



Asian Focus

Kidney transplantation in Indonesia: An update

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Update

Abstract *Objective:* Indonesia has overcome several barriers to the growth of kidney transplantation within the past decade. Currently, the procedure is increasingly performed in several centers across the country. However there are limited publications on kidney transplantation from Indonesia, especially from centers outside Jakarta. This study aims to give a brief overview on transplantation performed, discuss current efforts and progresses of transplantation in Indonesia and chiefly Semarang.

Methods: Retrospective analysis of 20 transplant cases in Semarang during 2014–2018 was performed. Information from other transplant centers was acquired through formal correspondences with 11 central teaching hospitals in Jakarta, Surabaya, Yogyakarta, Malang, Bali, Solo, Palembang, Aceh, Medan, Bandung, and Padang.

Results: There were 629 recorded kidney transplantations performed in 12 centers, and we report on 245 cases with viable data. The average age of kidney recipients were younger (35.4 years old) compared to the donors (41.3 years old). Approximately half of the kidneys were obtained from related donors (49.0%) and there was only one case of cadaveric donor. The three leading etiologies of end-stage renal disease were hypertension (37.4%), diabetes mellitus (26.1%), and autoimmune disease (11.3%). There is only one center that has performed more than 100 kidney transplants in Indonesia.

Conclusion: Indonesia has successfully overcome several major hurdles that had previously hindered the growth of transplantation. Further improvement should concentrate on the development of integrated organ transplant infrastructure, decentralization of transplant

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professionals, establishment of National kidney transplant database and changing the Nation's paradigm on cadaveric organ donor through public education.

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1. Introduction

The number of patients diagnosed with end-stage renal disease (ESRD) in Indonesia is increasing annually, showing a similar trend with the global prevalence [1,2]. With its superior outcome, kidney transplantation remains to be the treatment of choice for ESRD [3,4]. Aside from prohibitive cultural views and the governing law, the high medical cost of renal transplantation had hindered its growth in Indonesia [5,6]. The development of kidney transplantation in Indonesia has faced several ups and downs, affected by both global and national events [7]. Nonetheless, kidney transplantation in Indonesia is back on its feet and continues to improve since 2011, hallmarked by the establishment of National Transplant Committee and National health insurance coverage for kidney transplant [8]. The procedure is now routinely performed in several centers mainly located within Java. However, the number of transplantation still remains low, covering only a minority (<5%) of ESRD patients [9]. There are limited reports on kidney transplant from centers outside Jakarta. To address the issue, this article aims to provide the latest update on the number and demographics of kidney transplant in Indonesia, discuss current issues on its development and report on the progress of smaller-growing transplant center such as Semarang.

2. Materials and methods

2.1. Indonesia

Information on kidney transplant from 11 centers: Jakarta (Dr. Cipto Mangunkusumo hospital), Surabaya (Dr. Soetomo hospital), Yogyakarta (Dr. Sardjito hospital), Malang (Dr. Saiful Anwar hospital), Bali (Sanglah hospital), Solo (Dr. Moewardi hospital), Palembang (Dr. M. Hoesin hospital), Aceh (Dr. Zainoel Abidin hospital), Medan (H. Adam Malik hospital), Bandung (Dr. Hasan Sadikin hospital), and Padang (Dr. M. Djamil hospital) was acquired through formal correspondence started in September 2017 with the Department of Urology in each central teaching hospital. Participating urologists who performed the surgery varies between institutions and are listed in the acknowledgement section. Data from Jakarta were also taken from two recent publications [10,11].

2.2. Semarang

Data from Semarang were obtained through retrospective analysis of medical records from 26 transplants performed between January 2014 and July 2018 in Dr. Kariadi General

Hospital (Table 1). In-clinic patients with ESRD were actively screened as potential candidates for transplantation. Patients younger than 15 years old, older than 70 years, diagnosed with active systemic infection, active malignancy, significant cardiovascular, cerebrovascular or pulmonary disease, and drug/alcohol addiction were considered ineligible to become a recipient. Eligible, compliant patients with active National Health Insurance status were offered the renal transplant program. The patient and family members provided the list of potential kidney donors. Willing potential donors underwent preliminary screening before undergoing further tests to determine their suitability. Donor with history of malignancy, cirrhosis, left ventricular ejection fraction (LVEF) <40%, hepatitis B, hepatitis C, human immunodeficiency virus (HIV) infection, cytomegalovirus (CMV) infection, toxoplasma, tuberculosis infection, diabetes mellitus and obese (body mass index >35 kg/m²) was considered ineligible. The average waiting time from the time of transplant enrollment until the actual surgery was between 6 and 8 months.

Donors were hospitalized for 7 days and recipients for 3 days in isolation prior to surgery. Cardiologist, pulmonologist, gastroenterologist, dentists, otorhinolaryngologist, psychiatrist and nutritionist carried out a series of anamnesis, physical and diagnostics examinations. The standard induction therapy uses mycophenolate mofetil (CellCept®, Genentech, California, USA) 1 g every 12 h intravenously, tacrolimus (Prograf®, Astellas Pharma Inc., Illinois, USA) 0.2 mg/kg per day every 12 h orally, and basiliximab (Simulect®, Novartis Pharmaceuticals Corp., Florida, USA) 20 mg daily intravenously, 2 h pre-transplant and continued 4 days post-transplant. Kidney harvest was performed using open mini-flank nephrectomy, transplanted with open side-to-end anastomosis to the external iliac artery/vein followed by extravesical (Lich-Gregoir) ureter reimplantation. Post-transplant immunosuppression regiment consists of life-long tacrolimus and azathioprine (Imuran®, Prometheus Laboratories Inc., California, USA).

3. Results

3.1. Transplant in Indonesia

Responses from each transplant centers were acquired within a period of 2 months since the start of correspondence. There is a total of 629 kidney transplants recorded from 12 centers across Indonesia (Fig. 1). The significant majority of kidney transplant was performed in Jakarta ($n = 491$, 78.1%) between 2011 until the end of 2017. Surabaya has the second most transplants ($n = 41$, 6.5%)

Table 1 Demographics of kidney transplants in Semarang.

Characteristic	Value
Age, mean (range), year	
Recipient (<i>n</i> = 26)	33.0 (15–50)
Donor (<i>n</i> = 26)	46.1 (24–64)
Sex, male/female	
Recipient (<i>n</i> = 26)	18/8
Donor (<i>n</i> = 26)	15/11
Donor-recipient relationship, <i>n</i> (%)	
Related	19 (73.0)
Non-related	7 (27.0)
Etiology of ESRD, <i>n</i> (%)	
Hypertension	16 (61.5)
Diabetes mellitus	3 (11.5)
Autoimmune	1 (3.9)
Glomerulonephritis	2 (7.7)
Other	4 (15.4)
Recipient comorbidities, <i>n</i> (%)	
Coronary artery disease	3 (17.6)
Cerebrovascular disease	3 (17.6)
Pulmonary tuberculosis	2 (11.8)
Pleural effusion	2 (11.8)
Ascites	2 (11.8)
Hepatitis C	2 (11.8)
Gastric erosion	2 (11.8)
Depression	1 (5.8)
HLA Matching, <i>n</i> (%)	
Full match	20 (76.9)
4 miss match	1 (3.8)
3 miss match	1 (3.8)
2 miss match	2 (7.7)
1 miss match	2 (7.7)
Number of transplant, <i>n</i>	
In 2014	4
In 2015	3
In 2016	5
In 2017	8
In 2018	6
Mortality (%)	
In 2015	33.3 (1/3)
In 2016	40.0 (2/5)
In 2017	0 (0/8)
In 2018*	0 (0/6)
Procedural time, mean, min	
Cold ischemic time	8.1
Warm ischemic time II	27.9
Total ischemic time	36.9
Complications and outcome	
Mean intraoperative bleeding, mean $\pm$ SD, mL	384 $\pm$ 192
Recipient mean hospital stay, mean (range), day	11 (10–14)
Infection, <i>n</i> (%)	2 (7.7)
Cardiovascular, <i>n</i> (%)	3 (11.5)
Total number of deaths, <i>n</i> (%)	5 (19.2)
Redialysis, <i>n</i> (%)	3 (11.5)
Retransplant, <i>n</i> (%)	0 (0.0)

* data up to July 2018.

ESRD, end-stage renal disease; HLA, human leukocyte antigen.

followed by Yogyakarta (*n* = 36, 5.7%), Semarang (*n* = 26, 4.1%), and Malang (*n* = 14, 2.2%). Yogyakarta has the earliest starting timeline, reporting their data since 1991. There are also several unrecorded transplants in Indonesia before 1990, before the advent of proper medical record system such as in our center in Semarang. However, it is safe to assume the number is below 100 cases. The starting timelines from several smaller centers (e.g. Bali, Aceh, Medan, Bandung and Padang) are unknown (unreported).

The data from Jakarta were mainly extracted from a descriptive study published by Marbun et al. [11]. The center reportedly performed 491 transplants within a period of 7 years (2011–2017). However, complete follow-up were achieved in 108 patients and an additional 30 patient with partially known data. The data obtained from each center other than Jakarta were limited to patient demographics, etiology of ESRD and recipient-donor relationship. The abovementioned data are summarized in Table 2. The majority of transplant patients were in their 4th decade, with the average age of younger recipients (35.4 years old) compared to the donors (41.3 years old). There are more male recipients (65.7%) and donor (55.5%) with an almost equal proportion of related (49.0%) and unrelated (51.0%) transplant. The etiologies of ESRD in descending order of frequency are hypertension (37.4%), diabetes mellitus (26.1%), glomerulonephritis (14.8%), autoimmune (11.3%), and other (10.3%). All kidneys were acquired from living donor, except one case of cadaveric transplantation performed in Surabaya. Jakarta is the only center that has performed more than 100 kidney transplantations.

3.2. Transplant in Semarang

Since 1985, there were several renal transplantations performed in Telogorejo Hospital and Dr. Kariadi General Hospital, Semarang. We report 26 transplants performed in Dr. Kariadi General hospital from January 2014 until July 2018 (Table 1). Medical records and related data prior to January 2014 are considered to be permanently lost and irretrievable. There were four transplants in 2014, three in 2015, five in 2016, eight in 2017 and six until July 2018. Transplant recipients were within the 15–70 years of age criteria, with at least one human leukocyte antigen (HLA) match with the donor and absence of donor-specific antibody (DSA).

Patients in Semarang showed similar demographics with the overall Indonesian cases, where most recipients are younger (33.0 years old) compared to the donors (46.1 years old). Similarly, hypertension (61.5%) was the major etiology of ESRD. The recipient's comorbidities include cerebrovascular disease, coronary artery disease, history of pulmonary tuberculosis, pleural effusion, ascites, hepatitis C, gastric erosion and depression. The majority of recipient received kidney from blood related donors (*n* = 19, 73.0%). There were 20 (76.9%) full HLA match, two cases of one and two miss match, one case of four and three miss match. There were five (19.2%) cases of mortalities, two of which occurred during post-operative recovery period and the rest within 12 months after hospital discharge. The cause of the two "early" mortalities was

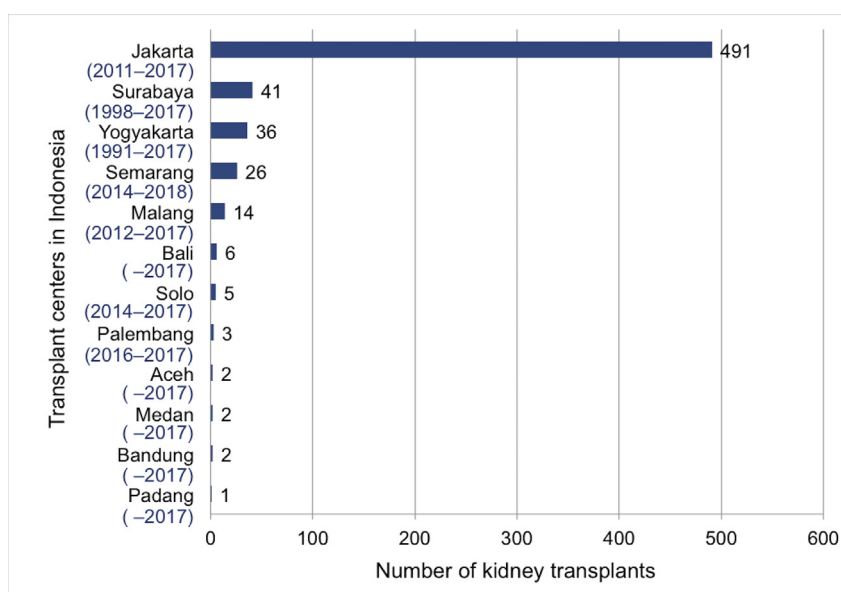


Figure 1 Total number of transplant performed in Indonesia. The number of kidney transplant is represented by the X-axis. The bracketed year under each center denotes the period of time, which the data were reported from. The starting timelines of Bali, Aceh, Medan, Bandung, and Padang are undefined.

acute myocardial infarction. Acute signs of allograft rejection or infection were not established in either patient. The third death occurred 7 months post-transplant in a 39-year-old male with history of myocardial infarction and gastric erosion. The cause of death was determined to be heart failure due to ischemic and hypertensive cardiomyopathy. Septic shock was the cause of death for the other two mortalities with one related to bacterial pneumonia and the other with unknown primary site of infection. There were three cases of allograft rejection, one patient with three pre-transplant HLA miss match and the other with two HLA miss match. Post-transplant immunosuppressive regiment was discontinued and all three patients underwent redialysis.

4. Discussion

This is the first report that presents the total number of kidney transplants performed in Indonesia. The number has risen significantly within the past 5 years, especially from centers in Java. However, it is still far below from what is needed or when compared to neighboring Southeast Asian countries like Vietnam, Thailand, and Philippines [12,13]. Several barriers to transplantation in Indonesia that had been previously elaborated include shortage of specialists, high cost, lack of easy access and information within the community, as well as amongst medical practitioners [1,6,14].

4.1. Insurance coverage and government rules

The majority of Indonesians with ESRD is still treated with hemodialysis (80%), which puts a significant burden on the National Health Insurance scheme (Jaminan Kesehatan Nasional, JKN), requiring an expense of 2.2 trillion IDR (1 USD $\approx$ 13.850 IDR) in year 2015 for hemodialysis [9].

Table 2 Overall demographic of kidney transplants in Indonesia.

Characteristic	Value
Age, mean (range), year	
Recipient ($n = 245$)	35.4 (15–57)
Donor ($n = 245$)	41.3 (17–64)
Age group ^a , recipient/donor, year	
≤ 20	6/3
21–30	33/19
31–40	29/25
41–50	32/35
51–60	8/21
≥ 60	0/4
Sex, male/female	
Recipient ($n = 245$)	161/84
Donor ($n = 245$)	136/109
Donor-recipient relationship, n (%)	
Related	120 (49.0)
Unrelated	125 (51.0)
Kidney source, n (%)	
Living donor	244 (99.6)
Cadaveric donor	1 (0.4)
Etiology of ESRD ^b , n (%)	
Hypertension	76 (37.4)
Diabetes mellitus	53 (26.1)
Autoimmune	23 (11.3)
Glomerulonephritis	30 (14.8)
Other	21 (10.3)
Number of transplant performed, number of centers	
< 10	7
10–50	4
> 50	1

^a Data excluding Jakarta and Bandung.

^b Data excluding Yogyakarta and Bali.

Budget impact analysis has shown that peritoneal dialysis-first policy for ESRD is much more economical compared to hemodialysis-first policy, requiring 75 trillion IDR for 100% coverage within 5 years compared to 166 trillion IDR for the later [8]. Although direct economical analysis for renal transplants in Indonesia has not been published, renal transplant is predicted to be more economical compared to life-long hemodialysis [15,16]. Officials and legislatures are aware of this predicament. Thus in year 2016 they established two regulations that would help mitigate the financial burden and promote the growth of organ transplantation in the country. 1) Revisions were made in the National Health Insurance (JKN) reimbursement scheme, covering the cost of kidney transplantation which is around USD 18 000 per case [17]. However, there are only seven out of 33 medical centers in the country that are fully covered by JKN [18]. 2) Organ transplant from unrelated donor are legalized by the Indonesian law [19]. With these two regulations in motion, two fundamental barriers to kidney transplantation in Indonesia are reduced.

4.2. Centralized transplant specialists

Lack of trained specialists and supporting infrastructure has been the major and well-known problem that impedes the growth of renal transplant in Indonesia. In 2017, there are 426 practicing urologists serving a nation with 263 991 379 population, resulting in a ratio of one urologist for every 619 698 Indonesians. Although the number of urologist has increased significantly from 229 in 2009, the urologist-to-patient ratio is severely low compared to the USA that has a ratio of 1:26 520 in 2016, and UK 1:73 330 in 2014 [20,21]. A similar problem of nephrologist and nephrology-trained nurses shortage is also present. One prominent trend from the presented data is the centralization of kidney transplant within Java, mainly in bigger cities such as Jakarta, Surabaya, and Yogyakarta. Several causes might have resulted in the uneven spread of specialists, but we think low incentive is the main reason for centralization.

Without full-time transplant specialists working in rural hospital, procurement of appropriate medical facilities is less likely to happen. Thus, the vicious cycle of specialists unwilling to work in a hospital without modern facilities ensues. Kidney transplant reimbursement by the National Health Insurance might have backfired in this aspect, since specialists working smaller hospital will eventually refer patients with complex diseases to bigger tertiary hospitals that are covered with larger insurance capitation. Continuous efforts are being made to rectify this problem, such as the expansion of urology residency training program, obligatory work program in rural area for new graduates, and continuous transplant supervision by the National Transplantation Committee headed by a team from Cipto Mangunkusumo Hospital (RSCM) [7]. However, such measures may only temporarily solve the problem. Complete decentralization of specialists into rural areas is a long-term goal that requires commitment from all responsible bodies: Government, medical associations, and individual specialists.

4.3. Cadaveric donor

Until now, there is only one report of cadaveric kidney transplant performed in Indonesia. Cadaveric kidney is a major source of kidneys donation, such as in Thailand where 2889 (50%) transplants were performed using kidneys from deceased donor [12]. Limiting the use of cadaveric donor prevents timely operation, worsens prognosis, and ultimately retards the growth of transplantation. The main reason for resistance against using cadaveric donor is misinformation and lack of community education among the general population. This is a major setback to the growth of kidney transplants in the country and has existed since the beginning. There exists a common misconception among Indonesians that organ transplantation is prohibited by religious law [5]. The resistance for cadaveric donor is based more on an individual cultural interpretation, considering a consensus by religious figures and health experts was reached in 1995 allowing organ transplantation. Another common misconception is living with one kidney will negatively affect the living quality of the donor, rendering them unable to lead a normal life. Such notion is evident that there is an urgent need for proper system for educating the public. Early education about end-stage renal disease, transplantation, and referral system has been proven to increase access to transplantation rate [22]. Overcoming this problem poses a great challenge since it requires changing one's spiritual paradigm and cultural believe. Consequently, government officials, health experts and religious figures must work hand-in-hand in a continuous effort to educate the community regarding the safety and religious permission of cadaveric organ transplantation.

4.4. Kidney transplant in Semarang

The situation of kidney transplantation in Semarang has also been affected by the events elaborated by Mochtar et al. [7]. The first recorded kidney transplant in Semarang was in 1977. Afterwards there were several unrecorded kidney transplants, mainly performed in Dr. Kariadi General Hospital. The renal transplant system was restarted in 2014 and since then the procedure has been regularly performed in the institution. In-hospital ESRD patients are individually offered the transplant program by the nephrologist team. Although there has been a constant annual increase of kidney transplant performed since 2014, the manual patient recruitment system will eventually limit the center from ever reaching its maximum potential. The average waiting time for Semarang patients was 6–8 months from the start of enrollment until the operation. The waiting time and total number of transplant can be greatly increased by a coordinated National database online system.

We report on 26 cases of living-donor transplantations from January 2014 until July 2018. In contrast, Cipto Mangunkusumo Hospital in Jakarta performed 491 transplants within 6 years [11]. There were five (19.2%) mortalities in Semarang, all within 12 months post-transplant. The mortality rate is similar to Jakarta ($n = 28$, 20.28%) as reported by Marbun et al. [11]. In Semarang two patients (40.0%) died during post-operative recovery due to acute myocardial infraction, one patient (20.0%) died because of

cardiomyopathy, and two patients (40.0%) caused by sepsis. The main cause of death in Jakarta was sepsis ($n = 8$, 40.0%), followed by unknown cause ($n = 7$, 35.0%), pulmonary edema ($n = 2$, 10.0%), hepatitis ($n = 2$, 10.0%) and stroke ($n = 1$, 5.0%). Marcelino et al. [10] published the only Indonesian data available for comparison, which was based on laparoscopic living-donor nephrectomy (LLDN) technique. In terms of procedural time, the average first warm ischemic time (WIT) of open technique in Semarang was longer compared to the LLDN in Jakarta (6.6 min vs. 4.3 min). Expectedly, the average intraoperative blood loss was also higher in open technique (384 ± 192 mL vs. 194 ± 198 mL). However, no urinary retention, operative wound site infection or severe pain (Visual Analogue Scale ≥ 7) was recorded.

Based on the outcome of 17 patients that surpassed the 12-month mark, the 1-year survival rate of transplant patient in Semarang is 70.6%. Compared to Jakarta, the 1-year survival is 88.5% and 3-year survival is 79.7% [11]. Compared abroad, the 1-year survival rates for living donor kidney transplants are 97.2% in USA, 98.0% in Australia and New Zealand, 95.8% in Europe, and 97.7% in Canada [23]. The limited number of transplant in Semarang contributes to the low number of survival rate. It also highlights the need of training and expertise. Better survival rate can be achieved with more transplants number as well as reaching the plateau of learning curve within the coming years. The transplant team in Semarang is also in the process of applying LLDN technique to achieve better operative results [10,24]. An exclusive hospital-patient communication and medical record system for kidney transplant patients is also being established to ensure a long-term and complete follow-up. The initial goal of our institution is to establish a firm kidney transplant center capable of covering Central Java, aiding the decentralization of kidney transplant.

5. Conclusion

This is the first report on the number of overall kidney transplantation data in Indonesia. Kidney transplantation in Indonesia can be considered to be still in its infancy. There has been a consistent increase of kidney transplantation, however still concentrated within the capital city. Major barriers that have been surmounted include the establishment of National Health Insurance full coverage in 11 appointed hospitals and a National law that permits organ transplantation. As of 2018, the five leading centers that performed the most transplants are Jakarta, Surabaya, Yogyakarta, Semarang and Malang. Currently, there are limited Indonesian data to compare the intra- and post-operative results of our center. However, improved experience and expertise are imperative to achieve better and satisfactory results in Semarang. In a national level, continuous efforts are being made in the expansion of specialist training program and kidney transplantation center. There is ongoing yet intangible effort by the Indonesian National Transplantation Society in establishing organ procurement system for cadaveric donor, public education, and the ever-needed Transplant National Database System.

Author contributions

Study conception and design: Tommy Supit, Eriawan Agung Nugroho, Ardy Santosa.

Data acquisition: Tommy Supit, Eriawan Agung Nugroho.

Data analysis: Tommy Supit, Eriawan Agung Nugroho, Ardy Santosa, Moh Adi. Soedarso, Nanda Daniswara, Sofyan Rais Addin.

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Critical revision of the manuscript: Tommy Supit, Eriawan Agung Nugroho, Ardy Santosa, Moh Adi Soedarso, Nanda Daniswara, Sofyan Rais Addin.

Performing kidney transplant: Eriawan Agung Nugroho, Ardy Santosa, Moh Adi Soedarso, Nanda Daniswara, Sofyan Rais Addin.

Conflicts of interest

The authors declare no conflict of interest.

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Bali: Anak Agung Gede Oka, Gede Wirya Kusuma Duarsa, Kadek, Budi santosa, and I Wayan Yudiana.

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