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# Differences in the Levels of Inflammation and Infection in the Thyroid Surgery Area Between Groups with and Without Antibiotic Prophylaxis

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## ABSTRACT

***Background:*** Surgical site infections (SSIs) are infectious complications associated with all surgical procedures, occurring within 30 days post-operation or up to 90 days. The prevalence of SSIs varies and comprehensive data collection on their incidence is lacking. This study aims to determine the difference in inflammation and thyroid surgical site infections between groups with and without prophylactic antibiotics. ***Methods:*** This research is a retrospective cohort study, where data will be obtained from secondary sources in medical records. The data collected includes age, gender, ASEPSIS scores, type of surgery, duration of surgery, length of hospital stay, incidence of inflammation, infection, type of antibiotic, and administration procedure. Descriptive statistical analysis, Chi-Square Test, independent t-test, and Mann-Whitney test were conducted using IBM SPSS version 26. ***Results:*** The results of the study showed the mean age to be over 50 years, with the majority being female. The ASEPSIS score for the antibiotic group had a mean of 11.15±8.31, while the non-antibiotic group had a mean of 11.92±6.10 (p=0.766). The median duration of surgery for both groups was 1 hour (ranging from 1 to 3 hours). The antibiotic used was Cefazolin, administered at a dose of 1 gram 30 minutes before surgery, followed by 1 gram every 8 hours for 24 hours post-operation intravenously. The incidence of inflammation had an OR of 3.44 (95% CI 0.52-22.43), p=0.185. The incidence of local infection had an OR of 1.65 (95% CI 0.22-11.99), p=0.619. ***Conclusions:*** This study concludes there is no difference in the levels of inflammation and thyroid surgical site infections between the groups receiving prophylactic antibiotics and those not receiving prophylactic antibiotics.

***Keywords:*** antibiotics; surgical site infection; thyroid surgery; ASEPSIS score; inflammation level.

## INTRODUCTION

Surgical site infection (SSI) is a common complication that can occur after surgery, typically within 30 days or up to 90 days for procedures involving implants [1,2]. To prevent SSIs, many surgeons use prophylactic antibiotics. Early studies from the 1970s and 1980s showed that these antibiotics could reduce SSI rates by 5-68% [3]. However, not all surgeries require the use of antibiotics. Guidelines from various health organisations, including the Infectious Diseases Society of America (IDSA) and the Surgical Infection Society (SIS), recommend against the use of prophylactic antibiotics for clean surgeries [4,5]. Research indicates that clean surgical procedures, such as thyroid surgery, do not typically need these antibiotics, as the SSI rate is low, around 2% in patients not receiving them [6,7].

Thyroid surgery is classified as a clean surgical procedure, characterised by small incisions and short duration [2]. Consequently, the use of prophylactic antibiotics is generally not recommended unless the operation is expected to exceed three hours. Studies indicate that the incidence of SSIs in thyroid surgery is relatively low, ranging from 0.1% to 2% [8–10]. In Asia, particularly in China, the previous research reported SSI rates of 0.1% and 0.2%, respectively [8,11]. Despite this, there is a lack of comprehensive research comparing SSI rates between groups receiving and not receiving prophylactic antibiotics in thyroid surgery.

In Indonesia, the practice of administering prophylactic antibiotics in clean surgeries persists, often without adherence to established guidelines and research findings.

Many surgeons routinely prescribe prophylactic antibiotics across all surgical types, disregarding the potential risks associated with unnecessary antibiotic use [8,12]. The compliance rate with prophylactic antibiotic guidelines in Indonesia is notably low, at only 43.1%, compared to the global average of 36.3% [13,14]. This issue is particularly pronounced in thyroid surgery, where nearly all procedures involve antibiotic administration [13].

The inappropriate use of prophylactic antibiotics not only incurs unnecessary costs but also contributes to the risk of developing antibiotic resistance [15]. Therefore, it is essential to eliminate the use of prophylactic antibiotics that do not align with established guidelines [16]. In Asia, the rate of prophylactic antibiotic use in thyroid surgery is alarmingly high at 58.3% (57.4-100%), in stark contrast to only 9% in developed countries [17,18].

In our pilot study at Prof. Dr. I.G.N.G Ngoerah General Hospital, we observed a divergence in practice among clinicians regarding the administration of prophylactic antibiotics in thyroid surgery. The prevalence of SSIs varied, and no comprehensive data has been collected to date. Additionally, the inflammatory response, which precedes the onset of SSIs, has not been adequately evaluated. Previous studies have suggested that sampling from drains and their fluids can provide insights into the levels of inflammation and infection at the surgical site [19].

This research is important because there have been no studies in Bali or Indonesia comparing SSI rates between groups that receive and do not receive prophylactic antibiotics. The results will help clinicians make informed decisions about antibiotic use in thyroid surgery. This study aims to assess the differences in SSI rates between these groups and evaluate inflammation levels through drain fluid analysis. We hope that our findings will guide the development of appropriate antibiotic policies for thyroid surgery in Indonesia, especially in Bali.

## METHOD

This study employs an analytical observational design, specifically a retrospective cohort study. Data will be collected from secondary sources available in the medical records of Prof. Dr. I.G.N.G Ngoerah Denpasar Hospital. This design allows for the examination of outcomes related to thyroid surgery and the use of prophylactic antibiotics. The research will be conducted in the medical records department of Prof. Dr. I.G.N.G Ngoerah Hospital, Denpasar, from June 15 to August 15, 2023. This timeframe is selected to ensure the collection of relevant data from patients who underwent thyroid surgery during this period.

The target population for this study includes all patients diagnosed with thyroid tumours who have undergone thyroid surgery. The accessible population consists of patients treated at Prof. Dr. I.G.N.G Ngoerah Hospital from January 2023 to June 2023, who have complete medical records detailing age, gender, duration of surgery, length of hospital stays, type of prophylactic antibiotics administered, ASEPSIS score, and signs of inflammation.

Samples will be selected using consecutive sampling from the accessible population that meets the inclusion criteria and does not fall under the exclusion criteria. The inclusion criteria specify that subjects must have undergone thyroid surgery at the hospital during the specified period and have complete data. Exclusion criteria include a history of other malignancies, haematological disorders, immunosuppressive diseases, or surgeries lasting more than three hours.

The required sample size was calculated using a standard formula for comparing proportions. With an alpha level set at 0.05 (95% confidence) and a power of 80%, the minimum sample size required for each group was determined to be 13 participants. This calculation is based on the expected proportions of surgical site infections (SSIs) in groups receiving and not receiving prophylactic antibiotics.

The independent variable in this study is the type of thyroid surgery performed, specifically whether prophylactic antibiotics were administered. The dependent variables include the rate of surgical site infection (SSI) and the level of local inflammation at the surgical site. Control variables encompass demographic factors such as age, gender, duration of surgery, type of surgery, length of hospital stay, type of prophylactic antibiotics, and timing of administration.

Data will be collected using a combination of medical record reviews and observational methods. Instruments include writing materials, research forms, and computers for data entry and analysis. Primary data will be gathered directly from patient follow-ups, while secondary data will include demographic information obtained from medical records.

The study will commence following the approval of the local ethics committee. Eligible subjects will be identified through a consecutive sampling of thyroid tumour patients scheduled for surgery. Those who meet the inclusion criteria and consent to participate will be included in the study. All subjects will undergo surgery using standardised techniques, and post-operative care will be consistent across participants. The level of inflammation will be assessed based on local signs of inflammation around the surgical site. The rate of surgical site infection will be monitored for 30 days post-surgery, using the ASEPSIS scoring system to evaluate wound status. Scores above 20 will indicate the presence of an SSI.

Data processing will involve editing, coding, entry, cleaning, and saving. Descriptive statistics will be used to summarise the characteristics of the subjects and variables. Normality tests will be conducted to determine the appropriate statistical analyses, with categorical data was compared using Fisher's exact test and numerical data analysed using independent T-tests or Mann-Whitney tests as appropriate. All statistical analyses will be performed using SPSS version 26.0.

**RESULTS**

In this study, a total of 26 subjects were included, divided into two groups of 13 participants each. The characteristics of the study population are presented in Table 1. The results of the normality test for numerical data, conducted using the Shapiro-Wilk test, are also shown in Table 2, indicating that the data distribution is normal for most variables, allowing for the presentation of means ± standard deviations.

**TABLE 1:** The Characteristics of the Research Data.

| Variable | Receiving Antibiotics (n=13) | Without Antibiotics (n=13) | p-value |
|---|---|---|---|
| Age (mean ± SD) in years | 53,62±5,74 | 50,92±15,14 | 0,584[a] |
| ***Gender*** | | | |
| Male | 1 (7,7%) | 3 (23,1%) | 0,593[b] |
| Female | 12 (92,3%) | 10 (76,9%) | |
| ASEPSIS Score (mean ± SD) | 11,15±8,31 | 11,92±6,10 | 0,766[a] |
| ***Type of Thyroid Surgery*** | | | |
| Ismolobectomy | 5 (38,5%) | 3 (23,1%) | 0,697[b] |
| Lobectomy | 4 (30,8%) | 5 (38,5%) | |
| Thyroidectomy | 4 (30,8%) | 5 (38,5%) | |
| Duration of Surgery [median (min-max)] in hours | 1 (1-3) | 1 (1-3) | 0,880[c] |
| Length of Hospital Stay [median (min-max)] in days | 2 (2-3) | 2 (2-3) | 0,336[c] |
| ***Local Inflammation*** | | | |
| Yes | 2 (15,4%) | 5 (38,5%) | 0,378[b] |
| No | 11 (84,6%) | 8 (61,5%) | |
| ***Type of Antibiotic Administered*** | | | |
| Cefazolin | 13 (100%) | 0 (0%) | 1,000[b] |
| ***Timing of Antibiotic Administration*** | | | |
| 1 gram given 30 minutes before surgery, then 1 gram every 8 hours for 24 hours intravenously. | 13 (100%) | 0 (0%) | 1,000[b] |

***Note:*** *[a]independent t-test; [b]Fisher's Exact test; [c]Mann-Whitney.*

**TABLE 2:** Normality Test Results.

| Variable | p-value (Shapiro-Wilk Test) | | Description |
|---|---|---|---|
| | Receiving Antibiotics (n=13) | Without Antibiotics (n=13) | |
| Age (mean ± SD) in years | 0,918 | 0,474. | Normal |
| ASEPSIS Score | 0,055 | 0,150 | Normal |
| Duration of Surgery | 0,002 | 0,002 | Unusual |
| Length of Hospital Stay | <0,001 | <0,001 | Unusual |

The age of participants in both groups was similar, with a p-value of 0.584. The group receiving antibiotics had a mean age of 53.62 ± 5.74 years, while the group without antibiotics had a mean age of 50.92 ± 15.14 years. In terms of gender distribution, females were predominant in both groups. The Fisher's Exact test indicated no significant difference between the groups (p=0.593), with 12 females (92.3%) in the antibiotic group and 10 females (76.9%) in the non-antibiotic group.

The ASEPSIS scores were also similar between the two groups, with a mean score of 11.15 ± 8.31 for the antibiotic group and 11.92 ± 6.10 for the non-antibiotic group, resulting in a p-value of 0.766. Both groups fell into the category of disturbance of healing. The types of thyroid surgeries varied between the groups. In the antibiotic group, 5 subjects (38.5%) underwent ismolobectomy, while 4 subjects (30.8%) underwent lobectomy and thyroidectomy.

In the non-antibiotic group, 3 subjects (23.1%) had ismolobectomy, and 5 subjects (38.5%) underwent both lobectomy and thyroidectomy. The Fisher's Exact test showed no significant difference in surgery types between the groups (p=0.697).

The duration of surgery was similar in both groups, with a median of 1 hour (range 1-3 hours), and the Mann-Whitney test indicated no significant difference (p=0.880). The length of hospital stay was also comparable, with a median of 2 days (range 2-3 days), and the Mann-Whitney test showed no significant difference (p=0.336).

Local inflammation occurrences post-surgery was not significantly different between the groups, with a p-value of 0.378. In the antibiotic group, 2 subjects (15.4%) experienced local inflammation, while 5 subjects (38.5%) in the non-antibiotic group did. All subjects in the antibiotic group received Cefazolin, administered as 1 gram 30 minutes before surgery, followed by 1 gram every 8 hours for 24 hours intravenous.

To assess the differences in the proportions of inflammation and infection occurrences between the antibiotic and non-antibiotic groups, a Chi-Square test was performed, and the results are presented in Table 3.

**TABLE 3:** Bivariate Analysis Results.

| Variable | Description | | OR | 95% CI | p-value |
|---|---|---|---|---|---|
| | Yes | No | | | |
| ***Local Inflammation*** | | | | | |
| Without Antibiotics | 5 (38,5%) | 8 (61,5%) | 3,44 | 0,52-22,43 | 0,185 |
| With Antibiotics | 2 (15,4%) | 11 (84,6%) | | | |
| ***Local Infection*** | | | | | |
| Without Antibiotics | 3 (23,1%) | 10 (76,9%) | 1,65 | (0,22-11,99) | 0,619 |
| With Antibiotics | 2 (15,4%) | 11 (84,6%) | | | |

The results in Table 3 indicate that local inflammation occurred in 2 subjects (15.4%) in the antibiotic group, compared to 5 subjects (38.5%) in the non-antibiotic group, with no significant difference (p=0.185). The odds ratio for local inflammation without antibiotics was 3.44 times greater than with antibiotics, with a confidence interval of 0.52-22.43.

For local infections, 2 subjects (15.4%) in the antibiotic group experienced infections, while 3 subjects (23.1%) in the non-antibiotic group did. The statistical analysis showed no significant difference (p=0.619), with an odds ratio of 1.65 for local infections without antibiotics compared to those with antibiotics, with a confidence interval of 0.22-11.99.

## DISCUSSION

The age distribution of subjects in this study revealed that both groups were predominantly in their 50s. Thyroid surgery cases can occur across all age groups, but they are more common in adults aged 45 to 54 years, with an average diagnosis age of around 50 years[20–22]. The previous research reported an average age of 52.2 ± 13.6 years in malignant cases and 48.6 ± 14.5 years in benign cases, with a significant difference ($p < 0.01$) [23]. Similarly, the previous research found significant age differences between malignant (49.3 ± 10.4 years) and benign (41.5 ± 9.65 years) groups [24]. In contrast, two reported no significant age differences between malignant and benign groups [25,26].

Age over 50 years has been associated with a 3.9% increase in the incidence of post-operative infections. The decline in immune function with age correlates with a higher risk of infection [27].

However, the previous research found no significant relationship between age and post-thyroidectomy infection rates (p = 0.80). Gender distribution in this study showed a predominance of females [28]. The previous research reported that out of 1,113 patients with thyroid nodules, 903 were female, with no significant correlation to malignancy [21]. Thyroid nodules are four times more common in women than in men [29], with 75% of cases occurring in women, particularly those under 55 years [30]. Some studies indicate an increased risk in men, particularly those under 20 or over 70 years. However, the previous research noted that age and gender are generally not associated with malignancy [31]. Additionally, gender does not appear to influence infection rates in thyroid surgery cases [27,28].

The ASEPSIS scores in both groups fell into the category of disturbance of healing. This finding aligns with a study of 143 patients undergoing head and neck surgery, where 93.98% had ASEPSIS scores between 0-20 [32]. In a larger cohort of 2,043 patients undergoing thyroidectomy, 92% also scored between 0-20, with a mean score of 12.34 ± 3.78 [28]. The types of thyroid surgeries varied between the groups. In the antibiotic group, 5 subjects (38.5%) underwent ismolobectomy, while 4 subjects (30.8%) underwent lobectomy and thyroidectomy. In the non-antibiotic group, 3 subjects (23.1%) had ismolobectomy, and 5 subjects (38.5%) underwent both lobectomy and thyroidectomy. A previous study at Prof. Dr. IGNG Ngoerah Hospital from 2011 to 2013 found that ismolobectomy was the most common procedure, accounting for 57.58% of cases, while thyroidectomy accounted for 42.42% [33]. In Italy, 78.6% of patients who developed infections underwent thyroidectomy, while 21.4% had lobectomy [34].

The average duration of surgery was similar between the groups, with the antibiotic group averaging 1.62 ± 0.76 hours and the non-antibiotic group averaging 1.54 ± 0.66 hours. The previous research reported an average duration of 102 ± 14.8 minutes for 305 patients undergoing thyroidectomy, noting that durations exceeding 120 minutes did not significantly increase the risk of post-operative complications [35]. In this study, 100% of the patients in the antibiotic group received Cefazolin, administered as 1 gram 30 minutes before surgery, followed by 1 gram every 8 hours for 24 hours intravenously. Prophylactic antibiotic use in thyroid surgery is generally low, with only 5.7% of cases receiving antibiotics, primarily Cefazolin. Antibiotic prophylaxis is rarely performed because thyroid surgery is considered clean, and it is only administered when there is a high risk of bacterial contamination [36].

At Prof. Dr. IGNG Ngoerah Hospital, a survey of 60 surgeons revealed that 50 respondents (83.3%) understood that thyroid surgery is a clean procedure and did not require prophylactic antibiotics, while 10 respondents (16.67%) were unaware and continued to administer them. Antibiotic administration occurred in 22.2% of thyroid surgery cases [34]. Local inflammation occurred in 2 subjects (15.4%) in the antibiotic group and 5 subjects (38.5%) in the non-antibiotic group, with no significant difference ($p = 0.185$). The odds ratio for local inflammation without antibiotics was 3.44 times greater than with antibiotics, with a confidence interval of 0.52-22.43. Local inflammation is a common complication following thyroidectomy, with incidence rates reported between 5-10% of all thyroid surgeries. Factors influencing inflammation include surgical technique, patient condition, and the cleanliness of the surgical environment. Symptoms of local inflammation may include redness, swelling, heat, and pain around the surgical site, with more severe cases potentially leading to drainage of fluid or pus. Management typically involves antibiotics, proper wound care, and close monitoring by healthcare professionals. Studies indicate that implementing infection and inflammation prevention protocols, such as ensuring the sterility of surgical instruments, controlling blood sugar levels, and administering prophylactic antibiotics, can significantly reduce the risk of post-operative inflammation [37].

Local infections were observed in 2 subjects (15.4%) in the antibiotic group and 3 subjects (23.1%) in the non-antibiotic group, with no significant difference ($p = 0.619$). The odds ratio for local infections without antibiotics was 1.65 times greater than with antibiotics, with a confidence interval of 0.22-11.99. The overall incidence of infections was found to be only 0.09% among 2,926 patients undergoing thyroid surgery [34]. Meta-analysis results indicate that the incidence of SSI after thyroidectomy ranges from 0.09% to 2.9%. International guidelines do not recommend routine prophylactic antibiotic use for thyroidectomy procedures [36].

Post-thyroidectomy, the risk of local infections varies. SSI can be classified into three types: superficial incisional infections, deep incisional infections, and organ/space infections. Data suggest that the incidence of SSI in surgical procedures, including thyroidectomy, can reach 5-10% [38]. Risk factors for increased infection likelihood include patient conditions such as weakened immune systems, prolonged pre-operative hospital stays, and microbial colonization. Prophylactic antibiotic use before surgery plays a crucial role in reducing infection risk. To minimize infection risk, implementing "Bundles SSI" protocols is highly recommended, which include measures before, during, and after surgery, such as pre-operative antiseptic bathing, blood sugar control, and maintaining aseptic techniques during the procedure.

## CONCLUSIONS

This study concludes that there is no significant difference in local inflammation or infection rates between patients who received prophylactic antibiotics and those who did not during thyroid surgery. Most patients were in their 50s, with a higher prevalence among females, which aligns with previous research. ASEPSIS scores indicated some disturbance in healing, but overall infection rates were low. These results support current guidelines that do not recommend routine use of prophylactic antibiotics for clean thyroid surgeries. The findings highlight the need for adherence to established protocols and suggest further research to improve patient outcomes while reducing unnecessary antibiotic use.


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