



Case Report

Kidney transplantation in Semarang : outcomes and prognosis

Eriawan Agung Nugroho¹, Tommy Supit², Ardy Santosa¹, Nanda Daniswara¹,
Sofyan Rais Addin¹, Anggun Ari Mukti²

¹Department of Urology, Faculty of Medicine Diponegoro University /
Dr. Kariadi General Hospital

²Department of Surgery, Faculty of Medicine Diponegoro University /
Dr. Kariadi General Hospital

Korespondensi : eriawanspu@gmail.com

Abstrak

Introduction & objective : Kidney transplantation is increasingly performed across Indonesia, including in Semarang. However there are limited publications on renal transplantation from Indonesia, especially from centers outside Jakarta. The objective of this case series is to give a brief overview on the transplantation performed in Semarang, discuss current issues and ongoing efforts to address them.

Case series : Twenty-seven renal transplants in Dr. Kariadi General Hospital from January 2012 until July 2018 were retrospectively analyzed. On average recipients were younger (32.5 years old) compared to the donors (46.8 years old). All kidneys were acquired from living donors with the majority of them to be blood-related (74.1%). The 3 leading etiologies of end-stage renal disease were hypertension (36.0%), diabetes mellitus (26.9%), and autoimmune disease (11.2%). The average total ischemic time was 36.9 minutes and the average length of stay was 11 days. We report 5 cases of mortality, 3 cases of allograft rejection and no re-transplantation.

Discussion : The demographics of kidney transplant patients in Semarang were similar compared to the National data. The limited number of transplant in Semarang contributes to the low number of survival rate and highlights the need of further 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.

Conclusion : The development of kidney transplant in Semarang follows the National milestones. In order to maximize the potential the institution, further improvements should concentrate on the development of integrated organ transplant infrastructure. The main goal of this institution is to establish a solid transplant center capable of covering Central Java, aiding the decentralization of kidney transplant in the Nation

Keywords : Kidney transplantation, end-stage renal disease, chronic kidney disease, Indonesia, Semarang, epidemiology, update

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, high medical cost of renal transplantation had hindered its growth in Indonesia.^{5,6} The development of kidney transplantation in Indonesia was also 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 across the Nation, including Semarang. 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.^{10,11} To address the issue, this review aims to provide the latest update and demographics of kidney transplants in smaller growing transplant center such as Dr. Kariadi General Hospital in

TABEL 1
Demographics of kidney transplantations in Semarang (Age and Sex)

Variabel		Recipient	Donor
Age	Mean (range)	32.5 (15 – 50)	46.8 (24 – 64)
Sex, n (%)	Male	17 (63.0)	14 (51.9)
	Female	10 (37.0)	13 (48.1)

Semarang, Central Java.

CASE REPORT

We report 27 transplants performed in Dr. Kariadi General hospital from January 2012 until July 2018 (Table 1). Medical records and related data prior to January 2012 are considered to be permanently lost and irretrievable. 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.

Donors were hospitalized for 7 days and recipients by 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 IV q12hr, tacrolimus (Prograf®, Astellas Pharma Inc., Illinois, USA) 0.2 mg/kg/day PO q12hr, and basiliximab (Simulect®, Novartis Pharmaceuticals Corp., Florida, USA) 20 mg IV qd 2 hours 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

TABEL 2
Demographics of kidney transplantations in Semarang based (Donor-recipient relationship, Etiology of ESRD, Recipient comorbidities, Recipients Body Mass Index and HLA Matching)

Variabel	n	%
Donor-recipient relationship		
Related	20	74.1
Non-related	7	25.9
Etiology of ESRD		
Hypertension	16	59.3
Diabetes mellitus	4	14.8
Autoimmune	1	3.7
Glomerulonephritis	2	7.4
Other	4	14.8
Recipient comorbidities		
Coronary artery disease	3	11.1
Cerebrovascular disease	3	11.1
Pulmonary tuberculosis	2	7.4
Pleural effusion	2	7.4
Ascites	2	7.4
Hepatitis C	2	7.4
Gastric erosion	1	3.7
Depression	1	3.7
Recipients Body Mass Index		
< 18.5 (underweight)	4	14.8
18.5 – 24.9 (normal)	14	51.9
25.0 – 29.9 (overweight)	6	22.2
≥ 30.0 (obese)	3	11.1
HLA Matching		
Full match	20	74.1
4 miss match	1	3.7
3 miss match	1	3.7
2 miss match	2	7.4
1 miss match	2	7.4

HLA : human leucocyte antigen

azathioprine (Imuran®, Prometheus Laboratories Inc., California, USA).

DISCUSSION

The incidence of ESRD patients in Indonesia who

TABEL 3
Demographics of kidney transplantations in Semarang (Year)

Year	No. of Transplant	Mortality
2012	1	0/1
2013	1	0/1
2014	3	2/3
2015	4	1/4
2016	4	2/4
2017	7	0/7
2018	7	2/4

TABEL 4
Demographics of kidney transplantations in Semarang (Procedural time)

Procedural Time	Minutes : Seconds
Warm ischemic time I	06 : 34
Cold ischemic time	08 : 04
Warm ischemic time II	27 : 55
Total ischemic time	36 : 56

TABEL 4
Demographics of kidney transplantations in Semarang (Complications and outcome)

Complications and outcome	
Intraoperative bleeding, mean (SD) in mL	384 (±192)
Hospital stay, mean (range) in days	11 (10 – 14)
Infection, n (%)	2 (7.7)
Cardiovascular, n (%)	3 (11.5)
Total number of deaths, n (%)	5 (19.2)
Re-dialysis, n (%)	3 (11.5)
Re-transplant, n (%)	0 (0.0)

underwent kidney transplantation from 1977 through 2017 was 629 patients. Kidney transplantation was first performed at Cipto Mangunkusumo Hospital, Jakarta in 1977. Since 1985, there were several renal transplantations performed in Telogorejo Hospital and Dr. Kariadi General Hospital, Semarang. The number of transplant performed steadily increased every year. 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).¹¹ 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 oneand twomiss match, one case of fourand threemiss 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 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. 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}

The situation of kidney transplantation in Semarang was affected by the events elaborated by Mochtar *et al* (Level Of Evidence 4).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 formally 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 68 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 27 cases of living-donor transplantations from January 2012 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 minutes vs. 4.3 minutes). 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 United States, 98.0% in Australia and New Zealand, 95.8% in Europe, and 97.7% in Canada.¹⁵ 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.^{10,16}

Based on this study, there was improvement in total number of kidney transplantation between January 2012 to July 2018 at Dr. Kariadi Hospital Semarang. The main cause of ESRD is hypertension. Most recipient are younger than the donor with majority kidney source are come from blood related donor. This report shows that 1-year survival rate in Semarang is lower than others center. 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

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.

REFERENCES

1. Prodjosudjadi W. Incidence, prevalence, treatment and cost of end-stage renal disease in Indonesia. *Ethn Dis.* 2006;16 (2 Suppl 2):S2-14-6.
2. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, *et al.* Global Prevalence of Chronic Kidney Disease - A Systematic Review and Meta-Analysis. *PLoS One.* 2016;11(7):e0158765.
3. Tonelli M, Wiebe N, Knoll G, Bello A, Browne S, Jadhav D, *et al.* Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant.* 2011;11(10):2093-109.
4. Yoo KD, Kim CT, Kim MH, Noh J, Kim G, Kim H, *et al.* Superior outcomes of kidney transplantation compared with dialysis: An optimal matched analysis of a national population-based cohort study between 2005 and 2008 in Korea. *Medicine (Baltimore).* 2016;95(33):e4352.
5. Markum HM. Renal transplantation problem in Indonesia. *Acta Med Indones.* 2004;36(3):184-6.
6. Bennett PN, Hany A. Barriers to kidney transplants in Indonesia: a literature review. *Int Nurs Rev.* 2009;56(1):41-9.
7. Mochtar CA, Alfarissi F, Soeroto AA, Hamid ARAH, Wahyudi I, B.H. M, *et al.* Milestones of kidney transplantation in Indonesia. *Medical journal of Indonesia.* 2017;26(3):229-36.
8. Afiatin, Khoe LC, Kristin E, Masytoh LS, Herlinawaty E, Weryingyong P, *et al.* Economic evaluation of policy options for dialysis in end-stage renal disease patients under the universal health coverage in Indonesia. *PLoS One.* 2017;12(5):e0177436.
9. 8th Report of Indonesian Renal Registry. *Perkumpulan Nefrologi Indonesia*, 2015.
10. Marcelino A, Mochtar CA, Wahyudi I, Hamid AR. Kidney

- transplantation: A new era of laparoscopic living donor nephrectomy in Indonesia. *Asian J Surg.* 2018;41(1):55-8.
11. Marbun MBH, Umami V, Susalit E. A 3-year survival rate of kidney transplant recipient in Cipto Mangunkusumo General Hospital in Indonesia. *Journal of Renal Medicine.* 2017;1(2):1-5.
 12. Noppakun K, Ingsathit A, Pongskul C, Premasthian N, Avihingsanon Y, Lumpaopong A, *et al.* A 25-year experience of kidney transplantation in Thailand: report from the Thai Transplant Registry. *Nephrology.* 2015;20(3):177-83.
 13. Chan-On C, Sarwal MM. A Comprehensive Analysis of the Current Status and Unmet Needs in Kidney Transplantation in Southeast Asia. *Frontiers in medicine.* 2017;4:84.
 14. Prodjosudjadi W, Suhardjono A. End-stage renal disease in Indonesia: treatment development. *Ethn Dis.* 2009;19 (1 Suppl 1):S1-33-6.
 15. Wang JH, Skeans MA, Israni AK. Current Status of Kidney Transplant Outcomes: Dying to Survive. *Advances in chronic kidney disease.* 2016;23(5):281-6.
 16. Kuo T, Yip SK, Ng CF, Ng LG, Cheng CW. Outcome of laparoscopic live donor nephrectomy and impact of double renal arteries: results from two transplant centres. *Asian J Surg.* 2010;33(2):70-5.