or being on treatment for DM (P=0.031; AOR 25.1 (95%CI 1.3, 467) were significantly associated with MS. These findings are also in line with findings of other similar studies(10, 14, 15, 24-26, 28, 29, 31).

The strength of the study is being original in our setup and addressing an important clinical problem. However, the study is underpowered by a small size and by short period of post-transplant follow up of most patients. This study can be used as a basis for further large-scale studies on prevalence of MS and associated factors in CKD patients or in the community at large.

Conclusion

Almost all of patients on our series didn't have many of the behavioral risk factors, except relatively lower number of daily servings of fruits and vegetables. The prevalence of MS was high in our transplant recipients. Only waist circumference and hyperglycemia were found to have significant association with MS. Comprehensive preventive strategies should be strengthened for optimal management of our transplant patients so that complications of MS could be averted.

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Competing Interest:

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

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ORIGINAL ARTICLE

KNOWLEDGE, ATTITUDE AND FACTORS ASSOCIATED WITH ORGAN DONATION AMONG MEDICAL STUDENTS, ADDIS ABABA

Mahteme Bekele Muleta, MD^{1*}, Mahlet Berhanu, MD¹, Sisay Tanie, MSC¹

ABSTRACT

Introduction: Organ transplantation is the most effective and desirable method of treatment for patients suffering from end stage organ failure secondary to any cause. The main problem currently facing transplant medicine lies in the discrepancy between global need for donor organs and the demand, which by many is believed to be because of lack of adequate knowledge and poor attitude towards organ donation among the public. Since medical students are the future physicians it is very important to assess their level of understanding and improve their knowledge and attitude towards organ donation.

Objective: To assess the knowledge, attitude and associated factors about organ donation among medical students of St. Paul Hospital's Millennium Medical College.

Methods: A descriptive cross-sectional study was conducted among medical students of St. Paul Hospital's Millennium Medical College, Addis Ababa, Ethiopia from March 12, 2018 to May 07, 2018. The study was conducted on a sample size of 240 medical students. Data was collected through structured self-administered questionnaire consisting of 31 questions on knowledge and attitude towards organ donation. Data was cleaned, coded and entered into computer and analyzed using SPSS version 20.0. Simple descriptive statistics such as frequency and percentage were used to summarize the results and chi-square and binary logistic regression was used to describe the association between variables. P -value < 0.05 was considered as statistically significant association.

Results: A total of 236 students participated in the study out of a sample size of 240, making the response rate 98.3%. Amongst which 88.6% had good knowledge but only 10.2% of the participants had positive attitude. Two of the independent variables were found to have significant association with having good knowledge. Female students were found to be five times more likely to be knowledgeable than male students $P=0.001$, $COR=5.383$, 95% CI 1.963-14.758) and those who reported internet as their primary source of information were found to be four times more knowledgeable than those who reported other outlets as their source ($P=0.004$, $COR=4.041$, 95% CI 1.567-10.420). Bivariate and multivariable analysis did not reveal other significant associations between the independent variables and having positive attitude.

Conclusion: Over a majority of the students were found to have good knowledge but negative attitude towards organ donation. Among the independent variables female gender and having internet as their primary source of information was found to have significant association with good knowledge. Thus, it is crucial that the college and clinical departments that practice transplantation medicine take part in the theoretical teachings as well as devising a curriculum that allows for students to raise and eliminate their perceived barriers to organ donation and transplantation to improve their attitude.

Key words: Knowledge, Attitude, Organ Donation, Students, Addis Ababa

INTRODUCTION

Organ transplantation is arguably one of the greatest scientific advances and remains one of the most challenging and complex fields of modern medicine (1). Organ donation can be defined as the removal and transfer of biological tissue or an organ of the human body legally from a living person through consent or from a dead person via ascent from next of kin to a living recipient in need of transplantation (2).

Experts say that the organs from one deceased donor can help up to 50 people. Transplantation of the kidney, liver, pancreas, intestine, heart, and lungs has now become commonplace in all parts of the world. In fact, transplantation is now so widely accepted and successful that the main problem facing the field today is not surgical technique, rejection primarily because of the development of safer and more effective immunosuppressive agents, or management of complications, but rather supply of organs (3-5).

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A live person can donate one kidney, a part of the lung, a part of the liver, blood or bone-marrow which can easily be transplanted. In deceased organ donation (after brain death), more organs such as the heart, pancreas and cornea can be transplanted if the patient is on the ventilator till the organs are extracted. Only healthy individuals can donate organs and the donor must be free of diseases including HIV (6). Live organ donation offers a valuable opportunity for transplantation, but cadaveric organ donation extends the possibility for reducing the gap between patients' needs and the organ supply (United Network for Organ Sharing, 2008). Living organ donation is often described as related or non-related (2). In the early days of transplantation, all donors were genetically related (7).

An enormous difference has been created between organ supply and demand for donor organs because of increase in the incidences of organ failures and lack of supply of organs (5). The waiting list of patients requiring organs is increasing day by day. Shortage of cadaveric organs for transplantation is a global problem. Some studies have suggested that knowledge, attitudes and determinants concerning this issue are influenced by many factors, including gender, educational level, occupation, socio-demographic status, income level, culture and religion. Although people generally express favorable views toward organ donation, very few actually agree to donate before they die or agree to have family members' organs donated upon their deaths. (7-11)

Efforts to increase donation rates have included public awareness and professional education programs, and law that require physicians to request that families donate the organs of deceased or dying relatives. Yet, public health attitudes to cadaveric organ donation and transplantation are a major public health problem and of importance, since prior consent of the donor or of a close relative at the time of death forms the basis for cadaveric organ donation in most developed and developing countries.

A total of 114,690 solid organs were reported to be transplanted in the year 2012 globally. Despite being a 1.8% increase in transplant rate as compared to year 2011, this still only amount to less than 10% of the global organ need (1).

Although there is scarcity of data regarding the statistics in Africa and particularly in Ethiopia. In Ethiopia, live organ donation first began in September 2015 at St. Paul Hospital's Millennium

Medical College (SPHMMC) upon the request of federal democratic Republic of Ethiopia Ministry of Health (FDRE, MOH). Preparations for recovery of organs from deceased donors began in November of 2015. For the past three years, SPHMMC has been the sole health institution providing the care of organ transplantation for patients with end stage kidney disease throughout the country. There is a worldwide shortage of donor organs in comparison to the need for transplantation. There is a significant relation between public attitude towards organ donation (OD) and availability of such organs. Thus, the main concern of most transplant surgeons is to increase the donor pool and spread the willingness of donation among healthy individuals (12).

Today's medical students are doctors of tomorrow and their awareness and attitude towards OD is equally as important. SPHMMC is a pioneer institution when it comes to transplant medicine in our country. Thus, this study aims to assess the knowledge and attitude of its undergraduate medical students towards OD. The findings of this research will shed light on the level of understanding of medical students about such an important aspect of modern medicine. Therefore, it can serve as background information for future studies. The results will be presented and if possible published on scientific journals. Outlining what can be done in relation to improving the service.

PARTICIPANTS AND METHODS

This study was conducted starting from March 20 to May 18, 2018 at St Paul's Hospital Millennium Medical College, Addis Ababa. Ethiopia is located in eastern part of Africa. The land is estimated to be about 1.1 million square kilometers. The country is among the three most populated countries in Africa with total population of 106 million (2017 estimates). Addis Ababa the capital city of Ethiopia has a total population of 3.6 million.

SPHMMC is the second largest public hospital in Ethiopia with the mission to provide preventive, promotional, curative and rehabilitative health care service in the country. The hospital was built in 1969 and since then it has been a source of medical care for the underserved population. The hospital currently has 20 departments, about 389 beds with six beds in the intensive Care Unit (ICU) and 5 in pediatric ICU. The hospital has about 2,508 clinical and non-clinical staff members, 800 medical students and 753 nursing students.

Currently, the hospital is advancing its medical training in undergraduate, post graduate and fellowship programs in addition to expanding medical services with the first center for kidney transplantation and future hematology, cardiology as well as oncology center already under construction. The study was conducted from March 20 to May 18, 2018.

An institution based cross sectional descriptive study was conducted on knowledge and attitude about organ donation among medical students in St. Paul's hospital millennium medical college Addis Ababa, Ethiopia. The source population was all undergraduate medical students currently enrolled in SPHMMC. The study populations were all undergraduate medical students of SPHMMC that full fill inclusion and exclusion criteria. In this study all undergraduate medical students who were learning at the school during time of the study, who are above age of 18 years and are willing to participate in the study were included. Undergraduate medical students who were not available during the period of sample collection; under the age of 18 years and who were not voluntary to participate were excluded from the study. Outcome of interest was Knowledge, attitude about organ donation Independent variables, age, sex, marital status, Religion and educational level.

Stratified random sampling technique was used to stratify medical students according to the year they are currently enrolled in. This was done by classifying the medical students by the year of study as follows. By using the formula, Sample size of the strata = $\frac{\text{Sample size}}{\text{Total population}} \times \text{Number of students in each strata}$. A random sampling technique used within each strata using a selection frame and selecting samples randomly from the frame.

After thoroughly reviewing the relevant literature, a self-administered questionnaire was used for data collection. The questionnaires consisted of a total of

The questionnaire was handed over to the respondents in person and collected by the principal investigator. Ethical clearance was obtained from the institutional review board (IRB) of SPHMMC. Participants in the study were briefed about voluntary nature of the study and confidentiality issues. Informed written consent was obtained and the questionnaire was distributed and collected by the principal investigator. Then the data was checked for completeness and internal consistency. Then it was entered onto SPSS version 20 software package (IBM Corporation, Armonk, NY, USA). Random checking was done to verify the validity of the entered data.

Simple descriptive statistics including frequency and percentage were used to summarize the results, and chi-square and binary logistic regression were done to describe the association between variables. $P < 0.05$ is considered as statistically significant association.

RESULTS

A total of 240 questionnaires were administered and 236 were completed and received, (three of the respondents returned incomplete questionnaire, one was not willing to participate in the study), making the response rate 98.3%. The age of the study participants varied from 18 to 26 with a median age of 22 years. The mean (\pm SD) age was 21.64 (\pm 1.87) years.

The gender distribution consisted of 50.8 % female and 49.2% male. When we come to religion, 57.2% of the respondents were orthodox Christian, Protestant and Muslim constituted for 20.8 % and 16.9%, respectively, and others were 5.1%. Of 236 students that were included in the study, preclinical year students accounted for 83 (35.2%) and clinical year students for 153 (64.8%), of which a majority was

Table 1: Socio-demographic characteristics of the undergraduate medical students 18-26 years of age, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia, May 2018.

Socio-demographic characteristics	Categories	Frequency (N=236)	Percent
Age	18-21	81	34.3
	22-26	155	65.7
Sex	Male	116	49.2
	Female	120	50.8
Religion	Orthodox	135	57.2
	Muslim	40	16.9
	Protestant	49	20.8
Educational level	Others	12	5.1
	1st year (Preclinical-1)	42	17.8
	2nd year (Preclinical-2)	41	17.4
	3rd year (Clinical-1)	34	14.4
	4th year (new clinical 2)	41	17.4
	5th year (old clinical 2)	44	18.6
	Intern	34	14.4

Assessment of knowledge of medical students about organ donation

Among 236 participants, a majority, 209 (88.6%), of the respondents had good knowledge. The mean (\pm SD) knowledge score was 10.67 (\pm 2.35). The minimum score was two and maximum was 16.

When we see the year wise distribution of their knowledge interns had the highest percentage of good knowledge (100%) followed by fourth- and third-year medical students, 95.1% and 91.2%, respectively (Figure 1).

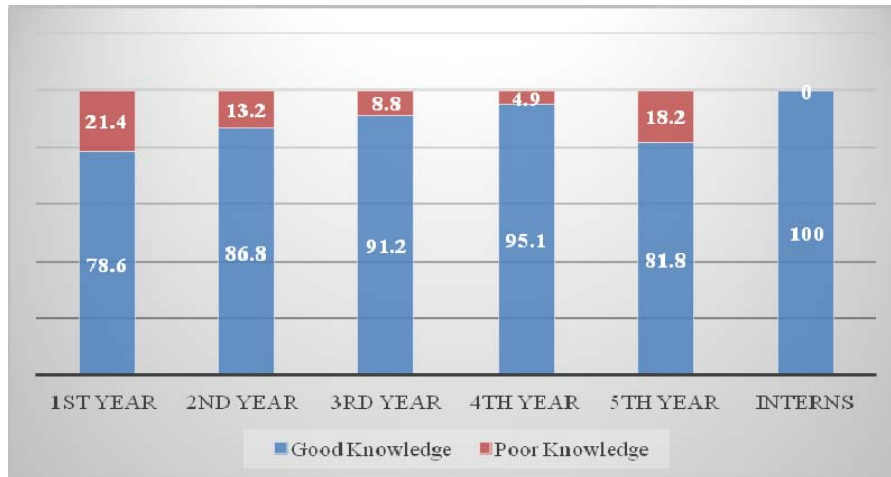


Figure 1: Knowledge among of student about organ donation, St. Paul’s Hospital Millennium Medical College, Addis Ababa, Ethiopia, May 2018

This research revealed that a majority, 232 (98.3%), of the study participants have heard of organ donation. When asked if they were aware that there was a law regarding transplantation of human organs 71.2% answered correctly. Most of the students were aware that brain dead organ donors had to be kept on ventilation support, 202 (85.6%) and, 161 (68.2%) knew brain dead patients can be organ donors.

them knew organ transplant recipients were more prone to developing cancer following transplantation.

A large majority of the participants had knowledge that donor’s and recipient blood group must be matched, 196 (83.1%), but only 102 (43.2%), knew human leukocyte antigen didn’t have to be matched. Nearly three-quarters, 176 (74.6%), of the students knew malignancy wasn’t always a contraindication to cadaveric organ donation, but only, 63 (26.7%), of

Two-thirds, 159 (67.4%), of them knew that hepatitis B patients couldn’t donate their solid organs and a similar percent, 158 (67.3%) knew transplant recipients were at increased risk for opportunistic infections. Knowledge about kidney donation was the highest (97%), followed by cornea (91.1%), liver (86%), heart (83%), lung (53%), skin (48%) and intestine (21%).

The sources of information among students at the College is given in Figure 1 and the knowledge of undergraduate medical students about organ donation is presented in Table 2.

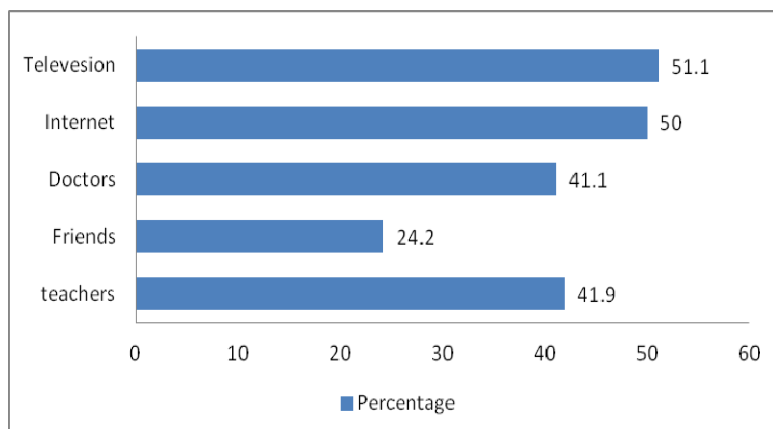


Figure 2: Source of information of medical students, St. Paul’s Hospital Millennium Medical College, Addis Ababa, Ethiopia, May 2018.

Table 2: Knowledge of undergraduate medical students about organ donation, St. Paul Hospital's Millennium Medical College, Addis Ababa, Ethiopia, May 2018.

Variables	Categories	Frequencies (N)	Percentage (%)	
Have you heard of the term "Organ donation"?	Correct	232	98.3	
	Incorrect	4	1.7	
Have you heard of the term "Organ Transplantation?"	Correct	231	97.9	
	Incorrect	5	2.1	
Are you aware of "transplantation of human organ act"?	Correct	168	71.2	
	Incorrect	68	28.8	
Can a brain-dead patient's organs be donated?	Correct	161	68.2	
	Incorrect	75	31.8	
Which one of the following organs can be donated?	Heart	Correct	196	83.1
		Incorrect	40	16.9
	Kidney	Correct	229	97.0
		Incorrect	7	3.0
	Liver	Correct	203	86.0
		Incorrect	33	14.0
	Lung	Correct	126	53.4
		Incorrect	110	46.6
	Intestine	Correct	51	21.6
		Incorrect	185	78.4
	Skin	Correct	114	48.3
		Incorrect	122	51.7
	Cornea	Correct	215	91.1
		Incorrect	21	8.9
Will certified brain-death registered organ donor be immediately disconnected from ventilation support?	Correct	202	85.6	
	Incorrect	34	14.4	
Can parents/guardians make substitute decision making for mentally disable person in regard of organ donation?	Correct	83	35.2	
	Incorrect	153	83	
Donor's and recipient's blood group MUST be matched?	Correct	196	83.1	
	Incorrect	40	16.9	
Donor's human leukocytes antigen MUST be identical to that of the recipient for any organ transplantation?	Correct	102	43.2	
	Incorrect	134	56.8	
People of all ages can be potential donors?	Correct	58	24.6	
	Incorrect	178	75.4	
Hepatitis B and C carriers can donate all of their solid organs except the liver organ?	Correct	158	67.3	
	Incorrect	78	32.7	
Malignancy is always a contraindication of cadaveric organ donation?	Correct	176	74.6	
	Incorrect	60	25.4	
Increased risk of opportunistic infections is a common complication of all transplantation?	Correct	159	67.4	
	Incorrect	77	32.6	
Organ transplant recipients are more prone to developing cancer after transplantation?	Correct	63	26.7	
	Incorrect	173	73.3	

Assessment of attitude among medical students about organ donation: Coming to the attitude section, this study revealed that only, 24 (10.2%), of the participants had positive attitude. Among the participants of the study, 221 (93.6%), said they support organ donation and, 190 (80.5%), believed it adds meaning to one's life. 83.1% of them said they were comfortable thinking or talking about organ donation but only, 34 (14.4%), said their families agree with OD (Table 3).

Only, 91 (38.9%), responded they would agree to donate when they die although only, 6 (2.5%), believed their body should be kept intact after death. More than one-half, 137 (58.1%), believed there will be premature termination of medical treatment for registered organ donors and only, 8 (3.4%), thought cadaveric donation was better than live donation in solving shortage.

Table 3: Attitude of undergraduate medical students about organ donation, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia, May 2018

Variables	Categories	Frequencies (N)	Percentage (%)
Do you support Organ donation?	Positive	221	93.6
	Negative	15	6.4
Do you feel comfortable to think or talk about Organ donation?	Positive	196	83.1
	Negative	40	16.9
Do you agree to donate your organs when you die?	Positive	91	38.9
	Negative	145	61.4
Does your family agree with organ donation?	Positive	34	14.4
	Negative	202	85.6
Do you think donating one's organ adds meaning to one's life?	Positive	190	80.5
	Negative	46	19.5
Do you have belief that your body should be kept intact after death?	Positive	230	97.5
	Negative	6	2.5
Do you believe your religion agrees with organ donation or transplantation?	Positive	80	33.9
	Negative	156	66.1
Do you have fear that your body will be disfigured, if you donate?	Positive	96	40.7
	Negative	140	59.3
Do you think there will be premature termination of medical treatment for registered organ donors?	Positive	99	41.9
	Negative	137	58.1
Do you think live organ donation is better than cadaveric organ donation in solving shortage?	Positive	8	3.4
	Negative	228	96.6

Only 80 (33.9%) believed their religion agreed with organ donation, of which majority were orthodox Christians (57.2%) followed by protestants (20.8%) and Muslims (16.9%).

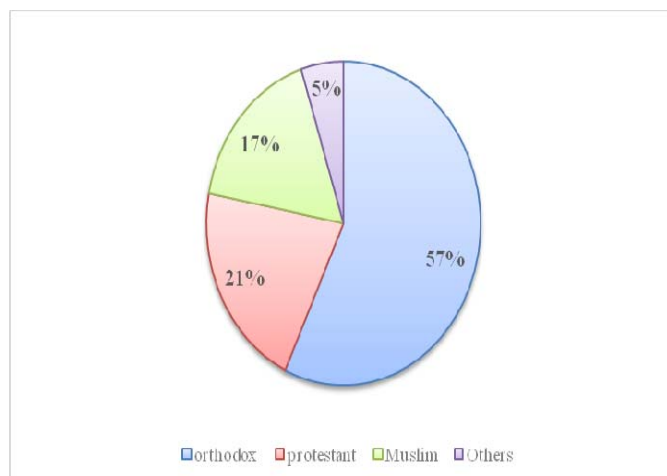


Figure 3: Distribution of students by their beliefs in organ donation and religion, St. Paul Hospital's Millennium Medical College, Addis Ababa, Ethiopia, May 2018.

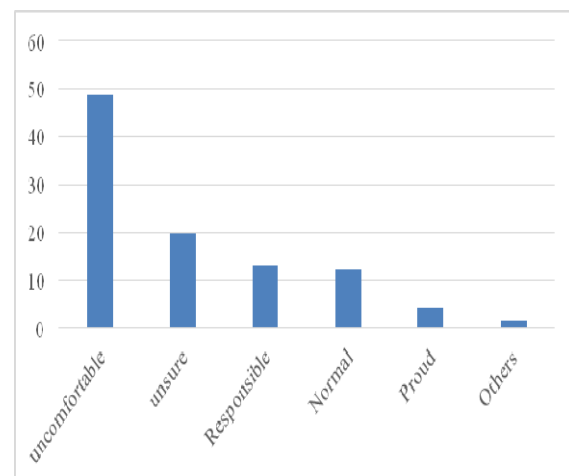


Figure 4: Students' feelings about asking families to donate organs of their deceased relatives, St. Paul Hospital's Millennium Medical College, Addis Ababa, Ethiopia, May 2018.

When the participants of the study were asked how they would feel if they were to ask families to donate organs of their diseased relatives majority answered uncomfortable followed by unsure and responsible.

Association of independent variables with knowledge and attitude: On bivariate analysis using chi-square and binary logistic regression on good knowledge and the independent variables (sex, educational level, source of information and religion), only two the of the independent variables were found to have significant association (Table 4).

Female students were five times more likely to be more knowledgeable than male students ($P=0.001$, $COR=5.383$, $95\%CI$ 1.963-14.758). Those who reported internet as their primary source of information were four times more knowledgeable than those who reported other outlets as their source ($P=0.004$, $COR=4.041$, $95\%CI$ 1.567-10.420). the clinical students were having 4 times better knowledge when adjusted for religion, sex and source of information ($p=0.011$, $AOR=4.09$ and $95\% CI =1.37-12.19$).

Table 4: Multivariable regression analysis of knowledge on independent variables* among undergraduate medical students, St. Paul Hospital's Millennium Medical College, Addis Ababa, Ethiopia, May 2018.

Variable	Category	P value	COR	95% CI	P value	AOR	95% CI
Sex	Male		1			1	
	Female	0.001	5.38	1.96 - 14.75	0.002	4.91	1.77 - 13.62
Internet	Yes	0.004	4.04	1.56 - 10.42	0.009	3.62	1.38 - 9.50
	No		1			1	
Education level	Clinical	0.058	0.458	0.20-1.02	0.011	4.09	1.37-12.19
	Preclinical		1			1	
Religion	Orthodox	0.907	1.136	0.133-9.717	0.454	2.50	0.23-27.43
	Protestant	0.559	.515	0.056-4.760	0.685	0.61	0.06 -6.59
	Muslim	0.347	.355	0.041-3.080	0.955	1.07	0.09 -12.21
	others		1			1	

DISCUSSION

The results of this research reveal that majority of the respondents were knowledgeable (88.6%). which is comparable to a study done on knowledge and willingness to donate among health care workers in south west Nigeria which found that (82.5%) of the respondents had desirable knowledge (13), but it was found to be significantly higher than another African study done in Egypt which found only (36%) of the respondents had good knowledge (12).

This research shows that majority (98.3%) of the study participants have heard of organ donation. which was similar to a study done in Pune, India in 2016 which reported that from a total of 394 medical students' awareness regarding organ donation 98.7-100% (14).

This was also consistent with the result of a study done in Saudi Arabia which reported 90.9% knew what organ donation meant (15). Regarding the presence of a law about transplantation of human organs 71.2% answered correctly.

Which is much higher than the results of a study done in Karnataka , India which stated only 13.9% (6) but in a similar study done in Pune, India knowledge of already existing laws was found to be 57.6% (14). When we compare with an Africa study done in Egypt still the knowledge was much higher than what was found in the Egyptian study which was only 33.3% (12).

Some 68% of the participants knew brain dead patients can be organ donors, which was lower than a report from India (76.3%) who knew brain dead persons can be considered for OD (6).

This could be because of the fact that currently Ethiopia is only practicing live donation even though attempts are being made to start cadaveric donation. Knowledge about kidney donation was the highest (97%) and heart was (83%), finding which concur with the result of a study by Karnataka in India (97.7%) and (89.1%), respectively.

Among the participants in our study, 93.6% said they support organ donation and 80.5% believed it adds meaning to one's life. This is similar to the results of the study done in Kankarta, where a majority of the students (90.4%) supported OD and believed it was a gift to life, but only 38.9% of the respondents in this research said they would agree to donate when they die, a figure lower than 57.3% willingness to donate reported by . Our observation is also lower than a finding from Saudi Arabia (50.9%), who were willing to donate (15-17). In contrast, it was higher than the finding from a study in south-west Nigeria, which reported only 29.5% that were willing to donate when they die (14).

In this research we found that female students were more likely to have good knowledge about the topic and those who reported internet as their source of information had better knowledge scores. Thus, this could lead to the assumption that in order to address these issues the responsible party could use the media and especially the web as a primary outlet.

Only 33.9% of our students believed their religion agreed with organ donation, which contrasts both the Nigerian and Saudi Arabian studies that reported 63.4% and 91.3%, respectively, believed it was allowed in their religion to donate (12-15). This could also be the reason why majority of the respondents did not agree to donate when they die.

Overall only 10.2 % of our study subjects were found to have positive attitude towards OD, which is lower the study done in Nigeria (29.5%) and also from Egypt where 37% of the students had positive attitude (12,13). Despite having desirable or good knowledge the students in our college showed a negative attitude towards OD. This could be due of

Strength and limitation

In the design of the study, we tried to make the sample representative by using probabilistic sampling method. The participants were stratified according to their current year of enrollment and simple random sampling was used within each stratum. The data was collected from the participants directly to minimize data collector bias. That we did not pre-test the study questionnaire in a pilot to examine applicability and level of understanding and acceptance by the students was a limitation in our study.

Conclusion

In conclusion the study participants had good knowledge but the negative attitude towards organ donation. Female gender and having internet as their primary source of information were found to be significantly associated factors with good knowledge. Higher Education level was having better knowledge when adjusted to sex, religion and source of information. The students had a good understanding of facts that pertain to organ donation and transplantation but had a negative attitude towards it. It is crucial that the college and clinical departments that practice transplantation medicine (department of surgery and internal medicine) involve in the theoretical teaching as well as devising a curriculum that allows students to raise and eliminate their perceived barriers to organ donation and transplantation.

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Competing Interest:

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CASE REPORT

A CASE OF BK VIRUS NEPHROPATHY POST RENAL TRANSPLANTATION: A CASE REPORT

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ABSTRACT

BK Nephropathy (BKVN) is a viral nephropathy that can lead to allograft failure. We report a 25 years old kidney transplant recipient who presented with asymptomatic progressive renal allograft dysfunction nine months after renal transplantation. He was worked up as inpatient and allograft biopsy came with a conclusion of viral nephropathy. Further work up for the etiology revealed the viral agent was BK Virus. As renal transplantation is still relatively new to developing countries, this case will highlight clinical feature, diagnosis and treatment options of the condition.

Keywords: BK Virus, Kidney Transplantation, Allograft, Nephropathy, Ethiopia

INTRODUCTION

BK Nephropathy (BKVN) was first described in 1971 in a renal transplant recipient with ureteric stenosis. [1,2,3] It is caused by a DNA virus of the genus polyomavirus and was named after the initials of the first patient in whom the virus was isolated (19). It was not until 20 years later that BK was recognized as a cause of interstitial nephritis and allograft failure in renal transplant recipients (1-3).

BK Virus is a 25 – 45 nm, non-enveloped, double stranded DNA virus from the genus polyomavirus. Seroprevalence ranges 60 – 90 % among adults worldwide. BK Virus is also known for its latency in the genitourinary tract, reactivation during immunosuppression and tropism for the genitourinary tract. It causes a range of clinical syndromes in kidney transplant recipients with higher degree of immunosuppression. The major ones are asymptomatic viruria (with or without viremia), ureteral stenosis and obstruction, interstitial nephritis and allograft BKVN (1-4). The prevalence of BKVN can reach to 10% in transplant recipients.

It can occur as early as the first week and even as late as six years post transplantation (4,6).

BKVN is a cause of allograft dysfunction, not allograft rejection. Identifying one from the other is important as their management is basically opposite. A causal relationship between the two were not identified but their coexistence is well described in the literatures (8,9,12,13). We report a case of BKVN, which was successfully treated with decreasing immunosuppression and Leflunomide.

CASE SUMMARY

A 25 years old man with end stage renal disease of unknown etiology received a live donor kidney transplant after staying two years on regular hemodialysis. His donor was his haplomatch brother. He had a smooth intra and post-operative courses. He underwent his induction immunosuppressive therapy with Basilixmab based regimen and was discharged with prednisolone, mycophenolate mofetil and tacrolimus.

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He was also given miconazole oral gel for fungal prophylaxis, valganciclovir for Cytomegalo Virus (CMV) prophylaxis, trimethoprim-sulfamethoxazole for Pneumocystis pneumonia prophylaxis and isoniazide for tuberculosis prophylaxis dosed as per our transplant center’s protocol.

The first eight months post renal transplant were uneventful. He came with his first abnormal renal function test (serum creatinine – 1.58 mg/dl, Urea – 57 mg/dl) on

December, 2016. He had no symptoms, no abnormal physical findings and no major laboratory additional abnormalities except records of leukopenia ranging from 1500-2900/mm³. His tacrolimus level stayed in target range with in the whole course of follow up.

Further deterioration of renal function required further work up as inpatient. Allograft biopsy revealed viral intra nuclear inclusions in the renal tubular cells with interstitial inflammation. (Figure 1).

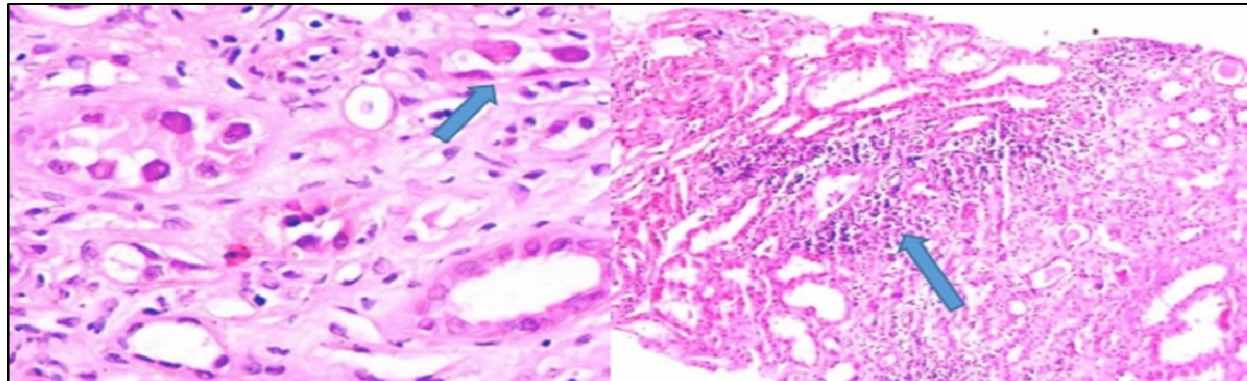


Figure 1A: Basophilic intra nuclear viral inclusions in the renal tubular cells (Arrow).

Figure 1B: Focal Interstitial inflammatory cells (Arrow).

Whole blood CMV PCR was negative. Plasma BK virus -DNA-PCR was 7,930,000 copies per ml. With the diagnosis of BK nephropathy(BKVN),patient underwent a month trial of immunologic Containment by discontinuing mycophenolate moefetil and decreasing the dose of tacrolimus to the minimum effective dosage.

After a month BK viral load decreased from 8 million copies to 2 million Copies but seum creatinine level remained in the range of 2.58 – 2.67 mg/dl. Leflunomide tablet at a dose of 20 mg once per day was added. After eight weeks of treatment with Leflunomide, our patient’s renal function started to recover and viral load declined to 40,000 copies per ml (Table 1).

Table 1: Patient’s progress as outpatient and in-patient

Date	5/9/16	19/9	20/10	19/11	19/12	27/12	2/1/17	26/1	30/1	2/2	9/2	14/2	16/2	21/4	2/6
WBC			5110	5400	3690	2900	BK DNA PCR 7,930,000	00		1500			6860		6330
Hgb			15.5	10.3		12.4	↓	11.7		13.2					
Pit			286	302	306	274	MMF – D/C Tac – ↓	41		241		BK DNA PCR 2,000,000			BK DNA PCR 40,300
Urea	23	22	34			57		0.3	60	47	82	68	58.4	43	44
Cr	1.16	0.97	1.16			1.59	1.81	2.58	2.13	2.59	2.76	2.6	2.67	2.49	2.02
LFT			N			N	Admitted	1qaz						N	N
Tac level								5.72							6.83
Alb									6.0	5.6	5.6				6.0
FBS								104		97	99				96

DISCUSSION

Our case is a twenty-five years old man who underwent live kidney donor renal transplantation. He was doing well for the first eight months after transplantation. On the ninth month, allograft dysfunction which required investigations including biopsy revealed BK Viral Allograft Nephropathy. He was successfully treated with immunologic containment and Leflunomide.

Kidney transplantation is still relatively new to developing countries. Here in Ethiopia, we began to give the service almost three years back. As the service continues to expand, post renal transplantation complications will be much more common. We report this case as its one of the typical complications which can be seen after renal transplantation.

As described in the introduction section of this report, BK Virus can cause a range of clinical syndromes in kidney transplant recipients. The major ones are asymptomatic viruria (with or without viremia), ureteral stenosis and obstruction, interstitial nephritis and BKVN (1,2,4). The prevalence of BKVN reaches 10 % in patients with viruria and graft loss can occur in up to 5% of the cases (2,6). The risk factors identified are degree of immunosuppression, extremes of age, male gender, delayed graft function, treatment for acute rejection, HLA or ABO mismatches, and high BK antibody titer in donor with a negative or low BK virus antibody titer in the recipients (4,6).

The commonest presentation is asymptomatic rise in serum creatinine during the first post-transplant year (2,8). The onset may be as early as a week and as late as six years (5,6). Definitive diagnosis requires allograft biopsy which may show characteristic cytopathic changes and positive immunohistochemistry staining using antibodies directed specifically against BK or the cross-reacting SV40 Large-T antigen. Non-invasive tests like BK virus DNA PCR from plasma and decoy cells from urine cytology serve as supportive evidences (1,9,12).

The main pathologic features of BKVN include BK viral intranuclear basophilic inclusions in the tubular cell nuclei and occasionally in the glomeruli parietal epithelium. Focal and demarcated areas of tubulointerstitial inflammations are also features (1,9). The degree of tubular atrophy and interstitial inflammation correlate with outcome (9).

Although histological findings in BKVN could resemble those of rejection, making the correct diagnosis is critically important as treatments for the two conditions is diametrically opposite. In BKVN, reduction rather than augmentation of the immunosuppressive regimen is warranted (1,2,7,11).

A trial of immunologic containment of BK viral replication is the accepted main stay of initial management to be followed by agents that have anti viral activity such as Leflunomide, cidofovir, Intravenous immunoglobulin (IVIg) or flouroquinolones. [8,13,18] Although head-to-head comparative studies between the management options are lacking, Leflunomide has good treatment outcomes in number of studies (2,9,14).

Preemptive treatment which means treating BK viremic patient with stable allograft function, is also another strategy which has shown clear benefit in number of Studies which were done in centers who do plasma screening for the virus after transplantation (15,16).

In this particular case, high index of suspicion, histopathology and serum viral load have played an important role in the diagnosis. Trial of immunologic containment with reduction of immunosuppressive agents has led to significant reduction in the viral load but rather initiation of leflunomide seems to be one responsible for halting allograft function deterioration.

In general, despite treatment, 30-60% of patients with established BKVN show progressive decline in renal function with graft loss (2,5,7,9). But early diagnosis and intervention was shown to result in better prognosis (15,16). Our case is a good example of this.

Conclusion

This report highlights one of the causes of allograft dysfunction after renal transplantation, which is relatively new modality of treatment in most third world countries. Differentiating BKVN from cellular rejection could be done on that basis of renal biopsy result. Early diagnosis and treatment is essential for better outcome. Preemptive screening with treatment and other cost effective ways of screening are points for further studies.

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Competing Interest:

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

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EMJ EDITORIAL POLICY

Overview

Ethiopia's oldest medical journal, *The Ethiopian Medical Journal (EMJ)* is the official organ of the Ethiopian Medical Association (EMA). The EMJ is devoted to the advancement and dissemination of knowledge pertaining to the broad field of medicine in Ethiopia and other developing countries. The journal first appeared in July 1962 and has been published quarterly (January, April, July, October) without fail since then. It has been published in both online (www.emjema.org) and hard copy (ISSN0014-1755) versions.

The EMJ continues to play an important role in documenting and disseminating the progress of scientific medicine, and in providing evidence base for health policy and clinical practice in Ethiopia and Africa at large.

Our online journal is open access. The hard copies are distributed to members of the Ethiopian Medical Association. Hard copies of the Journal are distributed to institutions and organizations (internal and external) based on subscription.

Reviewing procedure

Peer reviewers

The Ethiopian Medical Journal uses a double-blind review system for all manuscripts. Each manuscript is reviewed by at least two reviewers. The reviewers act independently, and they are not aware of each other's identities. The reviewers are selected solely based on their relevant expertise for evaluating a manuscript. They must not be from the same institution as the author(s) of the manuscript, nor be their co-authors in the recent past. The purpose of peer review is to assist the author in improving papers and the Editorial Board in making decision on whether to accept or reject a manuscript. Reviewers are requested to decline if they have a conflict of interest or if the work does not fall within their expertise.

Peer review process

Manuscripts are sent for review only if they pass the initial evaluation (pre-review by the Editorial Board) regarding their style, methodological accuracy, ethical review documentation and thematic scope. A special care is taken that the initial (pre-review) evaluation is done in 3-5 days.

The Journal policy is to minimize time from submission to publication without reducing peer review quality. Currently the total period from the submission of a manuscript until its publication takes an average of six months. Peer reviewers are requested to respond within four weeks. During the review process, the Editor-in-Chief may require authors to provide additional information (including raw data) if they are necessary for the evaluation of the manuscript. These materials shall be kept confidential and must not be used for any other purposes.

The entire review process takes place under the supervision of the Editor-in-Chief in an online environment, with the assistance of the Journal Secretariat. The online system also allows authors to track the manuscript review progress.

Resolving inconsistencies

In case that the authors have serious and reasonable objections to the reviews, the Editorial Board assesses whether a review is objective and whether it meets academic standards. If there is a doubt about the objectivity or quality of review, the Editor-in-Chief will assign additional reviewer(s).

Additional reviewers may also be assigned when reviewers' decisions (accept or reject) are contrary to each other or otherwise substantially incompatible. The final decision on the acceptance of the manuscript for publication rests solely with the Editor-in-Chief.

Responsibilities

Authors' responsibilities

This is provided in the '*Guidelines to Authors*' which appear in each issue of the Journal. Authors must guarantee that their manuscripts are their original work, that they have not been published before, and are not under consideration for publication elsewhere. Parallel submission of the same paper to another journal constitutes misconduct and eliminates the manuscript from further consideration. Work that has already been published elsewhere cannot be reprinted in the Ethiopian Medical Journal

Authors are exclusively responsible for the contents of their submissions and must make sure that the authors listed in the manuscript include all and only those authors who have significantly contributed to the submitted manuscript. If persons other than authors were involved in important aspects of the research project and the preparation of the manuscript, their contribution should be acknowledged in the Acknowledgments section.

It is the responsibility of the authors to specify the title and code label of the research project within which the work was created, as well as the full title of the funding institution. In case a submitted manuscript has been presented at a conference in the form of an oral presentation (under the same or similar title), detailed information about what was published in proceedings of the conference shall be provided to the Editor-in-Chief upon submission.

Authors are required to properly cite sources that have significantly influenced their research and their manuscript. Parts of the manuscript, including text, equations, pictures, tables and graphs that are taken verbatim from other works must be clearly marked, e.g. by quotation marks accompanied by their location in the original document (page number), or, if more extensive, given in a separate paragraph.

Full references of each quotation (in-text citation) must be listed in the separate reference section in a uniform manner, according to the citation style used by the journal. References section should list only quoted/cited, and not all sources used for the preparation of a manuscript.

When authors discover a significant error or inaccuracy in their own published work, it is their obligation to promptly notify the Editor-in-Chief and cooperate with him/her to retract or correct the paper.

Authors should disclose in their manuscript any financial or other substantive conflict of interest that might have influenced the presented results or their interpretation.

By submitting a manuscript, the authors agree to abide by the Editorial Policies of the Ethiopian Medical Journal

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Editorial responsibilities

The Editor-in-Chief is responsible for deciding which articles submitted to the journal will be published. The decisions are made based exclusively on the manuscript's merit. They must be free from any racial, gender, sexual, religious, ethnic, or political bias. When making decisions the Editor-in-Chief is also guided by the editorial policy and legal provisions relating to defamation, copyright infringement and plagiarism.

Members of the Editorial Board including the Editor-in-Chief must hold no conflict of interest about the articles they consider for publication. Members who feel they might be perceived as being involved in such a conflict do not participate in the decision process for a manuscript.

The information and ideas presented in submitted manuscripts shall be kept confidential.

Editors and the editorial staff shall take all reasonable measures to ensure that the authors/reviewers remain anonymous during and after the evaluation process in accordance with the type of reviewing in use.

The Editorial Board is obliged to assist reviewers with additional information on the manuscript, including the results of checking manuscript for plagiarism.

Reviewers' responsibilities

Reviewers are required to provide the qualified and timely assessment of the scholarly merits of the manuscript. The reviewer takes special care of the real contribution and originality of the manuscript. The review must be fully objective, and the judgment of the reviewers must be clear and substantiated by arguments.

The reviewers assess manuscript for the compliance with the profile of the journal, the relevance of the investigated topic and applied methods, the scientific relevance of information presented in the manuscript, and the pres-

entation style. The review has a standard format. It is submitted through the online journal management system where it is stored permanently.

The reviewer must not be in a conflict of interest with the authors or funders of research. If such a conflict exists, the reviewer is obliged to promptly notify the Editor-in-Chief. The reviewer shall not accept for reviewing papers beyond the field of his/her full competence.

Reviewers should alert the Editor-in-Chief to any well-founded suspicions or the knowledge of possible violations of ethical standards by the authors. Reviewers should recognize relevant published works that have not been considered in the manuscript. They may recommend specific references for citation but shall not require citing papers published in the Ethiopian Medical Journal, or their own papers, unless it is justified.

The reviewers are expected to improve the quality of the manuscript through their suggestions. If they recommend correction of the manuscript prior to publication, they are obliged to specify the way this can be achieved. Any manuscript received for review must be treated as confidential document.

Ethical Considerations

Dealing with unethical behavior

Anyone may inform the Editor-in-Chief at any time of suspected unethical behavior or any type of misconduct by giving the necessary credible information/evidence to start an investigation.

- Editor-in-Chief makes the decision regarding the initiation of an investigation.
- During an investigation, any evidence should be treated as confidential and only made available to those strictly involved in the process.
- The accused will always be given the chance to respond to any charges made against them.

If it is judged at the end of the investigation that misconduct has occurred, then it will be classified as either minor or serious.

Minor misconduct (with no influence on the integrity of the paper and the journal, for example, when it comes to misunderstanding or wrong application of publishing standards) will be dealt with directly with authors and reviewers without involving any other parties. Outcomes include:

- Sending a warning letter to authors and/or reviewers.
- Publishing correction of a paper, e.g. when sources properly quoted in the text are omitted from the reference list.

Publishing an erratum, e.g. if the error was made by editorial staff.

In the case of major misconduct, the Editor-in-Chief may adopt different measures:

- Publication of a formal announcement or editorial describing the misconduct.
- Informing officially the author's/reviewer's affiliating institution.

The formal, announced retraction of publications from the journal in accordance with the Retraction Policy.

- A ban on submissions from an individual for a defined period.

Referring a case to a professional organization or legal authority for further investigation and action.

The above actions may be taken separately or jointly. If necessary, in the process of resolving the case relevant expert organizations, bodies, or individuals may be consulted.

When dealing with unethical behavior, the Editorial Board will rely on the guidelines and recommendations provided by the Committee on Publication Ethics (COPE).

Plagiarism prevention

The Ethiopian Medical Journal does not publish plagiarized papers. The Editorial Board has adopted the stance that plagiarism, where someone assumes another's ideas, words, or other creative expression as one's own, is a clear violation of scientific ethics. Plagiarism may also involve a violation of copyright law, punishable by legal action.

Plagiarism includes the following:

- Self-plagiarism, which is using one's own previous work in another context without citing that it was used previously
- Verbatim (word for word), or almost verbatim copying, or purposely paraphrasing portions of another author's work without clearly indicating the source or marking the copied fragment (for example, using quotation marks) in a way described under Authors' responsibilities;
- Copying equations, figures or tables from someone else's paper without properly citing the source and/or without permission from the original author or the copyright holder.

Any manuscript which shows obvious signs of plagiarism will be automatically rejected. In case plagiarism is discovered in a paper that has already been published by the journal, it will be retracted in accordance with the procedure described under Retraction policy, including blacklisting the author(s).

To prevent plagiarism, the manuscripts are submitted to a plagiarism detection process. The results obtained are verified by the Editorial Board in accordance with the guidelines and recommendations of the Committee on Publication Ethics (COPE).

Retraction policy

Legal limitations of the publisher, copyright holder or author(s), infringements of professional ethical codes, such as multiple submissions, bogus claims of authorship, plagiarism, fraudulent use of data or any major misconduct require retraction of an article.

Occasionally, a retraction can be used to correct numerous serious errors, which cannot be covered by publishing corrections. A retraction may be published by the Editor-in-Chief, the author(s), or both parties consensually.

The retraction takes the form of a separate item listed in the contents and labeled as "Retraction".

The original article is retained unchanged, except for a watermark on the PDF indicating on each page that it is "retracted".

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Self-archiving policy

Authors are permitted to deposit publisher's version (PDF) of their work in an institutional repository, subject-based repository, author's personal website (including social networking sites, such departmental websites at any time after publication.

Full bibliographic information (authors, article title, journal title, volume, issue, pages) about the original publication must be provided and links must be made to the article's DOI and the license.

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GUIDELINES FOR AUTHORS

The *Ethiopian Medical Journal (EMJ)* is the official Journal of the Ethiopian Medical Association (EMA) devoted to the advancement and dissemination of knowledge pertaining to the broad field of medicine in Ethiopia and other developing countries. Prospective contributors to the Journal should take note of the instructions of Manuscript preparation and submission to EMJ as outlined below.

Article types acceptable by EMJ

Original Articles (*vide infra*) on experimental and observational studies with clinical relevance
 Brief Communications
 Case Series
 Case Reports
 Editorials, Review or Teaching Articles: by invitation of the Editorial Board.
 Correspondences/Letters to the Editor
 Monographs or set of articles on specific themes appearing in a Special Issues of the Journal
 Book reviews
 Perspectives,
 Viewpoints
 Hypothesis or discussion of an issue important to medical practice
 Letter to the Editor
 Commentaries
 Advertisements
 Obituaries

N.B. Articles are not acceptable if previously published or submitted elsewhere in print or electronic format, except in the form of abstracts in proceedings of conferences.

Content and format of articles:

Title: The title should be on a separate page. It should not have acronyms or abbreviations. The title should be descriptive and should not exceed 20 words or 120 characters including space. The title page should include the name(s) and qualification of the author(s); the department or Institution to which the study/research is attributed and address of the corresponding Author. If the author has multiple affiliations only use the most preferred one.

1. Original Articles

2,500 words, excluding Abstracts, References, Figures and Tables. The manuscript of the Article, should appear under the following headings:

a) **Abstract:** The abstract of the Article is prepared on a separate paper, a maximum of 250 words; it should be structured under the titles: a) Background; b) Methods; c) Results; d) Conclusions. Briefly summarize the essential features of the article under above headings, respectively. Mention the problem being addressed in the study; how the study was conducted; the results and what the author(s) concluded from the results. Statistical method used can appear under Methods paragraph of the Abstract, but do not insert abbreviations or references in the Abstract section.

Keywords: Provide three to six key words, or short phrases at the end of abstract page. Use terms from medical subject heading of Index Medicus to assist in cross indexing the Article.

b) **Introduction :** Should provide a short background and context of the study and provide the rationale for doing the study. It should not be a detailed review of the subject and should not include conclusions from the paper.

- c) **Patients or (Materials) and Methods:** should contain details to enable reproducibility of the study by others. This section must include a clear statement specifying that a free and informed consent of the subjects or their legal guardians was obtained. Corresponding author should submit a copy of institution review Board (IRB) clearance or letter of permission from the hospital or department (if IRB exempt) with the manuscript. For manuscripts on clinical trials, a copy of ethical approval letter from the concerned body should be submitted with the Manuscript. If confidential data is being used for publication (such as student grades, medical board data, or federal ethics board data), then appropriate support/agreement letter should be included. Photos of patients should disguise the identity or must have obtained their written consent. Reference number for ethical approval given by ethics committee should be stated. In general, the section should include only information that was available at the time the plan or protocol for the study was being written; all information obtained during the study belongs in the Results section.
- d) **Results:** This section should present the experimental or observational data in text, tables or figures. The data in Tables and Figures should not be described extensively in the text.
- e) **Discussion:** The first paragraph should provide a summary of key finding that will then be discussed one by one in the paragraphs to follow. The discussion should focus on the interpretation and significance of the results of the study with comments that compare and describe their relation to the work of others (with references) to the topic. Do not repeat information of Results in this section. Make sure the limitations of the study are clearly stated.
- f) **Tables and Figures:** These should not be more than six. Tables should be typed in triplicate on separate sheets and given serial Arabic numbers. Titles should be clearly place underneath Tables and above Figures. Unnecessary and lengthy tables and figures are discouraged. Same results should not be presented in more than one form (choose either figure or table). Units should appear in parentheses in captions but not in the body of the table. Statistical procedures, if not in common use, should be detailed in the METHODS section or supported by references. Legends for figures should be typed on separate sheets, not stapled to the figures. Three dimensional histograms are discouraged. Recognizable photographs of patients should be disguised. Authors should submit editable soft versions of the tables and figures.
- g) **Acknowledgement:** Appropriate recognition of contributors to the research, not included under Authors should be mentioned here; also add a note about source of the financial support or research funding, when applicable.
- h) **References:**
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 - References should be numbered consecutively in the order in which they are first mentioned in the text and identify references in text, tables, and legends by Arabic numerals in parentheses.
 - Type the References on a separate sheet, double spaced and keyed to the text.
 - Personal communications should be placed NOT in the list of references but in the text in parentheses, giving name, date and place where the information was gathered or the work carried out (e.g. personal communication, Alasebu Berhanu, MD, 1984, Gondar College of Medical Sciences). Unpublished data should also be referred to in the text.
 - References with six or less authors should all be listed. If more than six names, list the first three, followed by et al.
 - Listing of a reference to a journal should be according to the guidelines of the International Committee of Medical Journal Editors ("Vancouver Style") and should include authors' name(s) and initial(s) separated by commas, full title of the article, correctly abbreviated name of the journal, year, volume number and first and last page numbers.
 - Reference to a book should contain author's or authors' name(s) and initials, title of chapter, names of editors, title or book, city and name of publisher, year, first and last page numbers.

The following examples demonstrate the acceptable reference styles.

Articles:

- Gilbert C, Foster A. Childhood blindness in the context of Vision 2020: the right to sight. *Bull World Health Org* 2001;79:227-32
- Teklu B. Disease patterns amongst civil servants in Addis Ababa: an analysis of outpatient visits to a Bank employee's clinic. *Ethiop Med J* 1980;18:1-6
- Tsega E, Mengesha B, Nordenfelt E, Hansen B-G; Lindberg J. Serological survey of human immunodeficiency virus infection in Ethiopia. *Ethiop Med J* 1988; 26(4): 179-84
- Laird M, Deen M, Brooks S, et al. Telemedicine diagnosis of diabetic retinopathy and glaucoma by direct ophthalmoscopy (Abstract). *Invest Ophthalmol Vis Sci* 1996; 37:104-5

Books and chapters from books:

- Henderson JW. Orbital Tumors, 3rd ed. Raven Press New York, 1994. Pp 125-136.
- Clipard JP. Dry Eye disorders. In Albert DM, Jakobiec FA (Eds). Principles and Practice of Ophthalmology. W.B Saunders: Philadelphia, PA 1994 pp257-76.

Website:

- David K Lynch; laser History: Masers and lasers.
<http://home.achilles.net/jtalbot/history/massers.htm> Accessed 19/04/2001

2. Brief Communication

Short versions of Research and Applications articles, often describing focused approaches to solve a health problem, or preliminary evaluation of a novel system or methodology

- Word count: up to 2000 words
- Abstract up to 200 words; excluding: Abstract, Title, Tables/Figures and References
- Tables and Figures up to 5
- References (vide supra – Original Article)

3. Case Series

Minimum of three and maximum of 20 cases

- Up to 1,000 words; excluding: Abstract, Title, Tables/Figures and References
- Abstract of up to 200 words; structured; (vide supra)
- Statistical statements here are expressed as 5/8 (62.5%)
- Tables and Figures: no more than three
- References: maximum of 20

4. Case Report

Report on a rare case or uncommon manifestation of a disease of academic or practical significance

- Up to 750 words; excluding: Abstract, Title, Tables/Figures and References
- Abstract of up to 100 words; unstructured;
- Tables and Figures: no more than three
- References: maximum of 10

5. Systematic review

Review of the literature on topics of broad scientific interest and relevant to EMJ readers

- Abstract structured with headings as for an Original Article (vide supra)
- Text should follow the same format as what is required of an Original Article
- Word count: up to 8,000 words, excluding abstract, tables/Figures and references
- Structured abstract up to 250 words
- Tables and Figures up to 8

6. Teaching Article

A comprehensive treatise of a specific topic/subject, considered as relevant to clinical medicine and public health targeting EMJ readers

- By invitation of the Editorial Board; but an outline of proposal can be submitted
- Word limit of 8,000; excluding abstract, tables/Figures and references
- Unstructured Abstract up to 250 words

7. Editorial

- By invitation of the Editorial Board, but an editorial topic can be proposed and submitted
- Word limit of 1,000 words: excluding references and title; no Abstract
- References up to 15.

8. Perspectives

- By invitation of the Editorial board, but a topic can be proposed and submitted
- Word limit of 1,500
- References up to six

9. Obituaries

- By invitation of the Editorial board, but readers are welcome to suggest individuals (members of the EMA) to be featured.

Preparation of manuscripts

- Manuscripts must be prepared in English, the official language of the Journal.
- On a single separate sheet, there must be the title of the paper, with key words for indexing if required, and each author's full name and professional degrees, department where work was done, present address of any author if different from that where work was done, the name and full mailing address of the corresponding author, including email, and word count of the manuscript (excluding title page, abstract, references, figures and tables). Each table/figures/boxes or other illustrations, complete with title and footnotes, should be on a separate page.
- All pages should be numbered consecutively in the following order: Title page; Abstract and key-words page; main manuscript text pages; References pages; acknowledgment page; Figure-legends and Tables
- The Metric system of weights and measures must be used; temperature is indicated in degrees Centigrade.
- Generic names should be used for drugs, followed by propriety brand name; the manufacturer name in parenthesis, e.g. diazepam (Valium, Roche UK)
- Statistical estimates e.g. mean, median proportions and percentages should be given to one decimal place; standard deviations, odds ratios or relative risks and confidence intervals to two decimal places.
- Acronyms/Abbreviations should be used sparingly and must be given in full, at first mention in the text and at the head of Tables/foot of Figure, if used in tables/figures.eg. Blood Urea Nitrogen (BUN). Interstitial lung disease (ILD).
- Use the binomial nomenclature, reference to a bacterium must be given in full and underlined - underlining in typescript becomes italics in print (e.g. *Hemophilus influenzae*), and later reference may show a capitalised initial for the genus (e.g. *H. influenzae*)
- In the text of an article, the first reference to any medical phrase must be given in full, with the initials following in parentheses, e.g., blood urea nitrogen (BUN); in later references, the initials may be used.
- Manuscripts for submission should be prepared in Microsoft Word document file format

Submission of manuscripts

- As part of the submission process, authors are required to check off their submission's compliance with journals requirements

- All manuscripts must be submitted to the Editor-in-Chief of the Journal with a statement signed by each author that the paper has not been published elsewhere in whole or in part and is not submitted elsewhere while offered to the *Ethiopian Medical Journal*. This does not refer to abstracts of oral communications at conferences/symposia or other proceedings.
- It is the author's responsibility to proof-read the typescript or off-print before submitting or re-submitting it to the Journal, and to ensure that the spelling and numerals in the text and tables are accurate.
- Authors should submit their work through the Ethiopian Medical Journal website; ema.emj@telecom.net.et.

Conflict of interest

Authors should disclose at the time of submission of manuscripts any conflict of interest, which refers to situations in which financial or other personal considerations may compromise, or have the appearance of compromising their professional judgment in conducting or reporting the research results. They should declare that there is no conflict of interest to declare if there is none,

Manuscripts review procedures

The procedures for manuscripts review include:

- Within one week of receipt of a manuscript, the Editorial Board will review it in reference to (i) conformity with the Journal's "guidelines to authors (revised version available in all issues starting January 2020)", (ii) relevance of the article to the objectives of the *EMJ*, (iii) clarity of presentation, and (iv) plagiarism by using appropriate software
- The Editorial Board has three options: accept manuscripts for external review, return it to author for revision, or reject it. A manuscript not accepted by a board member is blindly reviewed by another board member. If not accepted by both, the manuscript is rejected by the Editorial Board. Decision will be made by the suggestion of a third Editorial Board member if the decisions of first two do not concur.
- Once accepted for external review, the Editorial Board identifies one (for brief communication, case reports, and teaching articles) or two (for original articles) reviewers with appropriate expertise. The reviewers will be asked to review and return manuscripts with their comments online within two weeks of their receipt. Reviewers have four options; accept, accept with major revision, accept with minor revision, or reject.
- A Manuscript accepted subject revision as suggested by reviewers will be returned to the corresponding author. Author(s) will be given four weeks to respond to reviewers' comments, make necessary changes, and return the manuscript to the Editorial Board. A Manuscript not returned within the specified time will be considered withdrawn by the author(s).
- Manuscripts with minor revisions will be cleared by the Editorial Board and accepted for publication. Those with major revisions will be returned to external reviewers and follow the procedures as outlined for the initial review.

General information

The Editorial Board reserves the right for final acceptance, rejection or editorial correction of papers submitted. However, authors are encouraged to write an appeal to the Editor-in-Chief for reconsideration of rejected manuscripts or any other complaints they might have.

Accepted papers are subject to Editorial revision as required and become the copy-right of the EMA. Twenty-five reprints of published articles are supplied free to the first/corresponding author.

The Editorial Board welcomes comments on the guidelines from Journal readers.

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Acknowledgment

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THE ETHIOPIAN MEDICAL JOURNAL

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