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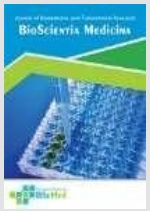

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# The Triad of Risk: Advanced Age, Female Gender, and High BMI in Patients Requiring Total Knee Replacement for Osteoarthritis at a Tertiary Indonesian Hospital

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**A B S T R A C T**

**Background:** Knee osteoarthritis (OA) imposes a substantial global burden, leading to significant disability, particularly within the elderly demographic. Total Knee Replacement (TKR) stands as the definitive surgical intervention for advanced knee OA cases that have proven refractory to comprehensive conservative management. A thorough understanding of the multifaceted characteristics of patients undergoing TKR is paramount for the development and implementation of targeted, effective healthcare strategies and resource allocation. This study aimed to meticulously identify and describe these characteristics in a cohort of patients receiving TKR at a tertiary referral hospital located in Bali, Indonesia. **Methods:** This investigation employed a descriptive quantitative cross-sectional study design. It involved a retrospective analysis of medical records pertaining to 54 patients who underwent primary TKR for diagnosed knee OA at Prof. Dr. I.G.N.G. Ngoerah General Hospital. The data collection period spanned from November 2023 to November 2024. The primary variables assessed included chronological age at the time of surgery, biological sex, body mass index (BMI) calculated from recorded height and weight, and the documented incidence of postoperative periprosthetic joint infection (PJI). All collected data were subjected to descriptive statistical analysis. **Results:** The demographic analysis revealed that the vast majority of patients were female, accounting for 85.2% (n=46) of the cohort. The predominant age group for TKR procedures was between 50 and 69 years, encompassing 85.1% of patients; specifically, the 50–59 years category included 44.4% (n=25), and the 60–69 years category included 40.7% (n=22). A notably high prevalence of overweight or obesity was observed, with 70.3% of patients falling into these BMI classifications (overweight: 37.0%, n=11; obesity class I: 27.8%, n=15; obesity class II: 9.3%, n=5). Periprosthetic joint infection, a significant postoperative complication, was documented in 5.6% of the patients (n=3) within this cohort. **Conclusion:** The findings of this study strongly indicate that advanced age, female gender, and an elevated body mass index collectively constitute a significant triad of risk characteristics among patients undergoing TKR for severe knee OA within this specific Balinese hospital setting. These observations underscore the critical necessity for focused preventive measures and tailored management strategies, particularly directed towards older women with increased BMI, to potentially mitigate the progression of OA and optimize the outcomes following TKR.

## 1. Introduction

Knee osteoarthritis (OA) is a highly prevalent and progressively debilitating degenerative joint disorder that profoundly impacts the global population, representing a substantial source of chronic pain, functional impairment, and diminished quality of life, especially among older adults. This complex musculoskeletal condition affects the entire synovial joint structure, including the articular cartilage, subchondral bone, synovium, menisci, ligaments, and

periarticular muscles. The pathological cascade in OA is characterized by the gradual breakdown of articular cartilage, aberrant bone remodeling leading to osteophyte formation, and varying degrees of synovial inflammation (synovitis). These structural alterations culminate in joint stiffness, crepitus, instability, and persistent pain, which often worsens with activity and progressively limits mobility. The global prevalence of knee OA is staggering, with estimates suggesting that hundreds of millions of individuals are affected worldwide, making it the most common form of arthritis. Data from the Global Burden of Disease studies consistently rank OA among the leading causes of disability globally, imposing immense socioeconomic costs through direct medical expenditures, indirect costs related to lost productivity, and the intangible costs of reduced patient well-being. In many developed nations, radiographic evidence of knee OA can be found in a significant majority of individuals over the age of 65, and a substantial proportion of these individuals experience clinically relevant symptoms that necessitate medical attention.[1,2]

The pathophysiology of knee OA is intricate and multifactorial, arising from a complex interplay of mechanical, biological, and inflammatory factors that disrupt the normal homeostasis of joint tissues. Historically viewed as a simple "wear and tear" disease, OA is now understood as an active and dynamic process involving aberrant chondrocyte metabolism, dysregulation of extracellular matrix synthesis and degradation, and a pro-inflammatory intra-articular environment. Key cellular players, primarily chondrocytes, become dysfunctional, leading to an imbalance between anabolic processes (synthesis of matrix components like type II collagen and aggrecan) and catabolic processes (production of matrix-degrading enzymes such as matrix metalloproteinases (MMPs) and aggrecanases (ADAMTS)). Inflammatory mediators, including cytokines like Interleukin-1β (IL-1β), Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6), and chemokines, are produced by chondrocytes, synovial cells, and infiltrating immune cells. These mediators perpetuate a cycle of inflammation and tissue degradation, contributing to cartilage erosion, synovial hypertrophy, and sensitization of nociceptive pathways, which underlie the chronic pain experienced by patients. Furthermore, the subchondral bone undergoes significant changes, including increased bone turnover, thickening (sclerosis), and the formation of bone marrow lesions, all of which are increasingly recognized as active contributors to OA pathogenesis and pain. Biomechanical factors, such as abnormal joint loading due to malalignment (varus or valgus deformity), obesity, previous joint injury (like meniscal tears or ligament ruptures), and muscle weakness, also play a critical role in initiating and propagating the degenerative process by concentrating stress on vulnerable areas of the articular cartilage.[3,4]

The management of knee OA is typically approached in a stepwise fashion, beginning with conservative, non-pharmacological interventions. These foundational strategies include patient education regarding the disease and self-management techniques, lifestyle modifications focusing on weight management for overweight or obese individuals, and structured exercise programs incorporating aerobic, strengthening, and neuromuscular exercises to improve joint stability, muscle support, and range of motion. Physical therapy plays a crucial role in designing individualized exercise regimens and providing modalities for pain relief. Pharmacological management aims to alleviate pain and reduce inflammation. Commonly used agents include simple analgesics like paracetamol (acetaminophen), topical non-steroidal anti-inflammatory drugs (NSAIDs), oral NSAIDs (both non-selective and COX-2 selective inhibitors), and in some cases, weak opioids for severe pain refractory to other treatments, though long-term opioid use is generally discouraged due to risks of dependence and side effects. Intra-articular injections are another therapeutic option. Corticosteroid injections can provide short-term relief from pain and inflammation, particularly during acute flares.

Viscosupplementation with hyaluronic acid aims to restore the viscoelastic properties of synovial fluid, though its efficacy remains a subject of ongoing debate. More recently, biologic injections, such as platelet-rich plasma (PRP) or mesenchymal stem cells, have been explored, but their role in routine OA management is still evolving and requires further robust evidence.[5,6]

When conservative measures fail to provide adequate pain relief and functional improvement, and the patient's quality of life is significantly compromised by end-stage knee OA, surgical intervention becomes the primary consideration. Total Knee Replacement (TKR), also known as total knee arthroplasty (TKA), is the definitive and most successful surgical procedure for advanced knee OA. This procedure involves the resection of damaged articular surfaces of the femur, tibia, and often the patella, and their replacement with prosthetic components typically made of metal alloys and ultra-high molecular weight polyethylene. TKR has demonstrated remarkable success in alleviating debilitating pain, restoring knee function, correcting deformity, and substantially improving the overall quality of life for the vast majority of patients. Long-term studies report excellent implant survivorship rates, often exceeding 90-95% at 10 to 15 years post-surgery. The procedure is considered highly cost-effective when compared to the ongoing costs and disability associated with unmanaged severe OA.[7,8]

Several well-established risk factors contribute to the development and progression of knee OA, ultimately leading to the necessity for TKR. Advancing age is one of the most significant non-modifiable risk factors; the prevalence and severity of OA increase markedly with each decade of life, reflecting the cumulative effects of joint loading, cellular senescence, and diminished tissue repair capacity over time. Female gender is another important risk factor, with women, particularly postmenopausal women, exhibiting a higher incidence and prevalence of knee OA compared to men. This disparity is thought to be influenced by hormonal factors (principally estrogen decline), as well as differences in joint anatomy, biomechanics, and potentially genetic predispositions. Obesity, defined by an elevated Body Mass Index (BMI), is a major modifiable risk factor. Excess body weight increases mechanical stress across the knee joints and also contributes to a systemic pro-inflammatory state through the release of adipokines from adipose tissue, both of which accelerate cartilage degradation. Other contributing factors include a history of significant knee injury (such as anterior cruciate ligament rupture or meniscal tears), certain occupational activities involving repetitive knee bending or heavy lifting, genetic susceptibility (with multiple genes implicated in OA development), and certain metabolic disorders.[9,10]

Indonesia, the world's fourth most populous country, is experiencing a rapid demographic transition characterized by an increasing proportion of elderly individuals in its population. This epidemiological shift, coupled with rising life expectancy, portends a significant increase in the burden of age-related chronic degenerative diseases, including knee OA. As the population ages and lifestyles potentially become more sedentary, the demand for TKR procedures is anticipated to grow substantially in Indonesia. Understanding the specific demographic and clinical characteristics of Indonesian patients undergoing TKR is crucial for effective healthcare planning, equitable resource allocation, optimization of surgical outcomes, and the development of culturally appropriate preventive strategies. While extensive research on TKR patient profiles exists from North American, European, and some other Asian countries, there is a relative paucity of detailed, contemporary data from specific regions within Indonesia, such as Bali. This knowledge gap limits the ability to tailor healthcare services and public health initiatives to the unique needs of the local population.

The novelty of this research is rooted in its focused, contemporary investigation of the key demographic and clinical characteristics—specifically age, gender,

body mass index (BMI), and the incidence of periprosthetic joint infection (PJI)—among patients with knee OA undergoing TKR at a prominent tertiary referral hospital in Bali, Indonesia (Prof. Dr. I.G.N.G. Ngoerah General Hospital) over a recent period (November 2023 to November 2024). This study provides valuable, localized data that contributes to a more nuanced understanding of the "triad of risk"—advanced age, female gender, and high BMI—within this specific Southeast Asian population, a demographic that has been less extensively characterized in the arthroplasty literature compared to Western cohorts. Furthermore, the study offers current insights into PJI rates in this particular institutional setting, which serves as a critical benchmark for assessing the quality and safety of arthroplasty services. By providing this specific regional profile, the research aims to fill an existing gap in the literature and offer a foundation for future comparative and analytical studies. Consequently, the primary aim of this study was to meticulously analyze and comprehensively describe the characteristics (specifically age distribution, gender ratio, BMI categories, and PJI incidence) of patients diagnosed with knee OA who underwent primary TKR at Prof. Dr. I.G.N.G. Ngoerah General Hospital between November 2023 and November 2024. This descriptive analysis endeavors to establish a detailed baseline profile of TKR recipients in this setting.

## 2. Methods

This investigation was meticulously designed and executed as a retrospective, descriptive quantitative cross-sectional study. The study was conducted within the Medical Records Department and the Orthopedic and Traumatology Clinic units of Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar, Bali, Indonesia. Prof. Dr. I.G.N.G. Ngoerah General Hospital serves as a major provincial and national referral hospital in Bali. It is a government-owned tertiary care facility equipped with specialized orthopedic services, including a dedicated arthroplasty unit performing a significant volume of TKR procedures annually for patients from across Bali and neighboring islands. The selection of this setting was purposeful, as it represents a key provider of advanced orthopedic care in the region, ensuring that the study cohort would be representative of patients accessing tertiary-level TKR services in this part of Indonesia. The retrospective data collection encompassed patients who underwent primary TKR procedures between November 1st, 2023, and November 30th, 2024, inclusive. This specific 13-month period was chosen to capture a contemporary cohort and allow for the observation of any potential variations across a full calendar year plus one additional month. The actual data abstraction from medical records, along with subsequent data cleaning, entry, and analysis, was conducted over a three-month period, from February 1st, 2025, to April 30th, 2025. This timeline was established to ensure thoroughness in data collection and processing.

The target study population consisted of all patients who had a confirmed diagnosis of primary knee osteoarthritis and subsequently underwent a primary TKR procedure at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar, during the defined 13-month study period, and whose medical records were complete and accessible. A consecutive sampling strategy was employed for the selection of study participants. This non-probability sampling method involves including all eligible patients who meet the predefined inclusion criteria as they are identified from the hospital's surgical registry or medical records database within the study timeframe. Consecutive sampling was chosen for its practicality in a retrospective setting and its ability to capture all available cases, thereby minimizing selection bias that might occur with other non-random methods and enhancing the representativeness of the sample for the period under review. All patient records that fulfilled the inclusion criteria and lacked any exclusion criteria were systematically included in the study until the data collection period concluded. Inclusion Criteria: Patients with a definitive diagnosis of primary knee osteoarthritis documented in their medical records as the principal indication for undergoing TKR. This

diagnosis would typically be based on clinical evaluation (history, physical examination) and radiographic findings (such as Kellgren-Lawrence grade III or IV); Patients who underwent a primary Total Knee Replacement procedure (unilateral or bilateral, if staged, and the first side fell within the period) during the specified timeframe of November 2023 to November 2024. Exclusion Criteria: Medical records with substantially incomplete or missing data for any of the primary study variables (age, gender, height, weight for BMI calculation, or definitive PJI status). Minor omissions of secondary data points not central to the core aims might be tolerated if the key variables were present; Patients undergoing revision TKR procedures (surgery to replace or repair a previously implanted knee prosthesis); Patients undergoing TKR for primary indications other than osteoarthritis, such as inflammatory arthropathies (like rheumatoid arthritis, psoriatic arthritis), post-traumatic arthritis where trauma was the clear primary cause without underlying advanced OA, avascular necrosis, or joint destruction due to tumor; Patients whose TKR surgery was performed outside the defined study period.

The study focused on a predefined set of variables extracted from patient medical records. These variables were: Demographic Data: Age: Recorded as the patient's chronological age in completed years at the time of the TKR surgery. For analytical purposes, age was categorized into four groups: <50 years, 50–59 years, 60–69 years, and ≥70 years; Gender: Recorded as either male or female, as documented in the patient's official medical record. Anthropometric Data: Body Mass Index (BMI): Calculated using the standard formula: weight in kilograms divided by the square of height in meters ($kg/m^2$). Height (in centimeters) and weight (in kilograms) at the time of pre-operative assessment or hospital admission for TKR were extracted from the records. BMI values were then categorized according to established classifications, specifically using Asian-Pacific guidelines where appropriate, or standard WHO cut-offs if these were the institutional norm. The categories used in the final data presentation were: Underweight ($<18.5$ $kg/m^2$), Normal (18.5–22.9 $kg/m^2$), Overweight (23–24.9 $kg/m^2$), Obesity Class I (25–29.9 $kg/m^2$), and Obesity Class II ($\geq 30$ $kg/m^2$). Clinical Outcome Data: Periprosthetic Joint Infection (PJI): Recorded as the presence or absence of a PJI diagnosed during the postoperative period, typically within 90 days of the index TKR, or later if clearly related to the index procedure. The diagnosis of PJI was based on the hospital's standard diagnostic protocols, which would ideally align with internationally recognized criteria, such as those proposed by the Musculoskeletal Infection Society (MSIS) or the International Consensus Meeting (ICM) on PJI. These criteria typically involve a combination of: Clinical findings: presence of a sinus tract communicating with the prosthesis, purulent drainage from the joint; Laboratory markers: elevated serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR); Synovial fluid analysis: elevated white blood cell (WBC) count and neutrophil percentage; Microbiological evidence: positive culture of the same organism from two or more separate intraoperative tissue or synovial fluid samples, or growth of a virulent organism in a single sample; Histopathological findings: presence of acute inflammation in periprosthetic tissues. The specific criteria applied by the institution for PJI diagnosis would have been consistently used.

Data were meticulously extracted from the physical and/or electronic patient medical records. A standardized data collection form was designed and utilized to ensure consistency and completeness in data. This form included clear fields for each variable and operational definitions where necessary. To enhance data quality, a random subset of abstracted records might have been cross-checked by a second reviewer for accuracy and inter-rater reliability, although this was not explicitly stated in the source document. All data were anonymized at the point of collection by assigning a unique study identifier to each patient record to protect patient confidentiality. Upon completion of data collection, the information

from the standardized forms was coded and entered into a digital database. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) software (the specific version, for instance, SPSS Version 25.0, IBM Corp., Armonk, NY).

The analytical approach was primarily descriptive, consistent with the study's aims. For categorical variables, such as gender, age categories, BMI categories, and the presence/absence of PJI, frequencies (n) and percentages (%) were calculated to describe their distribution within the study cohort. For continuous variables that were subsequently categorized (age and BMI), the distribution across these predefined categories was presented. The results were compiled and presented in a clear, tabular format, summarizing the key characteristics of the TKR patients. This table also included a disaggregation of the data by the year of surgery (2023 versus 2024) to allow for a preliminary observation of any potential temporal shifts or trends in patient characteristics over the relatively short study period. Narrative explanations and interpretations accompanied the table to highlight salient findings and provide context. The study was conducted with strict adherence to the ethical principles for medical research involving human subjects, as outlined in the Declaration of Helsinki and its subsequent amendments. Prior to the commencement of any data collection activities, formal ethical approval was sought and obtained from the Ethics Committee of Faculty of Medicine, Udayana University. The specific ethics approval number and date of approval should be documented in the final manuscript for transparency and verification.

**3. Results**

Figure 1, illustrating the gender distribution of patients undergoing total knee replacement (TKR) at Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali (2023-2024), reveals a striking and clinically significant finding: a profound predominance of female patients. The data indicate that out of 54 patients, a substantial 85.2% (n=46) were female, while males constituted a much smaller proportion at 14.8% (n=8). This pronounced disparity is not an isolated observation unique to this Balinese cohort but rather strongly resonates with extensive global epidemiological research on knee osteoarthritis (OA) and TKR utilization. The higher prevalence of severe, symptomatic knee OA necessitating surgical intervention in women is a well-documented phenomenon. This increased susceptibility is attributed to a complex interplay of biological, biomechanical, and potentially psychosocial factors that differentially affect women, particularly as they age. It underscores the necessity for heightened awareness and targeted healthcare strategies for women concerning knee OA. Preventive measures, particularly focusing on modifiable risk factors such as weight management (as obesity often interacts synergistically with female gender and age) and appropriate physical activity, should be emphasized for middle-aged and older women. Moreover, healthcare providers should be attuned to the earlier and potentially more severe presentation of knee OA in female patients, ensuring timely diagnosis and access to comprehensive management, including TKR when indicated. Figure 1 provides compelling visual evidence of the significant female predilection among TKR recipients in this Balinese study. This finding is deeply rooted in the complex pathophysiology of knee OA, where hormonal, biomechanical, and inflammatory factors converge to place women at a higher risk for developing debilitating forms of the disease requiring surgical intervention.

Figure 2, depicting the age distribution of patients undergoing total knee replacement (TKR) at Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali (2023-2024), highlights that the vast majority of procedures (85.1%) were performed on individuals aged between 50 and 69 years. Specifically, patients aged 50-59 years constituted the largest segment (44.4%, n=24), closely followed by those aged 60-69 years (40.7%, n=22). A smaller proportion of patients were under 50 years (5.6%, n=3) or 70 years and older (9.3%, n=5). This age profile is profoundly indicative of

the natural history and progressive nature of knee osteoarthritis (OA), which is strongly correlated with advancing age. The concentration of TKR recipients in the 50-69 year age bracket aligns with the understanding that knee OA is primarily a disease of middle and older age. The relatively smaller percentage of patients under 50 years undergoing TKR typically reflects cases of early-onset OA, which might be due to significant prior trauma, genetic predisposition, or inflammatory conditions. Conversely, while OA prevalence continues to rise beyond 70 years, the slightly lower TKR rates in the ≥70 group in this cohort could be influenced by factors such as increased surgical risk due to comorbidities, patient preference, or a perception of diminishing functional demands, though many individuals in this age group still benefit greatly from TKR. Clinically, this age distribution underscores that the 50-69 year period is a critical window where knee OA often becomes debilitating enough to warrant surgical intervention. It highlights the importance of early diagnosis and management strategies in middle age to potentially slow OA progression and delay the need for TKR. For those in this age group considering TKR, thorough preoperative assessment and optimization are crucial to ensure successful outcomes. Figure 2 effectively visualizes the age demographic most significantly burdened by end-stage knee OA requiring arthroplasty.

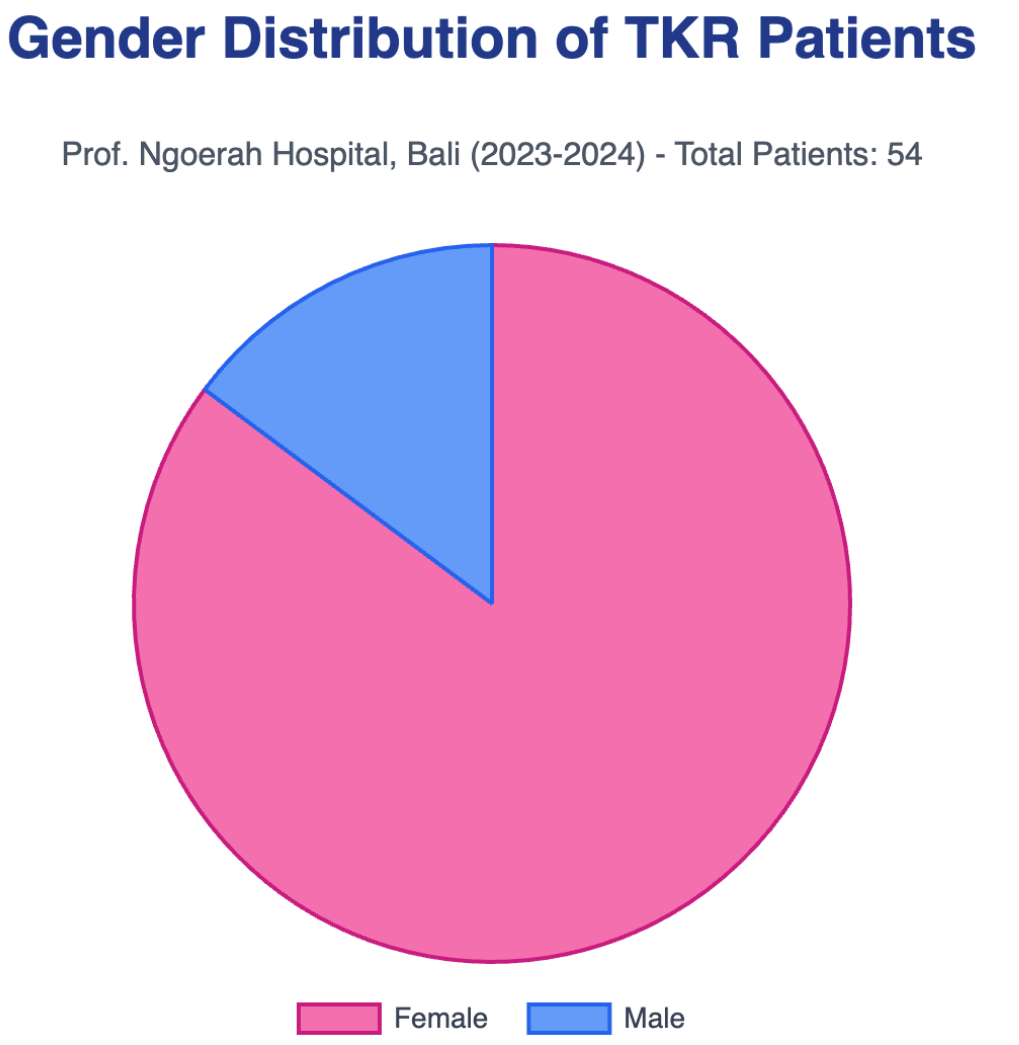


Figure 1. Gender distribution of TKR patients.

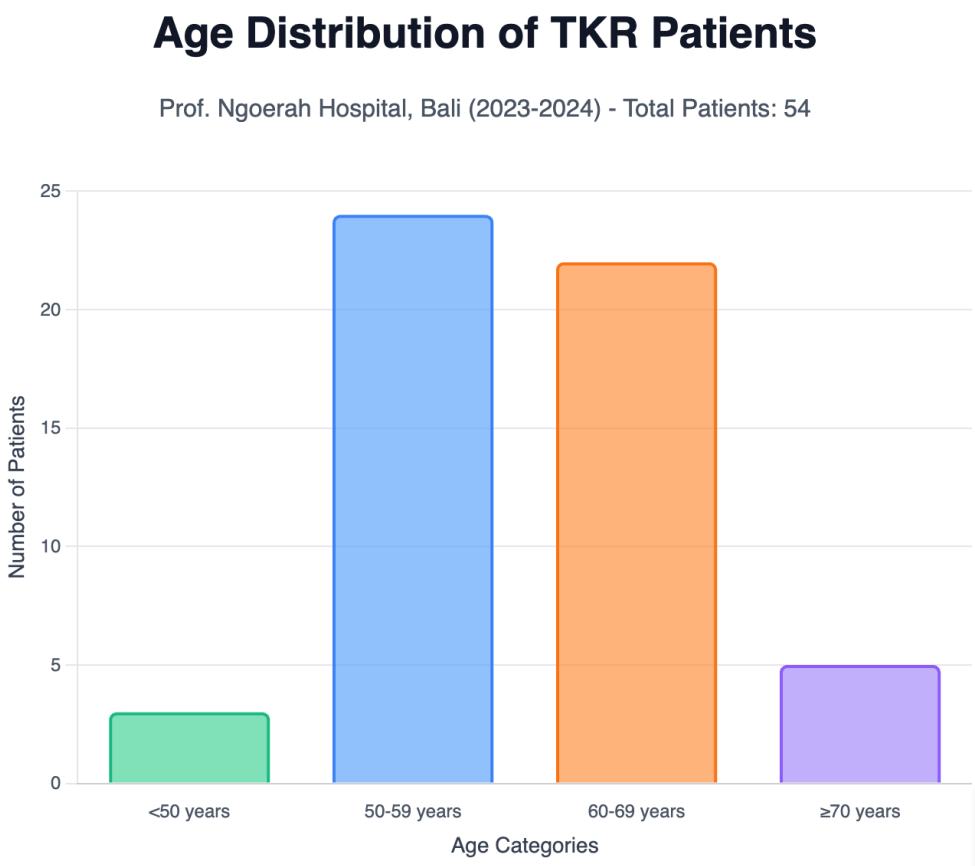


Figure 2. Age distribution of TKR patients.

Figure 3, which visually represents the body mass index (BMI) distribution of the 54 patients undergoing Total Knee Replacement (TKR) at Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali (2023-2024), presents a compelling picture of the significant role of body weight in the cohort requiring this surgery. The most striking feature is the high prevalence of patients classified as overweight or obese. Specifically, the largest single category is 'Overweight' (BMI 23-24.9 kg/m²), comprising 37.0% (n=20) of patients. This is followed by 'Obesity Class I' (BMI 25-29.9 kg/m²), accounting for 27.8% (n=15), and 'Obesity Class II' (BMI ≥30 kg/m²), representing 9.3% (n=5). Cumulatively, these three categories (Overweight, Obesity I, and Obesity II) constitute a remarkable 74.1% (n=40) of the TKR patients. In contrast, patients with a 'Normal' BMI (18.5-22.9 kg/m²) made up only 14.8% (n=8), and those classified as 'Underweight' (<18.5 kg/m²) were 11.1% (n=6). This distribution strongly underscores the well-established association between elevated BMI and the development and progression of severe knee osteoarthritis (OA) necessitating TKR. The predominance of overweight and obese individuals in Figure 3 highlights a critical target for public health interventions aimed at preventing or delaying the onset of severe knee OA. Weight management strategies, including dietary modifications and increased physical activity, are crucial. For patients with established knee OA, weight loss can significantly reduce pain, improve function, and potentially slow disease progression. The relatively small proportion of patients with normal or underweight BMI undergoing TKR suggests that while other factors (age, genetics, trauma) contribute to OA, high BMI is a powerful driver towards end-stage disease in this cohort. The

presence of underweight patients, though a minority, might indicate other underlying health issues or severe OA leading to reduced mobility and muscle wasting, which warrants further clinical consideration. Figure 3 vividly illustrates that a high BMI is a dominant characteristic among TKR patients in this Balinese study. This finding reinforces the critical importance of addressing overweight and obesity as a key strategy in mitigating the burden of knee OA and reducing the demand for TKR.

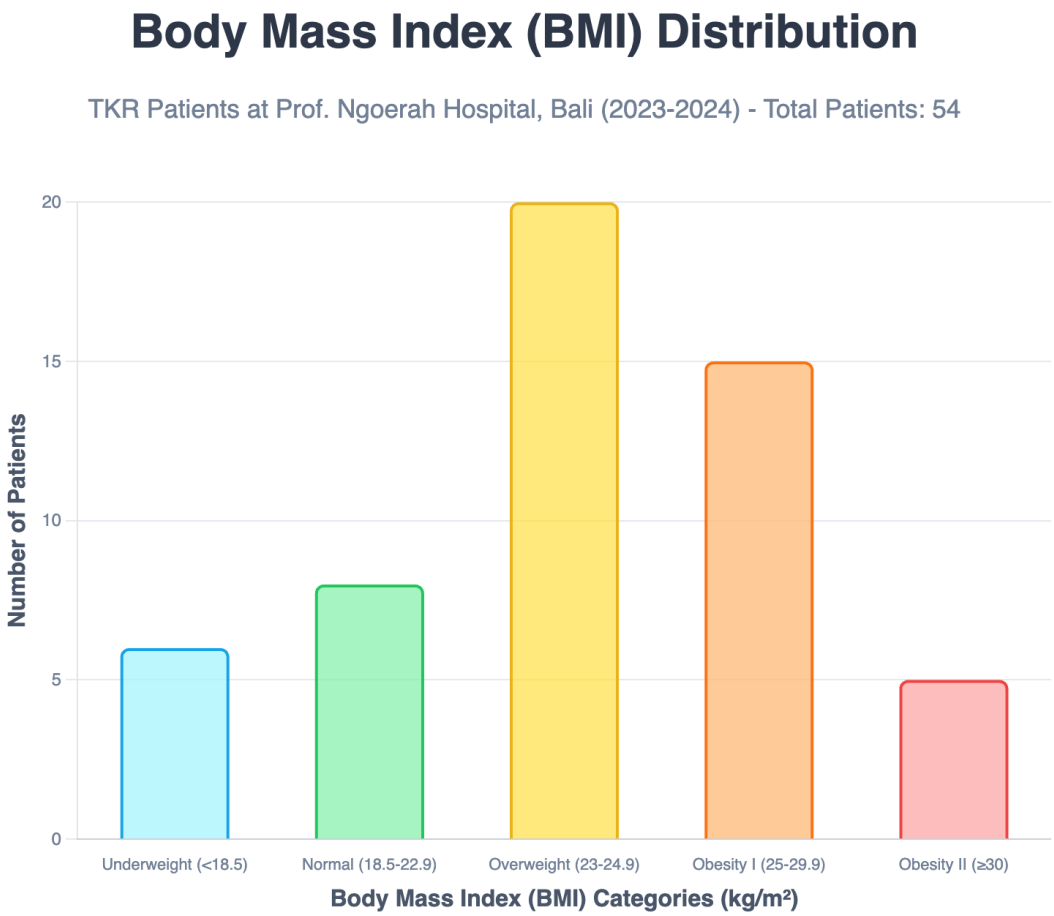


Figure 3. Body mass index distribution.

Figure 4 provides a critical insight into the safety profile of Total Knee Replacement (TKR) procedures at Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali (2023-2024) by illustrating the incidence of Periprosthetic Joint Infection (PJI). The doughnut chart clearly delineates that out of 54 patients who underwent TKR primarily for advanced knee osteoarthritis (OA), 3 patients (representing 5.6%) developed PJI, while the vast majority, 51 patients (94.4%), did not experience this severe complication. PJI is one of the most devastating complications following TKR, a surgery predominantly performed to alleviate pain and restore function in patients with end-stage knee OA. While TKR itself is highly successful, the occurrence of PJI can lead to catastrophic outcomes, including multiple subsequent surgeries, prolonged antibiotic therapy, significant patient morbidity, chronic pain, functional impairment, substantial healthcare costs, and, in rare cases, amputation or even mortality. The observed PJI

rate of 5.6% in this cohort is a crucial metric. For context, PJI rates in many high-volume arthroplasty centers in developed countries are often reported in the range of 0.5% to 2%. However, rates can vary significantly based on patient populations, healthcare settings, resource availability, and adherence to infection prevention protocols. A rate of 5.6%, while not alarmingly high compared to some global figures (which can range up to 10-15% in certain contexts), is higher than the lowest achievable benchmarks and warrants careful attention and continuous quality improvement efforts. The development of PJI is multifactorial. Patients with severe knee OA often present with risk factors that can also predispose them to PJI. These include advanced age, obesity (a common comorbidity also strongly linked to OA progression), diabetes mellitus, immunosuppression, and other systemic illnesses. These conditions can impair wound healing and the host's immune response to bacterial contamination, which can occur intraoperatively or, less commonly, via hematogenous spread. The implant itself provides a surface for bacterial adhesion and biofilm formation, making infections difficult to eradicate. From a clinical perspective, this 5.6% incidence underscores the paramount importance of rigorous infection prevention strategies in the entire perioperative pathway for TKR patients. This includes meticulous preoperative patient optimization (managing comorbidities like diabetes and obesity, smoking cessation, eradicating remote sources of infection), strict aseptic surgical techniques, appropriate antibiotic prophylaxis, maintaining a controlled operating room environment, and diligent postoperative wound care and surveillance. While knee OA itself doesn't directly cause PJI, the patient population debilitated by OA often carries inherent risks for such surgical complications. Therefore, understanding and reporting the local PJI rate, as visualized in Figure 4, is essential for benchmarking, guiding infection control policies, and ultimately improving the safety and outcomes for patients undergoing TKR to treat their disabling knee osteoarthritis.

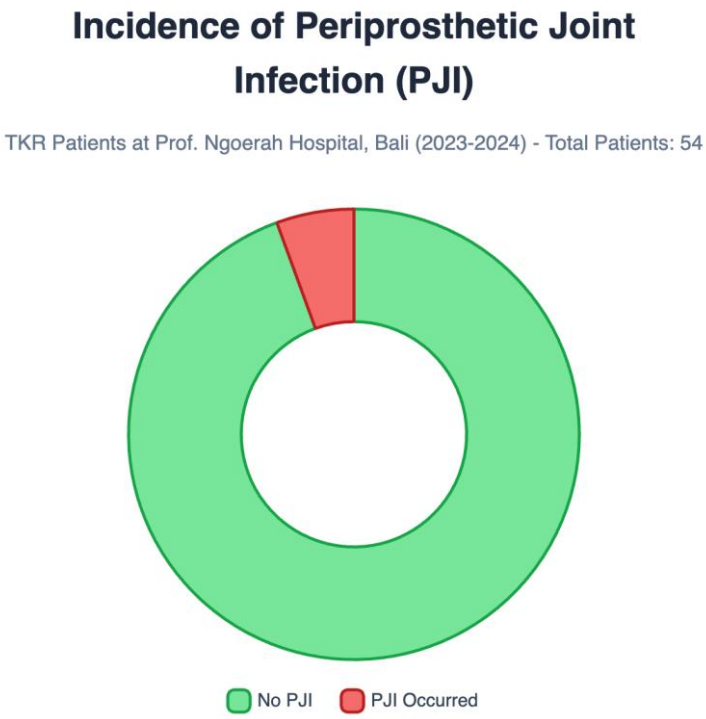


Figure 4. Incidence of periprosthetic joint infection.

## 4. Discussion

This descriptive cross-sectional study was undertaken to meticulously characterize the demographic and key clinical attributes of patients undergoing Total Knee Replacement (TKR) for advanced knee osteoarthritis (OA) at Prof. Dr. I.G.N.G. Ngoerah General Hospital, a significant tertiary care hospital in Bali, Indonesia, during the period spanning November 2023 to November 2024. The principal findings from this investigation delineate a distinct patient profile: the cohort was overwhelmingly composed of women, predominantly situated within the 50 to 69-year age stratum, and exhibited a remarkably high prevalence of body mass indices categorized as overweight or obese (specifically Class I). Furthermore, the incidence of the critical postoperative complication, periprosthetic joint infection (PJI), was found to be relatively contained. These observations not only resonate with established global trends in arthroplasty but also furnish specific, contemporary regional data that are invaluable for contextualizing the burden of severe knee OA and the characteristics of those seeking definitive surgical management in this particular Indonesian setting. The discussion will now delve into each of these key findings, exploring their alignment with existing literature, elucidating the underlying theoretical and pathophysiological mechanisms, and considering their clinical and public health implications. The observation that 85.2% of patients undergoing TKR in this Balinese cohort were female is a compelling finding, although it aligns strongly with a wealth of international literature consistently reporting a higher prevalence and incidence of severe, symptomatic knee OA, and consequently a greater utilization of TKR, among women compared to men. This female predominance has been documented across diverse geographical regions and ethnic populations. Our study noted a particularly high proportion of females (87.1%) in 2023.[11,12]

The underlying reasons for this marked gender disparity are multifaceted and involve a complex interplay of hormonal, anatomical, biomechanical, genetic, and potentially psychosocial factors. Hormonal Influences, Primarily Estrogen: The role of sex hormones, particularly estrogen, in joint health and OA pathogenesis is a significant area of research. Estrogen receptors (ERα and ERβ) are expressed in various joint tissues, including articular cartilage, subchondral bone, and synovium. Estrogen is generally considered to have chondroprotective effects. It influences chondrocyte proliferation, differentiation, and extracellular matrix synthesis, and it can modulate inflammatory responses within the joint. The sharp decline in estrogen levels experienced by women during and after menopause is strongly implicated in an accelerated rate of cartilage degradation and an increased susceptibility to OA. Postmenopausal women often exhibit a more rapid progression of OA and a higher incidence of severe symptoms necessitating TKR. Estrogen deficiency may lead to increased production of pro-inflammatory cytokines (such as IL-1β, TNF-α, IL-6) and matrix-degrading enzymes (MMPs), creating a catabolic intra-articular environment. Furthermore, estrogen influences bone metabolism, and its decline can affect subchondral bone integrity, which is crucial for overlying cartilage health. Some studies also suggest that progesterone and androgens may play roles, though their impact on knee OA in women is less clearly defined than that of estrogen. Anatomical and Biomechanical Differences: Women exhibit distinct anatomical and biomechanical characteristics in the lower limbs that may predispose them to knee OA. For instance, women typically have a wider pelvis relative to their height, which can result in a greater quadriceps angle (Q-angle). An increased Q-angle can alter patellofemoral tracking and increase lateral forces across the patellofemoral joint and potentially the tibiofemoral joint, leading to abnormal stress distribution and accelerated cartilage wear. Differences in femoral and tibial morphology, such as a narrower intercondylar notch or variations in condylar geometry, have also been reported. Furthermore, women often demonstrate greater ligamentous laxity compared to men, which can

contribute to subtle joint instability (micro-instability) and increased shear stresses on articular cartilage over time. Differences in muscle strength, particularly quadriceps strength, and patterns of muscle activation during dynamic activities may also contribute; weaker periarticular muscles provide less dynamic joint stabilization, potentially increasing loads on passive structures like cartilage and ligaments. Genetic and Inflammatory Factors: Genetic predisposition plays a role in OA, and some genetic factors may exhibit sex-specific effects. Variations in genes related to cartilage matrix proteins, inflammatory pathways, or hormonal regulation could contribute to the higher OA rates in women. Women may also exhibit different inflammatory responses compared to men. Some research suggests that women might have a more pronounced pro-inflammatory cytokine profile or a greater propensity for certain types of inflammatory responses within the joint, which could accelerate OA progression. Lifestyle and Psychosocial Factors: While not directly assessed in this study, differences in historical physical activity patterns, occupational exposures, and even psychosocial factors like pain perception and reporting could contribute. The observation in a Surabaya study, cited in the original manuscript, that many female TKR patients were homemakers, hints at potential unmeasured physical demands or cumulative exposures associated with domestic activities that might contribute to knee joint stress over decades. The consistent finding of female predominance underscores the need for sex-specific research into OA prevention and treatment, as well as targeted public health messaging for women regarding risk factor modification (especially weight management and appropriate exercise) and the importance of seeking timely medical attention for persistent knee pain.[13,14]

This study identified that the vast majority of TKR recipients (85.1%) were aged between 50 and 69 years, with the 50-59 year category being the most common (44.4%), followed closely by the 60-69 year category (40.7%). This age distribution is highly consistent with the well-established epidemiology of OA, which demonstrates a steep increase in prevalence and severity with advancing age. The age-related degenerative processes affecting joint tissues are central to OA pathogenesis. The increased susceptibility to severe OA in this age range can be attributed to several interconnected biological and biomechanical phenomena: Cellular Senescence and Chondrocyte Dysfunction: Articular chondrocytes, the resident cells of cartilage, have a limited capacity for proliferation and repair. With age, chondrocytes undergo cellular senescence, a state of irreversible growth arrest characterized by altered gene expression, reduced responsiveness to anabolic stimuli (like growth factors), and increased production of pro-inflammatory cytokines, chemokines, and MMPs – a phenomenon known as the senescence-associated secretory phenotype (SASP). Senescent chondrocytes contribute directly to matrix degradation and create a chronic, low-grade inflammatory environment within the joint ("inflammaging"). The accumulation of senescent cells in aging cartilage impairs its ability to maintain tissue homeostasis and respond to mechanical stress. Extracellular Matrix Alterations: The extracellular matrix (ECM) of articular cartilage, primarily composed of type II collagen and aggrecan, undergoes significant age-related changes. There is a decrease in proteoglycan synthesis and content, leading to reduced hydration and compressive stiffness of the cartilage. The collagen network can become more cross-linked and brittle, reducing its tensile strength and resilience. These changes make the cartilage more susceptible to mechanical damage from daily loading. The accumulation of advanced glycation end-products (AGEs) in the collagenous matrix, a result of non-enzymatic glycation over time, further stiffens the cartilage and can induce chondrocyte apoptosis and pro-inflammatory responses. Impaired Tissue Repair Mechanisms: The intrinsic repair capacity of articular cartilage is notoriously poor due to its avascular nature and the low mitotic activity of chondrocytes. With aging, these already limited repair mechanisms

become even less efficient. The recruitment and differentiation of progenitor cells may be impaired, and the response of chondrocytes to growth factors and anabolic signals diminishes. Sarcopenia and Neuromuscular Deficits: Age-related loss of muscle mass, strength, and function (sarcopenia) is common in individuals over 50. Weakness of the quadriceps, hamstrings, and hip abductor muscles reduces dynamic knee joint stability and shock absorption, leading to increased peak loads and altered load distribution across the articular surfaces. Age-related declines in proprioception (the sense of joint position) and neuromuscular control can also impair the ability to respond effectively to perturbations, increasing the risk of microtrauma and abnormal joint mechanics. Cumulative Mechanical Load and Microtrauma: Over a lifetime, knee joints are subjected to substantial cumulative mechanical loading from daily activities, occupational demands, and recreational pursuits. Even in the absence of major acute injuries, repetitive microtrauma can accumulate, leading to fatigue failure of cartilage and subchondral bone. The 50-69 age range often represents the point at which these cumulative effects, superimposed on age-related tissue degeneration, manifest as clinically significant OA requiring surgical intervention. Subchondral Bone Changes: The subchondral bone plays a crucial role in supporting the overlying cartilage and absorbing mechanical loads. Age-related changes in subchondral bone, including increased stiffness, microdamage accumulation, and altered vascularity, can negatively impact cartilage health. Increased subchondral bone stiffness may reduce its shock-absorbing capacity, transmitting greater forces to the articular cartilage. Bone marrow lesions, frequently observed on MRI in OA patients, are associated with pain and disease progression and are more common with increasing age. The concentration of TKR procedures in this age group highlights a critical window for interventions aimed at slowing OA progression and managing symptoms to potentially delay or, in some cases, obviate the need for surgery. It also underscores the importance of optimizing candidates in this age group for surgery to ensure successful outcomes, considering potential age-related comorbidities.[15,16]

The finding that 70.3% of TKR patients in this cohort were either overweight (37.0%) or obese (Class I: 27.8%; Class II: 9.3%) is a particularly salient observation and aligns with the overwhelming body of evidence identifying excess body weight as one of the most significant modifiable risk factors for the development, progression, and severity of knee OA. The proportion of patients with normal BMI notably decreased from 25.8% in 2023 to 0.0% in 2024 in this study, while underweight and overweight/obese categories saw increases, further emphasizing this trend in the more recent year of data collection. The detrimental effects of obesity on knee joint health are mediated through both mechanical and metabolic pathways: Increased Mechanical Loading: This is the most intuitive mechanism. Excess body weight directly increases the compressive and shear forces transmitted across the knee joints during weight-bearing activities such as walking, stair climbing, and rising from a chair. It is estimated that each additional pound of body weight can amplify the load on the knees by three to six pounds during walking. This chronic mechanical overloading accelerates the wear and tear of articular cartilage, can lead to meniscal damage, and contributes to subchondral bone changes. Altered gait patterns often observed in obese individuals (such as increased knee adduction moment) can further concentrate forces on specific compartments of the knee, typically the medial tibiofemoral compartment, predisposing it to more rapid degeneration. Metabolic and Inflammatory Effects (Adipokines and Metaflammation): Adipose tissue, particularly visceral adipose tissue, is now recognized as an active endocrine and immune organ that secretes a wide array of bioactive molecules collectively termed adipokines. Many adipokines, including leptin, resistin, and visfatin, have pro-inflammatory and catabolic effects on joint tissues. Leptin: While primarily known for its role in appetite regulation, leptin levels are elevated in obesity and

have been shown to promote cartilage degradation by stimulating the production of MMPs and pro-inflammatory cytokines by chondrocytes. Leptin receptors are expressed on chondrocytes. Adiponectin: Paradoxically, while adiponectin is generally considered anti-inflammatory in other contexts and its levels are often decreased in obesity, its role in OA is complex. Some studies suggest it may have pro-inflammatory effects within the OA joint under certain conditions. Resistin and Visfatin: These adipokines are also elevated in obesity and have been implicated in promoting inflammation and cartilage breakdown in OA. The systemic low-grade chronic inflammation associated with obesity, often termed "metaflammation," contributes to a pro-inflammatory intra-articular environment that is conducive to OA progression. This systemic inflammation can affect joints independently of mechanical loading, which helps explain the increased risk of OA in non-weight-bearing joints, such as those in the hand, among obese individuals. Lipid Metabolism and Oxidative Stress: Obesity is often associated with dyslipidemia (altered lipid profiles, such as high LDL cholesterol and triglycerides). Lipids and their metabolites can accumulate in joint tissues and contribute to chondrocyte dysfunction, inflammation, and apoptosis. Increased oxidative stress, another hallmark of obesity, can damage cellular components and matrix molecules within the joint, further exacerbating the degenerative process. Interaction with Other Factors: Obesity frequently coexists with other metabolic conditions like type 2 diabetes mellitus and hypertension, which are themselves independent risk factors for OA or can worsen its progression through shared inflammatory and metabolic pathways. For instance, hyperglycemia in diabetes can lead to the formation of AGEs, further damaging cartilage. The high prevalence of overweight and obesity in this TKR cohort underscores the critical public health challenge posed by rising obesity rates in Indonesia and globally. Weight management interventions, including dietary modifications and increased physical activity, are paramount in both the prevention of knee OA and the non-operative management of established disease. For obese patients undergoing TKR, pre-operative weight loss can potentially improve surgical outcomes and reduce complication rates, although achieving and maintaining significant weight loss can be challenging.[17,18]

The overall incidence of PJI in this study was 5.6% (3 out of 54 patients), with a rate of 6.5% in 2023 and a lower rate of 4.3% (or 3.2% per source table) in 2024. PJI is one of the most feared and devastating complications following TKR. Although relatively uncommon compared to the total number of successful arthroplasties performed, its consequences are severe, leading to significant patient morbidity, prolonged and often multiple hospitalizations, the need for complex and costly revision surgeries (often involving implant removal, debridement, antibiotic spacers, and subsequent reimplantation), extended courses of systemic antibiotic therapy with potential side effects, and, in some cases, permanent functional impairment, arthrodesis (joint fusion), or even amputation. The pathogenesis of PJI is complex and typically involves the introduction of microorganisms into the surgical site at the time of surgery (intraoperative contamination) or, less commonly, through hematogenous seeding from a distant infection site at a later stage. Bacterial Adhesion and Biofilm Formation: Once bacteria, most commonly Staphylococci (Staphylococcus aureus and coagulase-negative Staphylococci), gain access to the prosthetic implant surfaces, they can adhere and proliferate, forming a biofilm. A biofilm is a structured community of bacteria embedded within a self-produced matrix of extracellular polymeric substances (EPS). This EPS matrix protects the bacteria from host immune defenses (such as phagocytosis and antibodies) and significantly reduces their susceptibility to antimicrobial agents, often by factors of 100 to 1000 compared to their planktonic (free-floating) counterparts. Biofilm formation is a critical factor in the chronicity and recalcitrance of PJI. Host Immune Response: The host immune system attempts to clear

the infection, but the biofilm structure often thwarts these efforts. The inflammatory response mounted by the host, while intended to be protective, can also contribute to local tissue damage, pain, and implant loosening. Diagnostic Challenges: Diagnosing PJI can be challenging, particularly in low-grade or chronic infections where clinical signs may be subtle. Diagnosis relies on a combination of clinical evaluation, serum inflammatory markers (CRP, ESR), synovial fluid analysis (WBC count, differential, culture), intraoperative tissue cultures, and sometimes imaging or histopathology. Standardized diagnostic criteria, such as those from the MSIS or ICM, are crucial for accurate and consistent diagnosis. Risk Factors for PJI: Numerous patient-related and procedure-related factors can increase the risk of PJI. Patient-related factors include obesity, diabetes mellitus, immunosuppression (due to disease or medications), smoking, poor nutritional status, pre-existing skin infections or remote infections, male gender (in some studies), and prior surgery on the same joint. Procedure-related factors include prolonged operative time, inadequate antibiotic prophylaxis, breaks in sterile technique, operating room environment (air quality), and wound healing complications.[19,20]

The observed PJI rate of 5.6% in this Balinese cohort, while higher than the 1-2% often quoted from high-volume centers in some Western countries, falls within the broader range reported globally, especially in settings that may face different challenges in terms of patient populations or resource availability. The slight downward trend from 6.5% in 2023 to 4.3%/3.2% in 2024, if sustained and validated with larger numbers, would be a positive development, potentially reflecting ongoing efforts to optimize infection prevention protocols at the institution. These protocols typically include meticulous preoperative patient screening and optimization (addressing modifiable risk factors), standardized skin preparation, appropriate and timely administration of prophylactic antibiotics, strict adherence to sterile surgical techniques, minimizing operating room traffic, and diligent postoperative wound care and surveillance. Continuous monitoring of PJI rates and adherence to evidence-based prevention bundles are essential to minimize this serious complication.

The convergence of advanced age, female gender, and high BMI as dominant characteristics in this cohort of TKR patients in Bali paints a clear picture of the "at-risk" phenotype for end-stage knee OA in this region. This "triad of risk" is not unique to Bali, but its consistent appearance in this specific Southeast Asian setting, with contemporary data, is an important local confirmation of global trends. These findings have significant implications for the Balinese and broader Indonesian healthcare systems. Public health strategies must prioritize primary and secondary prevention of knee OA by addressing modifiable risk factors, particularly obesity, through community-based programs promoting healthy diets and physical activity. Clinical guidelines should emphasize early identification of individuals at high risk, especially older women, and advocate for proactive management strategies to slow disease progression. This could include tailored exercise programs, weight management support, and patient education on joint protection principles.

The data on PJI, while indicating a rate that warrants ongoing vigilance, also provides a local benchmark for quality improvement initiatives. Sharing such data, even from a single center, can contribute to national or regional registries and foster collaborative efforts to enhance arthroplasty safety and outcomes across Indonesia. The discussion in the original manuscript also alluded to other relevant clinical aspects often seen in TKR candidates, such as the high prevalence of bilateral disease and advanced Kellgren-Lawrence grades at presentation, suggesting that many patients endure significant symptoms and functional decline before undergoing surgery. This may reflect various factors, including access to care, patient preferences, or cultural attitudes towards surgery. The preference for spinal anesthesia and typical lengths of hospital stay also provide context for perioperative management practices in this setting. It

is also crucial to reiterate that the experience of OA pain is deeply personal and influenced by a complex interplay of biological, psychological, and social factors. Therefore, a holistic approach to patient care, extending beyond the technical success of the TKR procedure, is essential. This includes comprehensive pain management strategies, robust postoperative rehabilitation, and attention to the psychosocial well-being of patients to ensure optimal recovery and long-term satisfaction.

## 5. Conclusion

This comprehensive descriptive study, conducted at a tertiary referral hospital in Bali, Indonesia, between November 2023 and November 2024, has meticulously characterized the profile of 54 patients undergoing Total Knee Replacement (TKR) for advanced knee osteoarthritis. The investigation unequivocally identified a prominent "triad of risk" characteristics within this cohort. Firstly, there was a striking predominance of female patients, accounting for 85.2% of individuals receiving TKR. Secondly, the majority of patients were concentrated in the advanced age categories of 50 to 69 years, collectively representing 85.1% of the cohort. Thirdly, a significant proportion of patients (70.3%) presented with an elevated Body Mass Index (BMI), falling into overweight or obese classifications. These three factors—female gender, advanced age, and high BMI—emerged as the defining demographic and anthropometric features of patients progressing to end-stage knee OA requiring surgical intervention in this specific regional setting. Furthermore, the study assessed the incidence of postoperative periprosthetic joint infection (PJI), a critical indicator of surgical quality and patient safety. The overall PJI rate was found to be 5.6%. A slight decrease in PJI incidence was observed from 6.5% in 2023 to 4.3% (or 3.2%) in 2024, suggesting potential positive trends in infection control, although this requires further monitoring with larger datasets. The insights gleaned from this research bear substantial implications for both public health initiatives and clinical practice within Bali and, by extension, Indonesia. The clear identification of this high-risk patient profile underscores the urgent need for targeted preventive strategies. Public health campaigns should focus on raising awareness about modifiable risk factors for knee OA, particularly the critical role of weight management and the benefits of regular, joint-friendly physical activity, especially among middle-aged and older women. Clinicians should be vigilant in identifying patients exhibiting this risk triad early in the disease course to implement proactive management plans aimed at slowing OA progression, alleviating symptoms, and potentially delaying or obviating the need for TKR. For those patients who do require TKR, optimizing their preoperative status, particularly addressing obesity and other comorbidities, alongside meticulous perioperative care and comprehensive postoperative rehabilitation, is paramount to maximizing surgical outcomes and enhancing long-term joint function and quality of life.

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