Volume of Organ Failure in Syria and Obstacles to Initiate a National Cadaver Donation Program

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INTRODUCTION

The incidence of end-stage renal disease (ESRD) in developing countries is 48 pmp to 240 pmp, compared with 76 pmp to 268 pmp in the developed regions of North America, Europe, and the Asia-Pacific region.[1-3] In developing countries, ESRD seems to be at least as common, if not more common, as that in developed countries.[4] The figures given probably underestimate the true incidence, because most of the people live in rural areas where there is limited access to healthcare facilities and patients do not have access to dialysis facilities in urban areas.[5] In the absence of an established kidney transplant program, it is not viable economically to maintain large numbers of patients on a maintenance hemodialysis program in a developing country.[4] Kidney transplantation is the only viable option for most patients with irreversible kidney failure in the developing countries, because it is the most cost-effective form of renal replacement therapy, with the best promise of improved quality of life and an excellent chance of rehabilitation making a successful kidney transplant a greater necessity than elsewhere. There is a worldwide shortage of organs and the gap between supply and demand growths inexorably. Lack of resources, cultural factors, and ignorance all contribute to the ongoing shortage of organs.[6]

VOLUME OF ORGAN FAILURE IN SYRIA

In the absence of formal registry data, it is difficult to establish with certainty the prevalence and incidence of organ failure.[5,7] However, we have tried in the current study to address this point by collecting data from healthcare authorities and different medical institutions who are involved in caring of organ failure patients. Yet, kidney and cornea are the only 2 organs or tissue that could be transplanted in Syria. In the past, heart transplantation has been performed for few patients, and then, it was stopped. Whereas liver, other organs including the pancreas, lung, bone marrow, and intestine have never been transplanted in our country. However, bone marrow transplantation program might hopefully start in few months. The only 3 organs or tissues that we were able in this

study to collect sufficient data on their failure status are essentially the kidney followed by the liver and cornea.

Corneal Blindness

Of all the transplant surgery done today, corneal transplants are by far the most common and successful. According to the World Health Organization statistics, the estimated total number of patients suffering from severe poor vision or blindness in Syria is 125 000, which makes the estimated prevalence of blindness of 0.7%, 37% of which are diseased corneas as a cause of blindness.[8] Therefore, 46 250 patients have corneal blindness and the estimated prevalence of corneal blindness in Syria is 2.3 per 1000 people.

Eye Surgical Hospital in Damascus is the biggest ophthalmology center in Syria where the Eye Bank is located and 8032 patients with corneal blindness had been registered till April 2006 on waiting list, out of whom 2496 have unilateral diseased cornea and 5536 have bilateral diseased cornea; therefore, 13 568 eyes needed cornea transplantation. Of these, 1494 cornea transplant operations were performed at the Eye Surgical Hospital using donated cornea, and the remaining 4042 patients are still registered and waiting for a cornea, but unfortunately, for the past 2 years, the Eye Surgical Hospital did not receive any donated cornea; therefore, cornea transplantation is withheld in this center. Nevertheless, some private centers are still performing cornea transplants in a very occasional manner by using "purchased" corneas, while the vast majority of patients are still waiting for sight to be restored.

Liver Failure

Since national registry is lacking, the prevalence and incidence of chronic liver failure in Syria are unknown. As we all know, hepatitis virus-related liver disease in adults is the leading cause of liver failure (viral cirrhosis). Therefore, if we knew the estimated prevalence of both hepatitis B and hepatitis C in the country and the long-term clinical course and outcome of hepatitis B virus (HBV) and hepatitis C virus (HCV) carriers, we could make an estimation of the prevalence of viral cirrhosis.

In 2005, the Blood Transfusion Center of Damascus University has published its registered data of the prevalence of HBV and HCV among blood donors[9]; we have reviewed these data in details and thought they can be very representative of the Syrian population HBV and HCV carrier status as a whole. Though, in the current study, we have estimated the national carrier status of HBV and HCV by using the Blood Transfusion Center of Damascus University's figures as a good sample reflecting the real national HBV and HCV carrier status.

Hepatitis B virus-related liver disease. The estimated total number of HBV Syrian carriers is 540 000 patients which makes the estimated prevalence of HBV carriers of 2.7%. If we know already that 4% of those carriers have the risk of developing liver failure within 15 to 25 years,[10,11] then we have estimated that we would have around 865 new HBV-induced liver failure patients every year.

Hepatitis C virus-related liver disease. The estimated total number of Syrian HCV carriers is around 200 000 patients which makes the estimated prevalence of HCV carriers of 1%. Taking into account that 5% to 20% of those carriers have the possibility to develop chronic liver disease, and subsequently, 30% of those who have already HCV-induced chronic liver disease will ultimately reach the end-stage HCV-related liver disease within 15 to 25 years,[12,13] we could calculate the estimated number of new patients with HCV-induced liver failure to be between 118 and 482 every year.

We combined the estimated incidence of both HBV and HCV in 1 figure, and realized that there would be between 983 and 1347 new patients with HBV- or HCV-induced end-stage liver disease on a yearly basis; therefore, the estimated incidence of viral cirrhosis is 49 pmp to 67 pmp. Once more, it is worthwhile to mention that this figure does not include the other known causes of liver failure, and therefore, the true incidence of the end-stage liver disease in Syria would be definitely higher than the above mentioned figure.

Kidney Failure

The incidence of ESRD is estimated at anywhere from 100 pmp to 200 pmp per year. In 1997, the incidence of ESRD in Syria was estimated to be 75 pmp[14]; however, once more, as a national registry is lacking, we do not know the true incidence of ESRD, and we strongly believe that this figure probably underestimates the true incidence because most of the people live in rural areas where there is limited access to healthcare and patients do not

reach urban dialysis facilities. We estimated the incidence of ESRD in Syria to be 100 pmp, which means that every year, 2000 new cases with ESRD are registered in our country. This incidence is closer to what it has been reported in the neighboring countries; for example, 200 pmp in Egypt, and 120 pmp in Jordan.[15,16] The last available report of renal replacement therapy in Syria which was issued in May 2005 by the statistical department of the ministry of health has shown that there were 2750 patients on hemodialysis program and 111 patients were on continuous ambulatory peritoneal dialysis (CAPD); therefore, the total number of patients with ESRD undergoing either hemodialysis or CAPD was 2861. Regarding the Syrian population of about 20 million, we estimated the prevalence of patients with ESRD who receive renal replacement therapy in May 2005 to be 143 pmp. The 2750 patients hemodialysis were undergoing their dialysis sessions in 4 different health sectors as follows: 1448 patients in the Ministry of Health (MOH)-affiliated centers, 615 patients in 3 university hospitals, 490 patients in private centers, and 197 patients in military hospitals. We reviewed the number of patients who were undergoing their hemodialysis sessions in MOH centers for the past 3 years, and we pointed out that this number was not increasing as we might expect, but rather has sharply decreased in the year 2004, when there were 1371 patients compared to 1741 patients on hemodialysis in 2003, and then, it slightly increased to 1448 patients in 2005. These figures do not accurately reflect the whole picture of renal replacement therapy and ESRD incidence in our country, because they only speak of the MOH sector which provides healthcare for more than 50% of patients on hemodialysis, and more importantly, because there are other factors than the incidence of ESRD which have also their influences on the number of patients receiving dialysis at any given place or time. Some of these factors are the acceptance rate of renal replacement therapy, problems related to access of patients to long-term dialysis (particularly for those who come from rural areas which essentially precludes their inclusion in long-term dialysis programs),[4,5] technical and economical problems which are expected to be more and more deepened in the absence of an established kidney transplant program precluding the possibility to maintain large numbers of patients on a maintenance hemodialysis program in a developing country,[4] survival of the patients on maintenance dialysis, and the number of patients who receive transplantation.

We reviewed the reported mortality of patients receiving hemodialysis in several dialysis units in our country for the past 3 years, and we estimated the annual mortality rate of the patients on hemodialysis to be 15% (9% to 31%). The long-term outcome of maintenance dialysis as the treatment modality of choice has also been assessed in the current study and showed that the 3-year survival rate of these patients in Syria is 26% to 64%. This rate is far from being satisfactory although it is not that different from what it has been reported elsewhere in other developing countries; for instance, it was ranging from 25% to 52% at 5 years in Egypt, South Africa, and Taiwan.[15,17-18] In the developed countries, 56% to 60% of patients with ESRD receive dialysis, and in some countries the figure is higher.[19,20] Unfortunately, we do not have data on the percentage of patients with ESRD who receive dialysis in Syria although we know that the acceptance rate for renal replacement therapy is less than what it has been reported in the developed world where it ranged from 61% to 99%.[21]

Peritoneal dialysis is grossly underused in Syria; in 2005, less than 4% of patients on dialysis were receiving CAPD. This underuse of CAPD in Syria, as in some other parts of the world,[5,22] is partly due to physician bias. Other reasons in our country are as follows: lack of knowledge of patients and their subsequent less complaint, lack of skilled personnel which results in high rate of infection,[23] recurrent peritonitis, and other technical problems.

KIDNEY TRANSPLANTATION IN SYRIA

The number of kidney transplants performed pmp correlates with the socioeconomic status of a country.[24] In 2006, a total of 339 patients received a kidney transplant in Syria which made the number of kidney transplants to be slightly above 17 pmp per year. This figure is quiet better than those of most developing countries in which it ranges from 1 pmp to 5 pmp with an average of 2 pmp in the Middle East and the Afro-Arab region[25]; however, it is still far from being satisfactory because, as we have mentioned above, the estimated incidence of ESRD in our country is 100 pmp. Therefore, the remaining 83 pmp, which are equivalent to 1660

new patients with ESRD who did not receive a transplant, will be on a yearly basis either added to those who are on dialysis programs with a projected 3-year survival from 26% to 64%, or remained without dialysis, with all what it means in terms of mortality rate either due to the lack of access to dialysis or to a nonacceptance of dialysis by the patients themselves.

In perspective, if we are targeting to perform kidney transplantation for 75% of our new patients with ESRD which are equivalent to 75 pmp per year (since the remaining 25% might not be good candidates for transplantation due to a different setting of reasons including the medical contraindications), this optimal rate of transplantation is quiet higher than what is being done in reality (17 pmp per year). Therefore, we could figure out that in 2006, only 23% of the estimated optimal need for kidney transplantation is met in our country. Now, according to what is going on in the developed countries, we realize that most (> 90%) of all kidney transplants performed around the world are in the developed countries, in which they perform an average 20 to 40 transplants pmp per year.[26] An exemplary experience is that of Cyprus with an ESRD incidence of 80 pmp and a transplantation rate of 60 pmp, one-third of which being from cadaveric donors.[27] These results enable us to conclude that there is a marked discrepancy between the number of patients with ESRD and the number of patients who received a kidney transplant in Syria. Such a discrepancy might keep growing if no proper actions are going to be taken in the near future in order to reverse the curve and to narrow the gap between the supply and demand of kidneys in our country.

Obstacles to Initiate a National Cadaver Donation Program

Proponents of kidney transplantation argue that transplantation should be encouraged because it is the most cost-effective form of renal replacement therapy, with the best promise of improved quality of life and an excellent chance of rehabilitation. A national cadaveric donation program is a viable option to address the widening gap between organ request and availability; for instance, the increasing request for kidneys is not only due to the increased number of patients with ESRD awaited for kidney transplantation, but also to the fact that patients who previously would not have been considered for transplantation (eg, diabetics, the elderly, and children) are now on waiting lists.

Kidney transplantation in Syria, as in many other developing countries, is marked by its exclusive reliance on living donor transplantation. The use of cadaveric and or unrelated donors has been suggested as one possible solution to ameliorate the situation.[28] In November 2003, the "law number 30" has been enacted and constituted a landmark in the history of organ donation and transplantation in Syria as it recognized for the first time in our country of the concept of brain death and allowed the use of organs from cadaveric donors and also from living donors (either related or unrelated). Since the commencement of organ transplantation in Syria in the 1980s, transplantation activities have been exclusively relied on living related donors. This very important law has been preceded by another big stride in this regard which was the acceptance of the higher Islamic religious authorities in the country back in September 2001 on the principle of procurement of organs from cadaver providing consent to be given by one of his or her first-degree or second-degree relatives. Such a progress could only be achieved after several meetings which gathered religious authorities, legislators, lawyers, healthcare professionals, patients, and lay public. In November 2004, the ministry of health has issued guidelines which regulate almost all legal and medical aspects of organ donation and transplantation in Syria, including the definition of death and brain death criteria, informed consent for cadaveric organ donation, banding commercialism, defining who is a donor, and describing how to evaluate a potential donor of the kidney, liver, heart, lungs, intestine, or cornea.

Undoubtfully, some of the major obstacles to initiate a national cadaveric donation program in our country has been overcomed by the official recognition of brain death concept and by authorizing cadaveric organ donation as stated in the law number 30, and also by the support of most religious commentators, Islamic or Christian. It is worthy to say that Saudi Arabia is an excellent example of a conservative Muslim country that has implemented a cadaveric donor program successfully and made major strides in developing a cadaveric donor program through public education, excellent coordinators, and the efforts of its procurement

The Sequence of Events Preceding Cadaveric Donor Transplantation

1. Identification of potential donor
2. Notification of organ procurement organization
3. Diagnosis of brain death made by attending physicians; family informed
4. Suitability of donor ascertained
5. Permission for organ donation obtained from family
6. Tissue typing and ABO blood typing of donor
7. Kidneys removed and stored
8. Local and national computer listing of all potential recipients reviewed
9. Top recipient selected by ABO blood type and a national network scoring system
10. Transplantation program for recipients of marginal kidneys
11. Top recipient patient notified and admitted to hospital
12. "Backup" recipient prepared when recipient's panel reactive antigens are high
13. Donor lymphocytes and recipient serum cross-matched
14. Preoperative history and physical examination
15. Preoperative chest radiography, electrocardiography, ABO blood typing, and routine chemistry
16. Dialysis performed if necessary
17. Transplantation performed

agency, the Saudi Center for Organ Transplantation.[29] The sequence of events preceding cadaveric donor transplantation is displayed in the Table.

Even though, we are still lacking a cadaveric donation program despite all achievements, because there are still many other obstacles that have to be properly addressed. As a result, the practice of living unrelated donors has flourished, and consequently, an increasing number of kidney transplants from living unrelated donor was at the expense of decreasing living related donors in a very clear manner. Though, the practice of living unrelated donor transplantation has been marked in our country to have a negative impact on the potential of living related donors. Furthermore, it also might have a negative impact on the development of local cadaveric donation program in the future.[30] Although this source had fallen into disrepute because of exploitation by a few, it remains an important potential source of organs, and nowadays, very few patients with ESRD are going abroad to obtain kidneys from living unrelated donor in the neighboring countries. This is unlike what was happening before the enactment of the law number 30 where receiving transplant abroad from an unrelated donor was the unavoidable solution for those who could afford it and did not find a suitable living related donor inside the country.

Ignorance appears to be the major limiting factor inhibiting the institution and growth of cadaveric organ donation program in Syria as in many other developing countries.[31] That is the reason why we absolutely need a concerted and ongoing education campaign by the transplant community of both the healthcare professionals and the public to increase their awareness of the need for organ donation so as to change negative public attitudes that hinder discussion of this subject by family members and to gain societal acceptance. The success of this program definitely requires a high degree of public trust and acceptance.

The attitude of indifferent of health care professionals has also been identified as a major limiting factor to the initiation of cadaveric organ donation program, exactly as it has been pointed out in other developing countries,[6,31] and changing such indifferent attitudes should be given priority.

Establishment of a coordinating center for organ donation and transplantation requires appropriate legislation and financial support by the government. Such a center is fundamental for the success of cadaveric donation program as it supervises and coordinates the whole process of organ donation between the donating hospital and the transplant center, in addition to so many other functions like applying strategies to increase the awareness of the medical community and public at large to the importance of organ donation, and particularly, emphasizing ethics as the center is a nonprofit governmental agency. Later on, once this center is being well established, a network of regional *organ procurement organizations* has to be created, and ideally, it is supported financially by the national healthcare administration and health insurers.

Lack of trained transplant coordinators is one of

most important issues that have to be addressed before the initiation of cadaveric donation program in our country. Transplant coordination is still in its infancy in Syria. With an understanding of local social and cultural beliefs and sensitivity to the need and concerns of families, transplant coordinators could form a vital link between the community and the transplant team.[32] With the growth of cadaveric donor programs, the transplant coordinator will play a growing role in the identification and care of potential donors and their families. The transplant coordinator could increase the supply of organs by organizing and facilitating the logistics of organ procurement. Though, the program should not rely only on the enthusiasm of the transplant team who receive no additional remuneration for the extra work performed.

Adequate resources in term of finance personnel and services are crucial, because cadaveric donor programs tend to be more expensive than living donor transplants and are constrained in countries where health resources are stretched to the limit.[24] The costs have significant implications on the future of kidney transplantation in developing countries. Several reports have confirmed that transplantation is less expensive than dialysis in developing countries.[5,6,15,33] This issue has to be very clearly pointed out to all healthcare administrators and health insurers in order to get their support of our "overall less-costly" cadaveric donation program.

Access to intensive care facilities is required to allow the ventilation of donors; therefore, the shortage of intensive care beds can be a major limitation.[6,32] More ICU beds are absolutely needed before a cadaveric donation program could start. Moreover, the education and training of key personnel in the intensive care units is of equal if not more importance than increasing ICU beds, because they are the ones who will identify potential donors, and then, they will ascertain of the ICU standard care around the clock in order to improve the quality of recovered organs.

A reliable comprehensive tissue center where we can do human leukocyte antigen-typing, all methods of cross-matching tests, and panel reactive antibodies with a 24-hour service is of crucial importance, because such a national program cannot rely on private laboratories or on sending blood samples abroad, since it is costly, time consuming, and impractical procedure.

National registry and data bank for all organ failure cases are still lacking in our country; in the absence of which, it is impossible to have precise ideas of the prevalence and incidence of organs failure, which are substantial elements for profiling the national policy of organs transplantation.

Preemptive Kidney Transplantation in Syria

In the case of living donor transplantation, considerable costs can be saved if a patient receives a graft without prior dialysis. This early preemptive transplantation is an ideal choice for primary treatment of ESRD in developing countries. Avoiding hemodialysis not only saves costs, but also avoids the inconvenience and discomfort of dialysis and protects the patient from undue exposure to blood products.[34,35] Lastly, it results in a better graft survival.

Preemptive kidney transplantation practice in Syria is still restricted to a few patients; however, there is currently a tendency to apply it for an increasing number of patients as most transplant teams in our country had realized its lower costs and favorable outcomes since our entire performed kidney transplants are currently still being harvested from living donors only.

CONCLUSIONS

The success of a national cadaveric donation program requires several factors to be addressed, on the top of which are the government support for organ procurement efforts and the enactment of national laws and policies that facilitates transplantation. Finally, we must remember that for each grateful recipient of a transplanted organ, there is a family who is struggling with the loss of a loved one.

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CONFLICT OF INTEREST

None declared.

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