IOSR Journal of Nursing and Health Science (IOSR-JNHS)
e-ISSN: 2320–1959.p- ISSN: 2320–1940 Volume 13, Issue 2 Ser.2 (Mar. – Apr. 2024), PP 21-28
www.iosrjournals.org

Health Economic Evaluation of Hyperbaric Prilocaine vs. Hyperbaric/Heavy Bupivacaine as Spinal Anesthesia in Orthopedic Implant Surgeries in Indonesia

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Abstract:
Background*:During the past decade, there has been an increasing interest in orthopedic research in Indonesia. Due to an ageing population, the necessity for orthopedic joint replacement has grown, and therefore, new options are being sought, such as the same day discharge or day case surgery which aim to improve patient condition, outcomes, reduce length of hospital stay and improve the hospital's ability to treat more patients. Early mobilization is a key indicator which has major impact on patient satisfaction and better clinical outcomes in orthopedic knee and hip joint replacement surgeries. Spinal anesthesia enables early discharge leading to better clinical outcomes and more efficient use of healthcare resources. Several spinal anesthetics are available including heavy/hyperbaric bupivacaine and hyperbaric prilocaine. However, the evidence pertaining to cost effectiveness of hyperbaric prilocaine vs. hyperbaric/heavybupivacaine is scarce and would enable an informed policy decision in Indonesia from a public perspective.*
Methods: *A model based mathematical decision analytic model was parameterized to estimate the cost effectiveness of implementing hyperbaric prilocaine vs. hyperbaric bupivacaine in knee implant surgeries and plain prilocaine vs. heavy bupivacaine in hip implant surgeries in Indonesia. The analyses were carried out for knee and hip implant surgeries respectively. Input parameters included the cost of products, administration costs, costs related to multimodal analgesia, costs related to urinary retention and length of stay related costs in the hospital from a public payer perspective. A deterministic analysis was carried out to determine the incremental cost effectiveness ratio (ICER) along with a probabilistic sensitivity analysis to evaluate uncertainty in the variables.*
Results: *Base case deterministic cost effectiveness analysis showed hyperbaric prilocaine was dominant over hyperbaric/heavy bupivacaine as it demonstrated reduction in costs and better gains in quality adjusted life years (QALYs) (knee implant: savings of IDR 44,4720 per patient and incremental QALY gains 0.0023) and (hip implant: savings of IDR 48,9720 per patient and incremental QALY gains 0.0025). Probabilistic sensitivity analysis also demonstrated that hyperbaric prilocaine is cost effective at the willingness to pay threshold of Indonesia as the ICER scatter plot was in southeast quadrant (showing hyperbaric prilocaine is cost saving and demonstrates QALY gains in patients).*
Conclusions:*This study highlights cost savings associated with utilization of hyperbaric prilocaine vs. hyperbaric/heavybupivacaine in the public healthcare setting in Indonesia.*
Keywords:*HyperbaricPrilocaine, Hyperbaric Bupivacaine, Cost Effectiveness, Cost Utility, Length of stay, Incremental Cost Effectiveness Ratio (ICER)*

Date of submission: 14-03-2024 Date of acceptance: 24-03-2024

I. Introduction

During the past decade, there has been an increasing interest in orthopedic research in Indonesia. Early mobilization is a patient centric approach in orthopedic implants and an indicator of patient satisfaction and better clinical outcomes. The utilization of neuraxial versus general anesthesia for primary joint arthroplasty is associated with superior perioperative outcomes[1].

Current trend is moving towards day surgery supported by evidence from the enhanced recovery program pathways[2]. Spinal anesthesia is an established component of perioperative management for fast-track lower limbs arthroplasty. Short-acting local anesthetics may present an interesting option for primary non-complicated knee and hip arthroplasty. Published evidence underlines that spinal anesthesia enables early discharge leading to better clinical outcomes and more efficient use of healthcare resources. Bupivacaine is one of the most common options for spinal anesthesia in total hip (THA) or total knee (TKA) arthroplasty. It produces a well-known dose-dependent long-acting anesthesia and analgesia, associated with postoperative urinary retention and delayed motor function recovery, which have led to multiple studies looking for a minimally effective dose, with non-compromising anesthesia safety and fast-track protocols[3].

Prilocaine is a local anesthetic characterized by intermediate potency and duration and fast onset of action. As hyperbaric formulation of 5% solution, it was introduced and has been used for spinal anesthesia since 1960[3]. A new formulation of 2% plain and hyperbaric solution is currently available in Indonesia. In comparison with plain solutions, hyperbaricity remarkably accelerates the onset and offset times of intrathecal 2% prilocaine exhibiting a predictable intermediate duration of action. Literature indicates a dose ranging between 40 and 60 mg of prilocaine for lower extremities and lower abdominal procedures lasting up to 90 min, whereas a dose ranging from 10 to 30 mg is appropriate for perineal surgery[3].Readiness for discharge occurs in ~4 hours from spinal administration of hyperbaric prilocaine[3].Hyperbaric prilocaine (2%) has been investigated and showed promising therapeutic profile with low incidence of post anesthesia urinary retention, post anesthesia nausea and vomiting, as well as shorter time in post anesthesia care unit (PACU) and length of stay (LoS) as compared to bupivacaine[3].Hyperbaric prilocaine has also been utilized in advanced surgical pathways like SDD (same day discharge) and day case arthroplasty (DCA)[4]. However, the evidence pertaining to cost effectiveness/cost utility of hyperbaric prilocaine vs. hyperbaric/heavy bupivacaine is scarce and would enable an informed policy decision in Indonesia, from a public perspective.

Hence, we undertook a model-based cost effectiveness study to investigate the cost effectiveness of hyperbaric prilocaine vs. heavy/hyperbaric bupivacaine in orthopedic implants (knee and hip) based on published literature with a focus and perspective of the public healthcare system in Indonesia.

II. Material And Methods

A mathematical decision analytic model consisting of hypothetical patients was parameterized in Microsoft Excel to estimate the cost effectiveness of implementing hyperbaric prilocaine instead of hyperbaric bupivacaine in the orthopedic implant surgeries in Indonesia and report incremental cost effectiveness ratio (ICER). The analyses were carried out for knee and hip implant surgeries respectively **(Figure 1a and 1b)**.

Figure 1a: Analytical decision model designed to estimate cost effectiveness between hyperbaric prilocaine vs. hyperbaric bupivacaine in knee implant surgeries in Indonesia

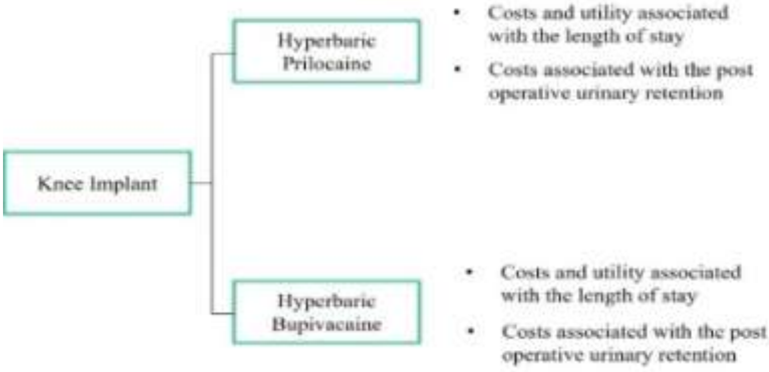
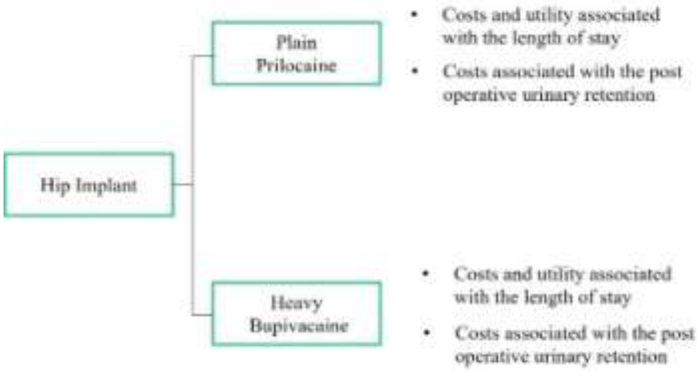


Figure 1b: Analytical decision model designed to estimate cost effectiveness between plain prilocaine vs.heavy bupivacaine in hip implant surgeries in Indonesia



A separate budget impact analysis was also carried out using the eligible patient population, set up to quantify the cost benefit scenario of using hyperbaric prilocaine instead of hyperbaric/heavy bupivacaine in Indonesia.

The study was conducted using a similar modeling approach in knee and hip implant surgeries. For knee implants the study by Thirunagari 2020[2] was available. This study was based on a single center experience in United Kingdom. It compares length of stay (in days) in hospital with hyperbaric bupivacaine (14mg) with hyperbaric prilocaine (60mg). It was taken care that outcome values for both the arms of model are taken from the same study[2].

For hip implants, a separate study by Birznieks 2019 was considered[5].The aim of this studywas to investigate the effects of same-day patient mobilization on pain, side effects, complications, duration of hospital stay, and recovery after primary hip replacement, using intermediate acting local anesthetics in spinal anesthesia (SA). Forty-six patients undergoing total hip replacement were selected and divided into two groups. Spinal anesthesia was performed in study group (P) with 70 mg plain prilocaine. The control group (B) received 18 mg heavy bupivacaine in spinal anesthesia[5]. In both knee and hip implant simulation cohorts, we considered multimodal analgesia as per a recent Indonesian study[6].We considered the usage of paracetamol 1 g and ibuprofen 800 mg by intravenous route 10 minutes before the end of surgery and every 6 hours up to 24 hours and 7.5 mg of morphine (over 24 hours)[6].

Input parameters included the cost of products (hyperbaric prilocaine and heavy/hyperbaric bupivacaine for a single surgery), and hospital length of stay (LoS) costs from a public perspective along with respective inputs from published evidence regarding the duration of LoS of prilocaine and bupivacaine for both hip and knee implants. The costs of drugs, needle, multimodal analgesia, were referred from the e-catalogue of Indonesia. The latest estimates were referenced to simulate post anesthesia urinary retention (POUR) in both the groups[7,8].The duration of length of stay was referenced based on available evidence[2,5].The utility values for orthopedic implant patients were based on study by Bischof 2023[9] and the per day length of stay related decrement in utility was factored in based on study by Cheng 2018[10]**(Table 1)**. All costs and cost savings were expressed in Indonesian Rupiah (IDR).

Table 1: Model input parameters

Sr No.	Variable	Value	Source
1.	Cost of 1 ampoule of prilocaine (IDR) (average cost*)	140,000	Market Data
2.	Cost of 1 ampoule of bupivacaine (IDR) (average cost*)	80,000	BPRS[15]
3.	24G spinal sprotte pencil-point needle (IDR) (average cost*)	90,000	BPRS[15]
4.	Cost of sterile pack of spinal tray, gloves and other sterile materials (IDR) (average cost*)	46,000	BPRS[15]
5.	Cost of ibuprofen injection 100 mg/ml (IDR)	60,384	e-katalog[16]
6.	Cost of paracetamol injection 100 mg/ml (IDR)	12,389	e-katalog[16]
7.	Cost of morphine injection 100 mg/ml (IDR)	29,900	e-katalog[16]
8.	Length of stay (prilocaine)knee implant (days)	0.5	Thirunagari 2020[2]
9.	Length of stay (prilocaine) hip implant (days)	6.91	Birznieks 2019[5]
10.	Length of stay (bupivacaine) knee implant (days)	1.5	Thirunagari 2020[2]
11.	Length of stay (bupivacaine) hip implant (days)	8	Birznieks 2019[5]
12.	Cost of one day length of stay (IDR)	500,000	e-katalog[16]
13.	Urinary retention % in hyperbaric prilocaine	1	Ambrosoli 2023[7]
14.	Urinary retention % in hyperbaric bupivacaine	9	Slaven 2023[8]
15.	Cost of urinary retention/episode (IDR)	59,000	e-katalog[16]
16.	Utility of orthopedic implant patients	0.85	Bischof 2023[9]
17.	Utility decrement due to one day length of stay in hospital	0.01	Cheng 2018[10]

*Average cost corresponds to arithmetic mean of the upper and lower range/limits of costs mentioned in BPRS

The model allows assessment of the trade-offs among various clinical and economic outcomes pertinent to both patients and decision-makers in Indonesia from a public payer perspective. The simulation was run for a cohort of 100 hypothetical patientsfor knee and100 hypothetical patients for hip implants, respectively, as two separate decision analytic models. The costs were calculated per patient by multiplying the resource use with unit costs. The cost savings and ICER were reported on a per patient basis. A deterministic analysis was carried out to determine the incremental cost effectiveness ratio (ICER) along with a probabilistic sensitivity analysis to evaluate uncertainty in the model input variables.

A time horizon of one year was considered in the model simulations and hence discounting was not included. All analysis was carried out from a public payer perspective in Indonesia. As per the availability of the data in the respective publications[2,5], we compared hyperbaric prilocaine vs. hyperbaric bupivacaine in knee implants and plain prilocaine vs. heavy bupivacaine in hip implants in our simulation model.

Due to lack of cost-effectiveness thresholds in Indonesia, treatment was considered costeffective when the calculated ICER was lesser than willingness-to-pay (WTP) thresholds of one to three times gross domestic product (GDP) per capita (GDP per capita Indonesia) (IDR 58,000,000) [17].

III. Result

The results demonstrated that hyperbaric prilocaine saves 32.58% costs as compared to hyperbaric Bupivacaine in knee implants whereas plain prilocaine saves 10.61% costs in hip implants compared to heavy bupivacaine **(Figure 2 and Figure 3)**.

Figure 2: Graph showing cost savings associated with hyperbaric prilocaine vs. hyperbaric bupivacaine in knee implants

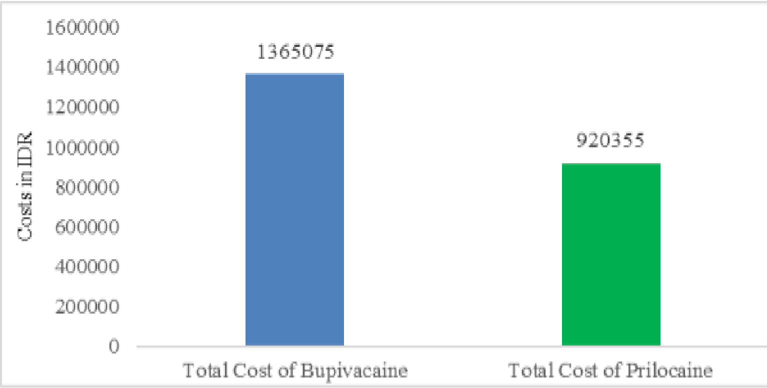
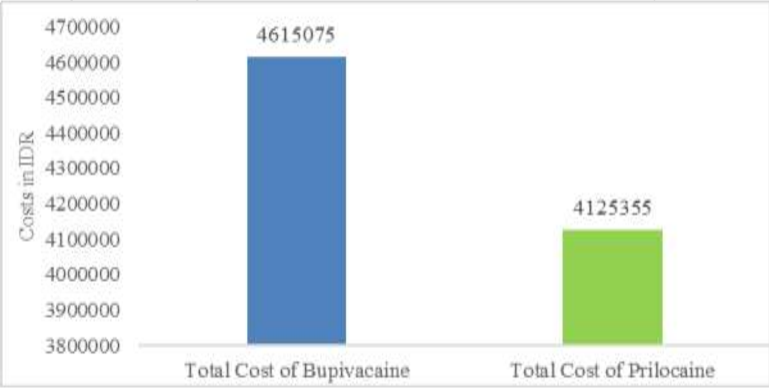


Figure 3: Graph showing cost savings associated with plain prilocaine vs. heavy bupivacaine in hip implants



Deterministic cost effectiveness analysis showed hyperbaric prilocaine was dominant over hyperbaric bupivacaine as it demonstrated reduction in costs and better gains in quality adjusted life years (QALYs) (knee implant: savings of IDR 4,44,720 per patient and incremental QALY gains 0.0023) and plain prilocaine showed similar dominance over heavy bupivacaine (hip implant: savings of IDR 4,89,720 per patient and incremental QALY gains 0.0025).**(Table 2 and Table 3)**

Table 2: ICER hyperbaric prilocaine vs. hyperbaric bupivacaine in knee implant patients

Treatment	Costs (IDR)	QALYs	Incremental Costs (IDR)	Incremental QALYs	ICER
hyperbaric prilocaine	9,203,55	0.8483	-4,447,20	0.0023	**-193241429**
hyperbaric bupivacaine	1365075	0.8460			

Table 3: ICER plain prilocaine vs. heavy bupivacaine in hip implant patients

Treatment	Costs (IDR)	QALYs	Incremental Costs(IDR)	Incremental QALYs	ICER
plain prilocaine	4,125,355	0.8335	-4,897,20	0.0025	**-195224771**
heavy bupivacaine	4,615,075	0.8310			

Probabilistic sensitivity analysis also demonstrated that prilocaine is cost effective at the willingness to pay threshold of Indonesia as the ICER scatter plot was in southeast quadrant (showing hyperbaric prilocaine is cost saving and demonstrates QALY gains in patients) **(Figure 4 and Figure 5)**.

Figure 4: ICER Scatter plot of hyperbaric prilocaine vs. hyperbaric bupivacaine in knee implant patients

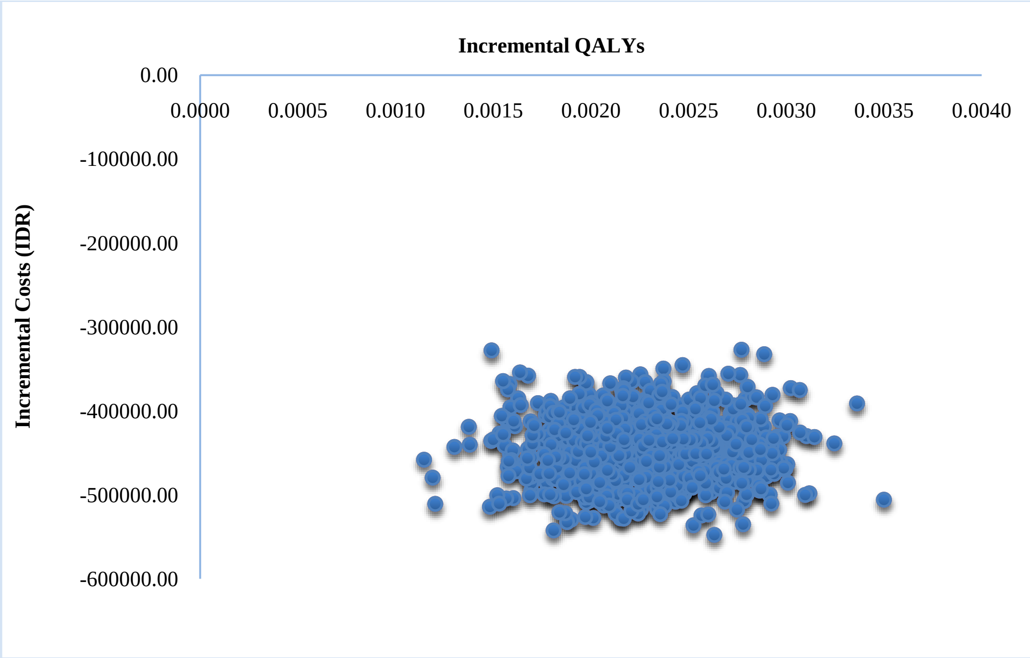
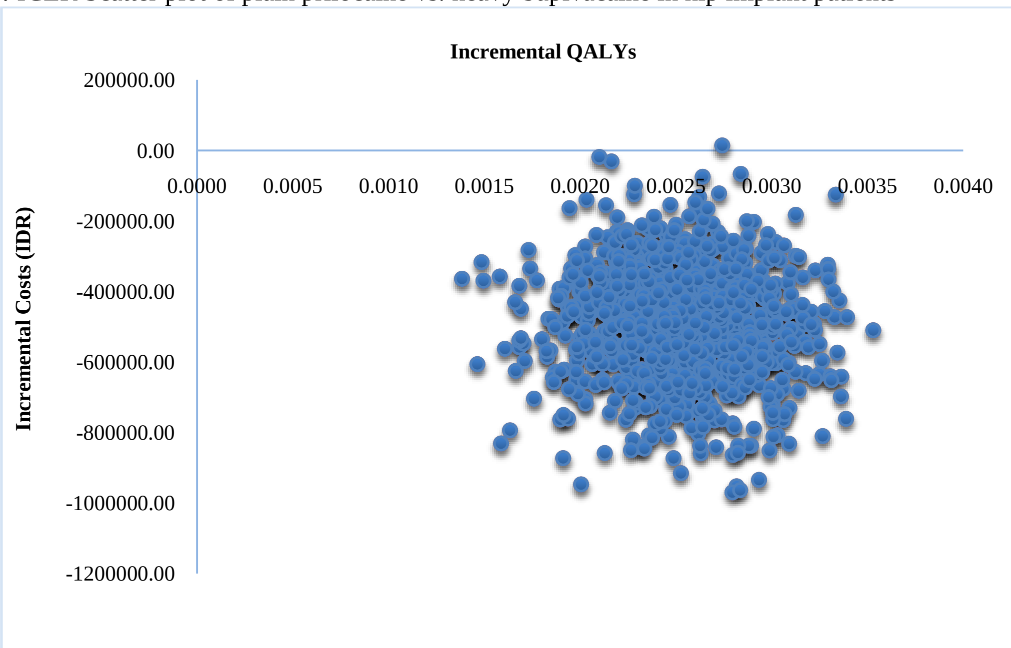


Figure 5: ICER Scatter plot of plain prilocaine vs. heavy bupivacaine in hip implant patients



NET analysis was also carried out showing cost savings across various prices of hyperbaric bupivacaine and heavy bupivacaine for both knee and hip implants **(Figure 6 and Figure 7)**.

Figure 6: NET results scatter plot comparing hyperbaric prilocaine vs. hyperbaric bupivacaine in knee implants

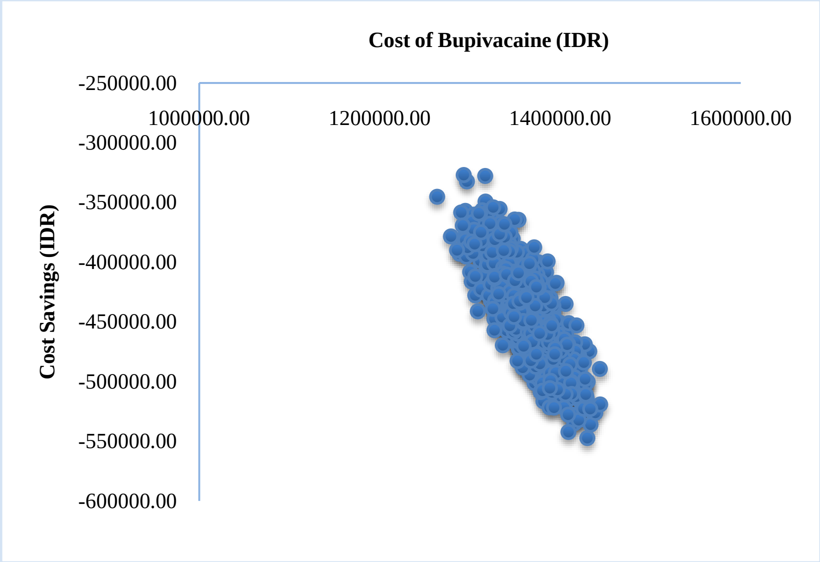
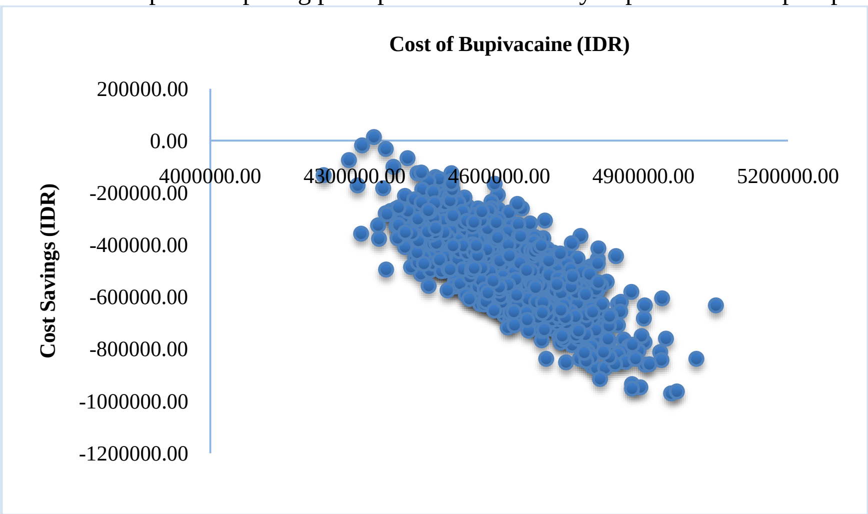


Figure 7:NET results scatter plot comparing plain prilocaine vs. heavy bupivacaine in hip implants



Cost savings comparing hyperbaric prilocaine and hyperbaric bupivacaine was plotted in a scatter plot for knee implants and plain prilocaine vs. heavy bupivacaine respectively **(Figure 8 and Figure 9)**.

Figure 8: Absolute and relative cost savings scatter plot hyperbaric prilocaine vs. hyperbaric bupivacaine in knee implant patients

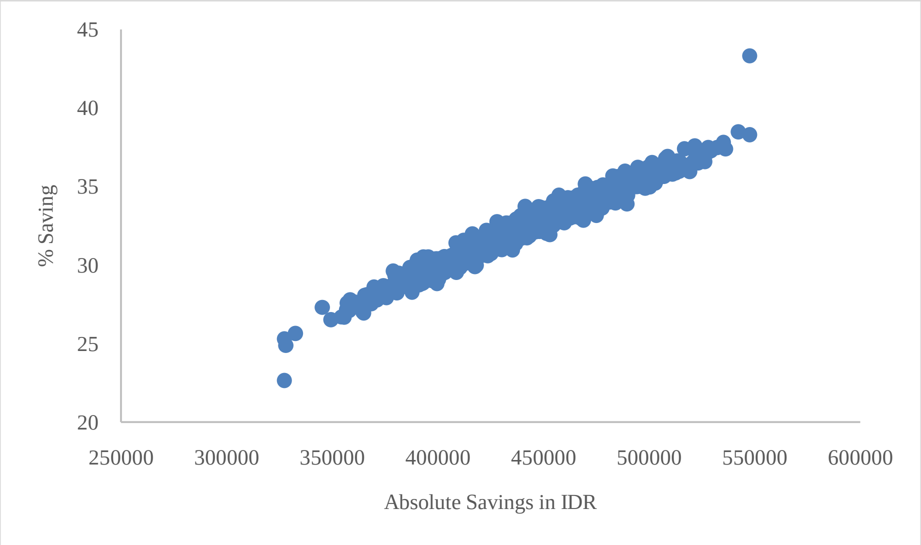
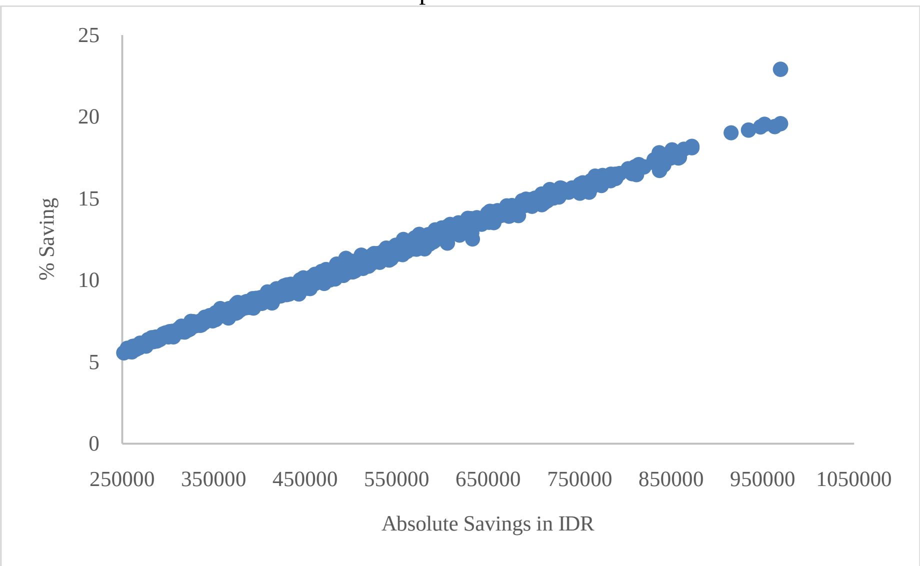


Figure 9: Absolute and relative cost savings scatter plot plain prilocaine vs. heavy bupivacaine in hip implant patients



The descriptive statistics of cost savings after probabilistic sensitivity analysis demonstrated a mean (95%CI) per patient cost savings of IDR 44,3558.48 (44,4336.96,35,719.67) for knee implants (hyperbaric prilocaine vs. hyperbaric bupivacaine) and IDR 49,3761.52 (49,7048.27,15,0808.89) comparing plain prilocaine vs. heavy bupivacaine **(Table 4)**.

Table 4: Descriptive statistics of absolute cost savings (IDR) of hyperbaric prilocaine vs. hyperbaric bupivacaine in Knee and plain prilocaine vs. heavy bupivacaine in hip implants respectively after probabilistic sensitivity analysis

Units	Knee Implants	Hip Implants
Mean	IDR 44,3558.48	IDR 49,3761.52
Median	IDR 44,3298.57	IDR 49,1407.59
SD	IDR 36,498.15	IDR 15,4095.64
Upper Confidence Interval	IDR 44,4336.96	IDR 49,7048.27
Lower Confidence Interval	IDR 35,719.67	IDR 15,0808.89

A budget impact analysis was also carried out. Considering the current population of Indonesia 27,907,2306, the number of males is 14,056,8720.53, and females is 13,850,3585.5. Out of these considering a prevalence of 15.5% in males and 12.7% in females, the approximate estimated eligible patient populationfor knee/hip implants is 21,788,151.68 males and 17,589,955.35 females[18,19]. The budget impact analyses results showed a per patient cost saving of IDR 44,4720 in knee and IDR 48,9720 per patient in hip surgeries, respectively. This demonstrated significant cost savings could be obtained if hyperbaric prilocaine is employed in orthopedic joint replacement surgeries in Indonesia.

IV. Discussion

Spinal anesthesia with prilocaine has been reported to enhance patient outcomes, reduce requirement of urinary catheters, increase patient turnover, and reduce costs across several publications[4,7,13,14].

Etriki and colleagues focused on hernia, piles, varicoceles, knee arthroscopy, hysteroscopy.[11]Similarly, some authors have focused on perianal surgeries[12] and abdominal wall herniorrhaphy[13].Similarly, length of stay has been studied by Thirunagari[2] in knee implants and Birzniecks[5] in hip implants respectively. Vagts and colleagues have reported cost benefit of using prilocaine over bupivacaine[14].

However, a formal cost utility analysis was not available in literature thus, laying the foundation of this model-based cost effectiveness investigation. The findings are in accordance with the report of Vagts and colleagues which demonstrates monetary savings via PACU time reduction using prilocaine[14].However, the current study looks at length of stay related costs and quality of life associated with orthopedic implant patients instead of PACU savings.

This is the first study which has quantified the cost and quality of life benefits due to reduced length of stay as well as reduced requirement of urinary catheters of prilocaine in comparison to bupivacaine as a spinal anesthesia in orthopedic implants.

Thus, the findings of this study might have important application as an evidence-based policy tool enabling tool for improving the efficiency of orthopedic implants in Indonesia. The utilization of prilocaine could save resource and budgets thus enabling better utilization of healthcare budgets.

Moreover, we must keep in consideration the benefits of hyperbaric prilocaine over plain prilocaine. In our study we analyzed hyperbaric prilocaine vs. hyperbaric bupivacaine in knee implants as the clinical data was available from published literature [2]. However, for hip implants we compared prilocaine vs. heavy bupivacaine owing to absence of a two-arm study of hyperbaric prilocaine vs. hyperbaric bupivacaine in hip implants. It is worth considering that even plain prilocaine demonstrated cost savings and dominance in cost effectiveness plain vs. heavy bupivacaine. A similar observation has been reported by Lovasz and colleagues,[4] who showed after launching the DCA program, using hyperbaric prilocaine, average length of stay of inpatients was reduced from 2.3 days to 1.8 days and rate of discharge with only one night stay increased from 12% to around 60%.

Our study has several limitations. Firstly, the clinical endpoints have been referenced from European populations and the model is designed for Indonesia which has an Asian population. Secondly, the studies used as inputs in the model as clinical end points in knee and hip implants have small sample sizes. To accommodate this limitation, we have included a robust probabilistic sensitivity analysis in our analyses.

V. Conclusion

Hyperbaric prilocaine provides a cost-effective option for spinal anesthesia in Indonesian population as compared to hyperbaric bupivacaine. This study highlights cost savings which could be realized with utilization of hyperbaric prilocaine in the orthopedic joint replacement surgeries in public healthcare setting in Indonesia.

References

[1]. Memtsoudis SG, Sun X, Chiu YL, Et Al. Perioperative Comparative Effectiveness Of Anesthetic Technique In Orthopedic Patients. Anesthesiology. 2013;118(5):1046-58. Doi: 10.1097/ALN.0b013e318286061d. Erratum In: Anesthesiology. 2016 Sep;125(3):610. PMID: 23612126; PMCID: PMC3956038.

[2]. Thirunagari S, Galitzine S, Alvand A.Anaesthesia For Unicompartmental Knee Replacement: Prilotekal Vs. Bupivacaine. AbstarctBritish Society Of Orthopaedic Anaesthetists. 2020. Available At: Https://Bsoa.Org.Uk/Media/Wmghha22/1thirunagari.Pdf

[3]. Manassero A, Fanelli A. Prilocaine Hydrochloride 2% Hyperbaric Solution For Intrathecal Injection: A Clinical Review. Local Reg Anesth. 2017;10:15-24.

[4]. Lovasz G, Aros A, Toth F, Va Faye J, La Malfa M. Introduction Of Day Case Hip And Knee Replacement Programme At An Inpatient Ward Is Safe And May Expedite Shortening Of Hospital Stays Of Traditional Arthroplasties. Journal Of Orthopaedic Surgery And Research. 2021;16(1):1-7.

[5]. Birznieks M, Golubovska I, Repša L, Et Al. Fast-Track Surgery And Early Rehabilitation For Total Hip Replacement In Hospital Of Traumatology And Orthopaedics. Inproceedings Of The Latvian Academy Of Sciences. Section B. Natural, Exact, And Applied Sciences. 2019; 73(5), 419-424.

[6]. Lubis AM, Maruanaya S, Tantri AR, Pontoh LAP, Ifran NNPPS. The Use Of Combination Paracetamol And Ibuprofen In Postoperative Pain After Total Knee Arthroplasty, A Randomized Controlled Trial. Pain Physician. 2021 Dec;24(8):E1199-E1204

[7]. Ambrosoli AL, Di Carlo S, Crespi A, Et Al. Safety And Effectiveness Of Prilocaine For Spinal Anesthesia In Day Surgery Setting: A Retrospective Study On A Sample Of 3291 Patients. Journal Of Anesthesia, Analgesia And Critical Care. 2023;3(1):40.
[8]. Slaven SE, Dedeogullari ES, Parks NL, Sershon RA, Fricka KB, Hamilton WG. Spinal Anesthesia For Primary Hip And Knee Arthroplasty: Comparative Rates Of Transient Neurological Symptoms And Urinary Retention Using Lidocaine, Mepivacaine, And Bupivacaine. The Journal Of Arthroplasty. 2023;38(6):S42-6.
[9]. Bischof AY, Steinbeck V, Kuklinski D, Et Al. What Is The Association Between Gender And Self-Perceived Health Status When Controlling For Disease-Specific Conditions? A Retrospective Data Analysis Of Pre-And Post-Operative EQ-5D-5L Differences In Total Hip And Knee Arthroplasty. BMC Musculoskeletal Disorders. 2023;24(1):914.
[10]. Cheng Q, Kinner SA, Lee XJ, Snow KJ, Graves N. Cost–Utility Analysis Of Low-Intensity Case Management To Increase Contact With Health Services Among Ex-Prisoners In Australia. BMJ Open. 2018;8(8):E023082.
[11]. Etriki RG, Abd Ellatif HK, Sayouh EF, Mohammed AM. Spinal Anesthesia Using Hyperbaric Prilocaine 2% Versus Hyperbaric Bupivacaine 0.5% For Day Case Surgery. The Egyptian Journal Of Hospital Medicine. 2022;87(1):1658-65.
[12]. Kaban OG, Yazicioglu D, Akkaya T, Sayin MM, Seker D, Gumus H. Spinal Anaesthesia With Hyperbaric Prilocaine In Day-Case Perianal Surgery: Randomised Controlled Trial. The Scientific World Journal. 2014;2014.
[13]. Gys B, Lafullarde T, Gys T, Janssen L. Intrathecal Prilocaine, 2-Chloroprocaine And Bupivacaine For Ambulatory Abdominal Wall Herniorrhaphy: A Prospective Observational Study. Ambul Surg. 2017;23:8-12.
[14]. Vagts DA, Bley CH, Mutz CW. Einsatz Von 2% Igem Hyperbarem Prilocain Zur Spinalanästhesie. Anaesthesist. 2013;62(4).
[15]. Bprssource:Http://Bprs.Kemkes.Go.Id/V1/Uploads/Pdffiles/Peraturan/32%20PMK%20No.%2069%20ttg%20Standar%20Tarif%20Pelayanan%20Kesehatan%20Program%20JKN.Pdf
[16]. E Katalog, Source : Https://E-Katalog.Lkpp.Go.Id/
[17]. The World Bank. GDP Per Capita (Current US$) - Indonesia | Data. The World Bank; 2022. Available From: Https://Data.Worldbank.Org/Indicator/NY.GDP.PCAP.CD?Locations=ID.
[18]. Worldometer. Available From: https://www.worldometers.info/world-population/indonesia-population/#:~:text=The%20current%20population%20of%20Indonesia,277%2C534%2C122%20people%20at%20mid%20year.
[19]. Macrotrends. Available From: https://www.macrotrends.net/global-metrics/countries/IDN/indonesia/population-growth-rate#:~:text=The%20current%20population%20of%20Indonesia,a%200.64%25%20increase%20from%202021.