Health Technology Assessment of Kidney Transplantation and Hemodialysis for the Treatment of End-Stage Kidney Disease

I Gde Raka Widiana (✉ rakawidiana@yahoo.com)

Nephrology and Hypertension Division, Faculty of Medicine Udayana University/Sanglah General Hospital <https://orcid.org/0000-0002-7523-9441>

Maruhum Bonar H. Marbun

Division of Nephrology and Hypertension, Departement of Internal Medicine, Faculty of Medicine University of Indonesia, Jakarta

Nyoman Paramita Ayu

Division of Nephrology and Hypertension, Departement of Internal Medicine, Faculty of Medicine University of Udayana, Denpasar, Bali

I Wayan Sudhana

Division of Nephrology and Hypertension, Departement of Internal Medicine, Faculty of Medicine University of Udayana, Denpasar, Bali

Yenny Kandarini

Division of Nephrology and Hypertension, Departement of Internal Medicine, Faculty of Medicine University of Udayana, Denpasar, Bali.

IB Mahendra

Division of Nephrology and Hypertension, Departement of Internal Medicine, Faculty of Medicine University of Udayana, Denpasar, Bali

Renny SP Duarsa

Division of Nephrology and Hypertension, Departement of Internal Medicine, Faculty of Medicine University of Udayana, Denpasar, Bali

Made Rama Putra

Division of Nephrology and Hypertension, Departement of Internal Medicine, Faculty of Medicine University of Udayana, Denpasar, Bali

Gede Wira Mahadita

Division of Nephrology and Hypertension, Departement of Internal Medicine, Faculty of Medicine University of Udayana, Denpasar, Bali.

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Abstract

BACKGROUND

Kidney transplantation is an expensive procedure, and it is an alternative treatment of end-stage renal disease other than dialysis. Cost-Effectiveness and the cost-utility study was undertaken at Sanglah Hospital Bali Indonesia, aiming to assess whether living-related kidney transplantation is more cost-effective and cost-utility than hemodialysis in the treatment of end-stage renal disease.

METHODS

A health technology assessment was done in living-related kidney transplant and hemodialysis during 2018. Data search from internet resources using the electronic library and critically appraised the best evidence of the data of the best data of five-year mortality and survival of kidney transplant and hemodialysis. A preliminary study about quality of life was also done among kidney transplant and hemodialysis patients. Data about kidney transplant costs and hemodialysis for five years was taken from the Sanglah General Hospital database.

RESULTS

During the study, Fourteen living-related kidney transplant patients at Sanglah Public Hospital Denpasar Bali Indonesia consisted of 14 recipients, 12 males, and 2 females aged 27 -55 years, and 14 donors, three males and 11 females aged 24-63 years were included. Thirty HEMODIALYSIS patients at the same hospital were recruited. They consisted of 20 males and ten females, with an average age of 50.9 years. The average five-year cost of kidney transplant was 741,078 M IDR. In comparison, hemodialysis's five-year cost was 581,514 M IDR, leading to a cost difference was 159,564 M IDR. Five-year mortality of kidney transplant was 55% (survival 45%), five years survival rate was 18.9%. Five years of survival difference between kidney transplant and hemodialysis was 26.1 %. Meanwhile, QOL for a kidney transplant was 0,7063, and QOL for hemodialysis was 0,5596, leading to a QOL difference of 0.15. Kidney transplantation will spend 6.11 M IDR for every 1% increase of survival for five years with 15% better QOL. In five years, kidney transplantation produces 67% ICER. From cost-utility perspective, kidney transplantation yields 31.04 M IDR per QALY or 2,217 USD per QALY.

CONCLUSION

Living-related kidney transplantation is more cost-effective and cost-utility than hemodialysis in the treatment of end-stage renal disease.

Background

As of 2016, Indonesia's population was estimated to be 260 million, thus making Indonesia the world's fourth most populous nation. End-stage renal disease occupies second place in the national medical

insurance budget for the catastrophic disease. a National Health Insurance of BPJS reported that the claim for renal failure was approximately US\$161.606.000 in 2014 alone. [1]

From 2007 to 2016, there were recorded more new hemodialysis patients and active hemodialysis patients. The Indonesian Society of Nephrology stated that an estimated 200,000 new end-stage renal disease patients require replacement therapy each year. Despite the increasing demand for dialysis, hemodialysis machines' shortage causing not all patients can receive dialysis treatment. In 2014, it was reported that most renal replacement therapies were hemodialysis (82.4%) and peritoneal dialysis (12.8%). From 2007 to 2016, the number of new and active hemodialysis patients showed an increasing trend. The IRR (Indonesian Renal Registry) reported that there were 4977 new patients and 1885 active patients in 2007, while 5,029 new patients and 7381 active patients were in 2014, by 2015 there were 7465 new patients and 9382 active patients. By 2016 there were 6288 new patients and 14,869 active patients. [2] The seventh report of the Indonesian Kidney Registry in 2014. Indonesian Society of Nephrology.³ The 2016 IRR report stated that Indonesia has 460 hemodialysis unit and 6604 hemodialysis machines. Generally, patients with end-stage renal disease undergo hemodialysis twice a week. BPJS, as the National Health insurance, covered this treatment frequency.[3]

Kidney transplantation is another treatment for end-stage renal disease. It has been practiced in Sanglah General Hospital in Bali as one of Indonesia's tertiary referral hospitals. So far, most kidney transplants have used living-related donors. To this date, Indonesia has no Health Technology Assessment (HTA) to compare living-related kidney transplants and hemodialysis.

The HTA aims to evaluate whether living-related kidney transplantation is more cost-effective and cost-utility than hemodialysis in treating end-stage renal disease.

Methods

A retrospective analysis was done in living-related kidney transplant and hemodialysis at Sanglah General Hospital, Bali Indonesia, during 2018. The study was started with a focus group discussion involving evidence-based medicine appraisals to search data resources on the internet using the electronic library and critically appraised the best evidence of the data. This appraisal is undertaken by two independent appraisals to obtain the best data of five-year mortality and survival of kidney transplant and hemodialysis patients in cohort study both in Indonesia and abroad. Whenever there are no full five years of survival data, a linear trend is assumed to obtain five years of survival using the maximum existing data. A preliminary study about quality of life was done among kidney transplant and hemodialysis. Data about a kidney transplant and hemodialysis costs for five years was taken from the Sanglah General Hospital database after obtaining a letter of permission. The costs included were tangible direct, tangible indirect, and intangible cost. This study was approved by the ethics committee of the Medical Faculty of Udayana University/Sanglah General Hospital.

Outcome data was determined, including median survival, quality of life, quality-adjusted life years (QALY), total cost, incremental cost-effectiveness ratio (ICER) of kidney transplantation over

hemodialysis. In contrast, the ICER is $(\text{cost}_{\text{transplant}} - \text{cost}_{\text{hemodialysis}})/(\text{QALY}_{\text{transplant}} - \text{QALY}_{\text{hemodialysis}})$. QALY gain and cost per QALY, is also calculated. This study was supported by grants from the HRD Department Ministry of Health of Indonesia. This study was approved by the National Health Research Ethics Commission, Research and Development Unit Ministry of the Health Republic of Indonesia.

Results

Cost of lived related kidney transplantation and hemodialysis

During the study, Fourteen living-related kidney transplant patients at Sanglah Public Hospital Denpasar Bali Indonesia consisted of 14 recipients, 12 males, and two females aged 27–55 years and 14 donors, three males and 11 females (all-female donor are recipient's mother) aged 24–63 years were included. Thirty hemodialysis patients at the same hospital were recruited, consisting of 20 males and ten females, aged 50.9 ± 9.9 years.

Costs of hemodialysis patients were estimated by direct tangible cost for predialysis surgery (double-lumen catheter and AV fistula), hemodialysis cost twice weekly, medicines (erythropoietin and iron injection, and oral medicines), labs and radiology during out-patient visits; indirect tangible cost including transportation and meals and intangible costs due lost of income due to absence from work when hemodialysis was undertaken (estimated from regential minimum wages, stipulated by the regent regulation). Costs of kidney transplantation were estimated by direct tangible cost screening and preliminary tests and immunological tests, operation procedures (during preparation, surgery, and post-operative care), out-patients visit including medicines, labs, and tacrolimus blood assay, post-transplant hospitalization costs due to complication (infection, sepsis, severe hyperglycemia and acute kidney injury, dehydration, and malnutrition); indirect tangible cost including transportation and meals and intangible costs for loss of income due to absence from work when transplant and post-transplant procedures were undertaken (also estimated from regential minimum wages, stipulated by the regent regulation). The cost for regular visits for the recipient is considered flat after 1-year transplantation. This cost estimation is mainly applied for a recipient under five years.

Selection procedure and operation costs for recipients and donors were calculated from selection procedures, during, and post-operative care until discharge, which varied due to the patient's medical condition. Lab tests were 334,000 to 772,000 IDR according to medical conditions; blood tacrolimus assay costs were 53,340,000 IDR (for five years total), and monthly medicines costs were 3,995,000 to 19,808,000 IDR, which was calculated for regular visits according to standard procedures and hospitalization due to post-transplant complications.

Insert Table 1 here

Table 1
Costs of Living Related Kidney Transplantation during 5 years

Category	Minimum (IDR)	Maximum (IDR)	Mean (IDR)	SD (IDR)
Recipient				
Selection and operation	138,456,100	337,695,400	182,255,442	46,921,425
Labs	72,000,000	99,660,000	81,107,142	7,076,603
Medicines	141,295,029	776,716,497	391,191,966	227,452,101
Transportation and meals	6,000,000	18,000,000	7,071,428	3,191,678
Lost of income	6,000,000.	12,000,000	6,857,142	1,833,749
Donor				
Selection and operation	36.171.900	87.849.600	58.165.000	13. 087.900
Transportation and meals	1.500.000	9.000.000	3,107.100	2,294.880
Income lost	3.000.000	9.000.000	6,000.000	2,353.390
Total	437,067,200	1,122,686,080	734,950,894	246,825,190

Hemodialysis cost was 765,000 IDR per session twice weekly, Epo 997,920 IDR (twice a week in a month), intravenous iron 45,000 IRD (once a month), and oral medicine 153,800 (once a month), labs 2,718,000 IDR (once a month for 12 months), chest X-ray 145,000 IDR (once a year), and USG 270,000 IDR (once a year). Transportation cost was 15,000 to 150,000 IDR according to the distance of the patient's address to HD center and meals 20,000 to 100,000 IDR according to the distance of the patient's address to HD center. Income loss was estimated according to regential minimum wages.

Insert Table 2 here

Table 2
Costs of Hemodialysis during 5 years (N = 30)

Category	Minimum (IDR)	Maximum (IDR)	Mean (IDR)	SD (IDR)
Double lumen catheter	2,358,900	8,000,000	4,180,526	1,268,290
AV fistula	2,494,900	17,900,000	5,537,683	3,427,830
Hemodialysis	397,800,000	397,800,000	397,800,000	N/A
Medicines	71,803,200	71,803,200	71,803,200	N/A
Labs and radiology	15,665,000	15,665,000	15,665,000	N/A
Transportation and meals	13,000,000	130,000,000	41,981,333	28,979,392
Income lost	31,200,000	65,000,000	44,546,666	8,013,253
Total	554,085,000	682,327,100	581,514,410	30,302,376

One year mortality of kidney transplantation was 13%, 3-year mortality 20.3%, mean mortality of second and third year is 10.15%. If linear assumption after one year is made, then 5 year mortality is 13% plus $4 \times 10.5\% = 55\%$, with survival 45%.⁴

Six months of follow up, there were 18 deaths from 222 hemodialysis patients who underwent regular hemodialysis. The incidence of death outcomes was 8.11%, with a cumulative average survival time of 177.34 ± 2.00 days.⁵ If linear trend is assumed, five years mortality = $10 \times 08.11\% = 81.1\%$ and survival rate 18.9%.

Cost-effectiveness of kidney transplant versus hemodialysis

The five-year cost of kidney transplant was 741,078 M IDR, while the five-year cost of hemodialysis was 581,514 M IDR, then the cost difference was 159,564 M IDR. Five-year mortality of kidney transplant was 55%, (survival 45%), while six-month mortality of hemodialysis was 8.11%, then five years mortality hemodialysis will be ten times 8.11% equals 81.1% (if linear trend assumed) and survival rate was 100% minus 81.1% equals 18.9%. Five years of survival difference between kidney transplant and hemodialysis was 45.0% minus 18.9% equals 26.1%, higher kidney transplant than hemodialysis.

The quality of life for a kidney transplant was 0,7063, while QOL for hemodialysis was 0,5596, then the QOL difference was 0.15. Suppose we calculate cost-effectiveness from a survival perspective, then in comparison to hemodialysis. In that case, kidney transplantation will spend 159,564 M IDR/26.1% equal 6.11 M IDR for every 1% increase of survival during five years with $0,71 - 0,56 = 0.15$ point or 15% better QOL.

Data from Pakistan showed that in 5 years, 85% of kidney transplant patient was alive. With linear assumption, 50% (median survival) patients will survive $85/50 \times 5 \times 12$ months equal to 102 months⁶.

The median survival of hemodialysis patients was 15 months among females and 22 months in males, therefore in average median survival of HD patients was 18.50 months.⁷

The difference between QOL for transplant versus hemodialysis was 71% minus 56% was 15%. QALY of the transplant was $102/12 \times 0.71$ equal 6.03, and QALY of hemodialysis was $18.50/12 \times 0.56$ equal 0.85. QALY difference transplant over hemodialysis was 6.03, minus 0.85 equals 5.14. Meanwhile, the cost difference of were 159,564 M IDR. Then, the ICER was 159,564 M IDR/5.14 and yielding 31.04 M IDR per QALY

Discussion

Our study showed that total transplantation cost was for five years was 741,078 M IDR and total hemodialysis cost for five years was 581,514 M IDR, yielding a cost difference between transplantation and hemodialysis for five years was 159,564 M IDR. If we calculate QALY for transplant and hemodialysis by multiplying median survival in one year with QOL, we found QALY for transplant 6.03 and QALY for hemodialysis 0.85 yielding QALY gain between transplant and hemodialysis 5.14. Five-year survival was 45% for transplant and survival rate 18.9% for hemodialysis, yielding five years survival difference between transplant and hemodialysis 26.1% higher for transplant than hemodialysis. Epidemiologically, his cost-effectiveness data produced $159,564 \text{ M IDR} / 26.1\% = 6.11 \text{ M IDR}$ for every 1% increase of surviving patients during 5 years, with $0.71 - 0.56 = 0.15$ point or 15% better QOL. If we calculate ICER for transplant versus hemodialysis for five years, it was shown that cost-utility for lived kidney transplantation in our hospital was 31.04 M IDR per QALY or 2,217 USD per QALY (exchange rate 14,000 IDR per USD). It means that in comparison to hemodialysis, lived kidney transplantation produced needs 2,217 USD for complete health status for end-stage kidney disease patients who survived one year longer.

Several studies regarding the cost comparison of kidney transplantation and hemodialysis exist. For the first year in Palestine, the total per-patient cost for kidney transplantation was 13 317 USD and 2960 USD (a total 16 277 USD). In comparison, the mean cost for hemodialysis for each patient was 16 085 USD per year. Both costs are similar. While after transplant, the cost continues at 2960 USD per year for each patient. Therefore, the first-year cost (16 277 USD) of kidney transplantation was fully offset in just 1.24 years by the yearly cost savings of 13 125 USD (16 085 USD for dialysis minus 2960 USD for kidney transplantation).[8]

Some similar studies on cost-effectiveness between kidney transplantation and hemodialysis have been conducted. A study by Sanchez-Escuredo et al. was done in 2014 with the use of prospective descriptive study. They compared the cost between LDKT (*living-donor kidney transplantation*) during one year after transplantation and hemodialysis. The total cost of LDKT was 29,879.91 Euro, in which 8,128.44 Euro for the cost for donor and 21,769.47 Euro for a recipient. Hemodialysis's total cost was 43,000.88 Euro, which 37,917 Euro for hemodialysis treatment and related procedures and 5,028 Euro for transportation, respectively. Thus, it could be concluded that LDKT had produced cost-saving 13,102.97 Euro per patient per year capital payback period for less than one year. On the other hand, the quality-adjusted life-year

(QALY) of LDKT was higher in LDKT than hemodialysis. It was known that LDKT is associated with a higher quality of life within one year after transplantation and more cost-effective.[9] Another study by Dominguez J and Atal R in 2011 conducted *cost-effectiveness analysis* and quality of life. They implemented the Markov model between kidney transplantation and dialysis. It was found that the cost estimation of dialysis was 134,000 USD with 4.32 *quality-adjusted life-year* (QALY). Simultaneously, the cost for transplantation was 106,000 USD, with 7.3 QALY, which produced 28,000 USD *net saving* and 2.98 *QALY gain*. Assuming, if 25,000 USD is considered yielding perfect health condition within one year; therefore, the subsequent transplantation can produce an *estimated total saving* of 102,000 USD. [10]

As for Pakistan's situation, the “free” transplantation costs to SIUT (Sindh Institute of Urology and Transplantation) are \$1640 for transplant surgery and \$300 per month for immunosuppressive drugs. A total of \$1.6 million was spent by SIUT each year only on transplantation with overall, the one- and five-year graft. Patient survival is 88% and 65% and 90% and 75%, respectively.[6] Although the cost of the first year after transplantation is expensive for Korea, over two years it becomes more effective and less costly than hemodialysis. It has been recommended that kidney transplantation is more cost-effective than hemodialysis. Kidney transplantation was less exorbitant and had a better result than hemodialysis. The cost per QALY gained was 19,450 thousand won in transplantation patients. In contrast, it was 36,514 thousand won per QALY gained in hemodialysis patients.[11]

In Indonesia, in 2013, a presidential decree on national health insurance has been issued. This national health insurance is run by BPJS, a national insurance body. Since 2014 the BPJS has reported that renal failure patients are the second top among catastrophic diseases after heart disease, which claimed 161.606.000 USD.[1] Compared to Greece, hemodialysis cost more than €171 million, or €182 per session, and €229 per inpatient day. It is also calculated that 2,046 years are lost due to mortality, and €9.9 million for the potential productivity cost, according to the human capital approach, and €303.000, based on the friction method. It was estimated as more than €273 million for total morbidity cost due to absence from work and early retirement, based on the human capital approach; the friction method was estimated as €12.5. In Greece, the population of ESRD patients depletes around 2 percent of total health expenditure. The mortality and morbidity of the disease also contribute to production loss.[12]

Problems of high economic and health burden due to end-stage renal disease make the government seek another approach. Our kidney transplantation is more costly; however, it is more cost-effective than hemodialysis. The QALY for transplant and QALY for hemodialysis was 6.03 and 0.85, respectively. The cost-utility for lived kidney transplantation was 31.04 M IDR per QALY or 2,217 USD per QALY (exchange rate 14,000 IDR per USD). A study by Dominguez et al., found that QALY for dialysis and QALY for kidney transplantation was 4.32 and 7.3, respectively, leading to 2.98 QALY gain and 25,000 USD per QALY (a condition of perfect health condition within one year). Less efficient procedures in our hospital due to an expensive blood test, laboratory examination such as HLA matching and blood tacrolimus measurement conducted in another region, and CT angio conducted in another center, may be responsible for the higher cost kidney transplantation. These problems may occur since our program still in the early phase

Conclusion

Living-related kidney transplantation is more cost-effective and cost-utility than hemodialysis in the treatment of end-stage renal disease.

Abbreviations

IRR	
Indonesian Renal Registry	
HTA	
Health technology assessment	
QALY	
Quality-adjusted life years	
HD	
Hemodialysis	
IDR	
Indonesian Rupiah	
QOL	
Quality of life	
LDKT	
Living-donor kidney transplantation	
SIUT	
Sindh Institute of Urology and Transplantation	

Declarations

Ethics approval and consent to participate

This study was approved by the National Health Research Ethics Commission, Research and Development Unit, Ministry of the Health Republic of Indonesia, written informed consent, after a verbal explanation was obtained from all study participants and their legal guardian before study enrollment.

Consent for publication

Not applicable

Availability of data and materials

The data that support the findings of this study are available from the corresponding author. However, restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of the corresponding author.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

IGRW designed the research, collect material and clinical data, analyzed the data, and writing the manuscript; MBHM, NPA, IWS, YK, IBM, RSD, and MRM designed the research, collect material and clinical data, and writing the manuscript; WM collects material and clinical data, revised the manuscript. All authors read and approved the final manuscript.

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