

Assessment of perioperative antibiotic prophylaxis for gynecological surgeries at an academic hospital in Brazil

Avaliação da profilaxia antibiótica perioperatória para cirurgias ginecológicas em um hospital universitário no Brasil

Evaluación de la profilaxis antibiótica perioperatoria para cirugías ginecológicas en un hospital académico de Brasil

Received: 06/17/2021 | Reviewed: 06/24/2021 | Accept: 06/29/2021 | Published: 07/13/2021

Denise Ramos dos Santos

ORCID: <https://orcid.org/0000-0002-0945-1129>

Federal University of Rio de Janeiro, Brazil

E-mail: deniseramos@ig.ufrj.br

Milene Rangel da Costa

ORCID: <https://orcid.org/0000-0001-8153-1492>

Federal University of Rio de Janeiro, Brazil

E-mail: milene@ufrj.br

Abstract

The aim of this study was to assess the adequacy of physicians' practice patterns regarding the use of perioperative antibiotic prophylaxis for gynecological surgeries in an academic hospital specialized in gynecology located at Rio de Janeiro city, Brazil. This is a retrospective study assessing all gynecological surgeries performed over one year. Appropriateness of antibiotic prophylaxis was determined according to criteria adapted from evidence-based guidelines. Clinical practice regarding the use of perioperative antibiotic prophylaxis was considered appropriate for 58.4% of 416 surgeries. The non-indicated use of antimicrobial prophylaxis was the main factor determining the low percentage of overall adequacy. Three variables were independently associated with inappropriate administration of perioperative antibiotics: patients age, breast surgeries and longer procedures. Antibiotic prophylaxis compliance to published recommendations is low. Women undergoing gynecological surgery are exposed to unnecessary risks associated to non-indicated use of antibiotic prophylaxis. Strategies aimed to improve compliance to evidence-based guidelines are necessary.

Keywords: Antibiotic prophylaxis; Gynecologic surgical procedures; Practice patterns, physicians'.

Resumo

O objetivo deste estudo foi avaliar a adequação da prática clínica quanto ao uso de profilaxia antimicrobiana em cirurgias ginecológicas em um hospital universitário especializado em ginecologia localizado na cidade do Rio de Janeiro, Brasil. Este é um estudo retrospectivo que avaliou todas as cirurgias ginecológicas realizadas ao longo de um ano. A adequação da profilaxia antimicrobiana foi determinada de acordo com critérios adaptados de diretrizes clínicas nacionais e internacionais. As condutas médicas quanto ao uso de profilaxia antimicrobiana foram consideradas adequadas em 58,4% de 416 cirurgias. O uso não indicado de profilaxia antimicrobiana foi o principal fator determinante do baixo percentual de adequação geral. Três variáveis foram independentemente associadas à administração perioperatória inadequada de antimicrobianos: idade da paciente, cirurgias mamárias e procedimentos de maior duração. Conclui-se que a profilaxia antimicrobiana praticada no hospital diverge das recomendações disponíveis. Mulheres submetidas às cirurgias ginecológicas estão expostas a riscos desnecessários associados ao uso não indicado da profilaxia antimicrobiana. Estratégias de promoção da adesão dos profissionais a diretrizes baseadas em evidências são necessárias.

Palavras-chave: Antibioticoprofilaxia; Procedimentos cirúrgicos em ginecologia; Padrões de prática médica.

Resumen

El objetivo de este estudio fue evaluar la adecuación de los patrones de práctica de los médicos con respecto al uso de profilaxis antibiótica perioperatoria para cirugías ginecológicas en un hospital académico especializado en ginecología ubicado en la ciudad de Río de Janeiro, Brasil. Se trata de un estudio retrospectivo que evalúa todas las cirugías ginecológicas realizadas durante un año. La idoneidad de la profilaxis antimicrobiana se determinó de acuerdo con criterios adaptados de las guías basadas en evidencia. La práctica clínica sobre el uso de profilaxis antibiótica perioperatoria se consideró apropiada para el 58,4% de 416 cirugías. El uso no indicado de profilaxis antimicrobiana fue el principal factor determinante del bajo porcentaje de adecuación global. Tres variables se asociaron de forma

independiente con la administración inadecuada de antibióticos perioperatorios: edad de las pacientes, cirugías de mama y procedimientos más prolongados. El cumplimiento de la profilaxis antibiótica con las recomendaciones publicadas es bajo. Las mujeres sometidas a cirugía ginecológica están expuestas a riesgos innecesarios asociados al uso no indicado de profilaxis antibiótica. Son necesarias estrategias destinadas a mejorar el cumplimiento de las pautas basadas en la evidencia.

Palabras clave: Profilaxis antibiótica; Procedimientos quirúrgicos ginecológicos; Pautas de la práctica en medicina.

1. Introduction

Surgical site infections (SSI) are the most frequent surgical complication in developing countries and affect as many as 11% of patients undergoing surgical procedures (Allegranzi et al., 2011). In Brazil, they account for 14% to 16% of all nosocomial infections (ANVISA, 2009), with the highest incidence being among obstetric or gynecological patients (Clifford & Daley, 2012; Jaiyeoba, 2012). Most of SSI are preventable if perioperative antimicrobial prophylaxis (PAP) is available (Allegranzi et al., 2011). According to the World Health Organization (WHO), appropriate PAP is defined as "administering an effective antimicrobial agent prior to exposure to contamination during surgery" (WHO, 2018).

PAP is widely accepted as an effective measure to reduce the risk of SSI and their undesirable outcomes, such as increased length of postoperative hospital stay, healthcare costs, and mortality (Bratzler & Hunt, 2006; Çakmakçı, 2015; Clarke-Pearson & Geller, 2013; Kamat et al., 2000; Kirkland et al., 1999). Different national and local clinical practice guidelines recommend PAP as the standard of care for different types of obstetric and gynecological procedures (ACOG, 2018; ANVISA, 2017; ASBrS, 2018; Bratzler et al., 2013; van Eyk, 2010; van Eyk, 2012; Leaper et al., 2008; Morrill et al., 2013).

However, improper use of antibiotic prophylaxis compromises its efficacy. Many studies have shown that irrational antibiotic use for PAP is still a common problem worldwide and it is frequently related to inappropriate selection of a broad-spectrum antibiotic, prolonged duration of PAP, incorrect timing of prophylaxis and un-indicated use (Abubakar et al., 2018; Alemkere, 2018; Viamonte & Cherres, 2016; Wright et al., 2013). There is great variability in PAP used for gynecological surgeries and it frequently does not conform to the published recommendations (Abubakar et al., 2018, Joyce et al, 2015; Kremer et al., 2018; Schimpf et al., 2015; Wright et al., 2013). The consequences of improper utilization include adverse drug reactions, development of bacterial resistance and increased healthcare costs (Burke, 2001; van Kasteren et al., 2003).

Therefore, the quality and use of PAP have been the subject of various studies (Abubakar et al., 2018; Burke, 2001; Joyce et al, 2015; Kremer et al., 2018; van Kasteren et al., 2003; Schimpf et al., 2015; Wright et al., 2013). Drug utilization studies could give useful insight about PAP patterns and provide valuable information for the improvement of PAP practices to ensure proper and effective administration of PAP. Nevertheless, there is scarce literature on PAP utilization for gynecological procedures in Brazil. Thus, the objective of this study was to assess physicians' practice patterns regarding the use of PAP in the light of evidence-based guidelines at a university hospital in Brazil.

2. Methodology

This is a retrospective cross-sectional study on the adequacy of PAP in gynecological and breast surgery. All women over 18 years old who underwent surgery in the Gynecology Institute of the Federal University of Rio de Janeiro, Brazil, in 2017 were included in the study population. Women whose medical records were incomplete or those undergoing antibiotic treatment were excluded.

Data were obtained manually from patients' medical charts by a clinical pharmacist. Data collection was carried out using a standardized form and included: age, weight and height of the patient; admission and discharge dates; type of surgery; date timing and duration of surgery; type of antibiotics used (if used), dose, timing of administration and duration (including first and subsequent doses); blood loss greater than 1,5 L. Surgeries were classified into two groups: gynecological surgery

(which included all types of procedures except of those on breasts) and breast surgery.

PAP appropriateness was assessed according to criteria adapted from the recommendations of the American Society of Health-system Pharmacists (ASHP) (Bratzler et al., 2013) American College of Obstetricians and Gynecologists (ACOG, 2018), American Society of Breast Surgeons (ASBrS, 2020) and the Brazilian Health Regulatory Agency (ANVISA, 2017). Practice pattern regarding the use of PAP was considered adequate if: (i) it was not indicated and was not used or (ii) it was indicated and used properly, which meant meeting all following five criteria:

1. choice of antibiotic: first-generation cephalosporin cefazolin as first choice.
2. dose and administration: 2.0 g intravenous or 3.0 g if patient weight > 120 Kg.
3. timing of administration relative to time of surgery: administration within 60 min before incision.
4. duration of administration: do not exceed 24 h after conclusion of surgery.
5. perioperative re-administration: only necessary if surgery lasts longer than 4h after first dose or in case of blood loss > 1.5 L.

Antibiotic consumption was calculated as the number of Defined Daily Dose (DDD) per 100-procedures using the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) index (2020) by the World Health Organization (WHO) Collaborating Centre for Drugs Statistics Methodology (WHO, 2020).

Bicaudal Student's t-test and z-tests were used to compare means and proportions, respectively. The relationship between categorical variables and PAP appropriateness was evaluated by the Chi-square test or Fisher exact tests, as appropriate. A logistic regression model was estimated to evaluate the effect of different variables on PAP adequacy. Statistical analysis was performed using R software considering a 5% level of significance. Both authors contributed equally to the design of the study and analysis of data. This research was approved by the University's Research Ethics Committee under the reference number CAAE: 44399715.4.0000.5403.

3. Results

In total, 555 women underwent gynecological or breast surgical procedures during the study period. Among them, 416 were eligible for inclusion in the analysis. The mean age, weight and body mass index (BMI) were 47.7 ± 14.1 years, 71.8 ± 15.5 Kg and 28.2 ± 5.6 Kg/m², respectively. A total of 306 (73.6%) women underwent gynecological surgery and 110 (26.4%) breast surgery. The most frequent gynecological procedures were total abdominal hysterectomy, cervical tissue excision and gynecological exeresis/biopsy. Regarding breast surgeries, mastectomy (bilateral or unilateral) was the most frequent followed by nodulectomy. Mean duration of the surgeries and hospitalization were 103.1 ± 63.9 min and 2.5 ± 1.5 days, respectively. Patient and surgery characteristics are shown in Table 1.

Overall proportion of PAP use was 92.8%. Intravenous cefazolin (ATC J01DB04) was used as single antibiotic for PAP in all procedures. Antimicrobial prophylaxis was administered within 60 min prior to incision in 97.4% of the surgeries. Duration of PAP was within intraoperative phase for 89.4% of procedures and a second dose of cefazolin was used in 5.7% of the cases. PAP characteristics are shown in Table 2.

Clinical practice regarding the use of PAP was considered appropriate for 58.4% of 416 surgeries. Overall adequacy of PAP was significantly different ($p < 0.05$) between surgery types. Gynecological procedures showed a lower proportion of PAP adequacy (52.9%) compared to breast surgeries (73.6%). The use of antimicrobial prophylaxis when it was not recommended was the main factor determining the low percentage of overall adequacy. Out of 113 surgeries with no indication for PAP, it was performed in 101 (89.4%). The opposite also occurred as PAP was not performed in 21 (6.9%) out of 303 surgeries for which antibiotic prophylaxis should be used. Adequacy proportion per criteria and type of surgery is shown in Table 3. It is worth noting that among the cohort of patients for whom PAP was recommended and performed (N=282),

antibiotic use met all five quality criteria in 231 cases, resulting in a overall adequacy of 81.9% in this group of patients.

Table 1: Patient and surgery characteristics.

Characteristic	Total population (N = 416)
	<i>Mean ± SD</i>
Age (years)	47.7 ± 14.1
Weight (Kg)	71.8 ± 15.5
BMI (Kg/m ²)	28.2 ± 5.6
Surgery duration (min)	103.07 ± 63.88
Hospitalization lenght (days)	2.47 ± 1.46
	<i>Count (%)</i>
<i>Gynecological surgeries</i>	306 (73.6)
Hysterectomy	99 (23.8)
Cervical tissue excision	53 (12.7)
Exeresis/biopsy	44 (10.6)
Prolapse repair	37 (8.9)
Myomectomy	21 (5.0)
Others	52 (12.5)
<i>Breast surgeries</i>	110 (26.4)
Mastectomy	68 (16.3)
Nodulectomy	32 (7.7)
Others	10 (2.4)

BMI: body mass index, SD: standard deviation. Source: Authors.

Table 2: Perioperative antibiotic prophylaxis characteristics.

Characteristic	Total population (N=386)*
<i>Type o antibiotic</i>	386 (100)
cefazolin	
<i>Administration route</i>	
intravenous	386 (100)
<i>Dose</i>	
2,000 mg	386 (100)
<i>PAP administration</i>	
within 60 min prior to incision	376 (97.4)
above 60 min prior to incision	6 (1.6)
after incision	4 (1.0)
<i>PAP duration</i>	
within intraoperative phase	343 (89.1)
above intraoperative phase	42 (10.9)
above 24h after surgery	11 (2.8)
<i>Second dose of antibiotic</i>	
no	364 (94.3)

*Patients that received antibiotic prophylaxis. PAP: perioperative antibiotic prophylaxis. Source: Authors

Table 3: Perioperative antibiotic prophylaxis adequacy according to quality criteria and type of surgery.

Criteria	Adequacy proportion (%)		
	Total	Gynecological surgery	Breast surgery
Indication*	70.7	66.3	82.7
Choice of antibiotic	100	100	100
Dose and administration route	100	100	100
Timing of administration relative to time of surgery	97.9	97.4	98.9
Duration of administration*	96.1	99.0	90.4
Perioperative re-administration*	85.6	81.2	94.7
Overall adequacy*	58.4	52.9	73.6

*Statistically significant differences ($p < 0.05$) between gynecological and breast surgeries. Source: Authors.

Univariable analysis revealed that patient age, type of surgery and procedure duration were significantly associated ($p = 0.000$) with practice pattern appropriateness. Obese patients and those who spent more than 2 days in hospital after surgery were no more likely to receive adequate PAP (Table 4). According to the multivariate analysis, clinical practice regarding PAP for patients older than 45 years old was more likely to be adequate (OR = 2.280; 95% CI, 1.503 – 3.457), the same occurred in the case of breast surgeries (OR = 2.823; 95% CI, 1.687 – 4.724) and surgeries that lasted more than 100 minutes (OR = 2.537; 95% CI, 1.456 – 4.421). The variables obesity and hospitalization length did not significantly affect the odds of PAP adequacy (Table 5). Antibiotic consumption was 72,9 DDD of cefazolin per 100 surgeries. Inappropriate use of PAP accounted for 27,1% of all antibiotic doses that were administered.

Table 4: Proportion of patients receiving adequate preoperative antibiotic prophylaxis according to patient and surgery characteristics.

Characteristic	Adequacy (%)	<i>p</i> -value
<i>Age</i>		
45 years old or younger	47.4	0.000
older than 45 years old	68.2	
<i>Obesity (BMI > 30 kg/m²)</i>		
yes	57.7	0.915
no	58.7	
<i>Type of surgery</i>		
gynecological	52.9	0.0000
breast	73.6	
<i>Surgery duration</i>		
100 minutes or less	49.8	0.0000
> 100 minutes	68.2	
<i>Hospitalization length</i>		
2 days or less	55.6	0.115
> 2 days	62.8	

p-values based on Chi-square test or Fishers exact test as appropriate. Source: Authors.

Table 5: Logistic regression predicting adequacy of preoperative antibiotic prophylaxis according to patient and surgery characteristics.

Variable	Adjusted odds ratio	CI95%	p-value
<i>Age</i>			
45 years old or younger	referent		
older than 45 years old	2.280	[1.503 – 3.457]	0.0000
<i>Obesity (BMI > 30 kg/m²)</i>			
no	referent		
yes	1.054	[0.675–1.647]	0.8180
<i>Type of surgery</i>			
gynecological	referent		
breast	2.823	[1.687 – 4.724]	0.0000
<i>Surgery duration</i>			
100 minutes or less	referent		
> 100 minutes	2.537	[1.456 – 4.421]	0.0000
<i>Hospitalization length</i>			
2 days or less	referent		
> 2 days	1.024	[0.580 – 1.809]	0.9341

CI95%: 95% confidence interval. Source: Authors.

4. Discussion

The aim of this study was to analyze the compliance of physicians' practice patterns with evidence-based guidelines regarding the use of antibiotic prophylaxis. Our data suggest that while the density of perioperative antimicrobial use is high, the incidence of inappropriate utilization is frequent and affected 58,4% of the analyzed procedures. Non-indicated use of PAP was the determinant factor for the poor alignment to guidelines recommendations.

The inadequacy of antibiotic prophylaxis for gynecological procedures has already been described in the literature. Wright et al. (2013) studied 545,332 gynecological procedures performed at more than 500 hospitals in the United States between 2003 and 2010 and found that 40.2% of women received non-indicated preoperative antibiotics. Joyce et al. (2015) who studied 326 surgeries performed from 2012 to 2013 at tertiary care hospital found that PAP was used in 53.7% of procedures with no indication. More recently, Kremer et al. (2018) analyzed 2,961 gynecological cases at a tertiary hospital and found that the overall proportion of preoperative antibiotic use for procedures in which antibiotics were not indicated was 19%. The study from Abubakar et al. (2018) that evaluated compliance with surgical antibiotic prophylaxis in obstetrics and gynecological surgeries performed at 3 tertiary hospitals in Nigeria found the proportion of unnecessary antianaerobic combination to be as much as 89.3%.

In our study, the proportion of non-indicated preoperative antibiotics was significantly high, reaching almost 90%. In fact, there was no record of occurrences that could justify such use, for instance, prolonged surgery, unplanned entrance into the abdomen or excessive blood loss (Kremer et al., 2018). The overuse of antibiotics is well known to increase patient morbidity and healthcare costs. Besides subjecting patients to unnecessary toxicity, it may contribute to antimicrobial resistance. These consequences emerge as even more important considering the scarcity of resources and budget constraints of the Brazilian healthcare system.

Some factors were significantly associated with appropriateness of PAP when other variables were controlled. Older patients were more likely to receive adequate PAP as well as patients undergoing breast surgery and those requiring longer surgeries. Interestingly, Wright et al. (2013) also found that older age is protective from using non-indicated PAP in

gynecological procedures whereas the study conducted by Kremer et al. (2018) revealed that inappropriate use of PAP is less likely to occur the longer the surgery lasts. One possible explanation could be that older patients would require more complex procedures which in turn could result in longer surgeries. Perhaps such characteristics could influence physicians' practice, making them more prone to comply with recommendations.

Even though previous studies about antibiotic prophylaxis adequacy in gynecological procedures were carried out in different settings and countries, their findings are aligned regarding the unsatisfactory PAP compliance to evidence-based guidelines. In our study, although the surgeries were performed at a teaching hospital specialized in gynecological procedures, there is no established local guideline for antibiotic prophylaxis nor explicit recommendations for the adoption of published ones. The fact that literature on antibiotic prophylaxis in various gynecological procedures is scarce, and hence recommendations on specific procedures are unavailable could, at least in part, explain practice variations and PAP misuse.

Patients and students could both benefit from the implementation of strategies designed to promote evidence-based practice dissemination. Besides the reduction of unnecessary treatments and their consequent economic burden (Brook, 2011), the adoption of a formalized protocol could improve patient security and health outcomes (Stulberg et al., 2010).

5. Conclusion

Inappropriate use of antibiotic prophylaxis in women undergoing gynecological surgeries is prevalent and the results of the present study corroborate it. The implementation of antibiotic stewardship strategies in our institution is necessary to reduce the use of PAP in women that are unlikely to benefit from it. Additionally, further broadening of existing guidelines and the inclusion of other types of gynecology procedures would contribute to reduce antibiotic misuse. Future studies addressing the factors that influence PAP could contribute to improvement of clinical practices.

References

- Abubakar, U., Sulaiman, S. A., & Adesiyun, A. G. (2018). Utilization of surgical antibiotic prophylaxis for obstetrics and gynaecology surgeries in Northern Nigeria. *Int J Clin Pharm*, 40(5), 1037–1043. <https://doi.org/10.1007/s11096-018-0702-0>
- Agência Nacional de Vigilância Sanitária. (2009). *Sítio cirúrgico. Critérios nacionais de infecções relacionadas à assistência à saúde*. Gerência Geral de Tecnologia em Serviços de Saúde, Gerência de Investigação e Prevenção das Infecções e dos Eventos Adversos. https://www.anvisa.gov.br/servicosaude/manuais/criterios_nacionais_isc.pdf
- Agência Nacional de Vigilância Sanitária. (2017). *Medidas de prevenção de infecção relacionada à assistência à saúde* (2nd ed.). Gerência de Vigilância e Monitoramento em Serviços de Saúde, Gerência Geral de Tecnologia em Serviços de Saúde. <http://www.riocomsaude.rj.gov.br/Publico/MostrarArquivo.aspx?C=pCiWUy84%2BR0%3>
- Alemkere, G. (2018). Antibiotic usage in surgical prophylaxis: A prospective observational study in the surgical ward of Nekemte referral hospital. *PLoS One*, 13(9), e0203523. <https://doi.org/10.1371/journal.pone.0203523>
- Allegranzi, B., Nejad, S. B., Combescure, C., Graafmans, W., Attar, H., Donaldson, L., & Pittet, D. (2011). Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. *Lancet*, 377(9761), 228–241. [https://doi.org/10.1016/S0140-6736\(10\)61458-4](https://doi.org/10.1016/S0140-6736(10)61458-4)
- American College of Obstetricians and Gynecologists. (2018). Prevention of infection after gynecologic procedures: ACOG practice bulletin, number 195. *Obstet Gynecol*, 131(6), e172–e189. <https://doi.org/10.1097/AOG.0000000000002670>
- American Society of Breast Surgeons. (2017). *Consensus Guideline on Preoperative Antibiotics and Surgical Site Infection in Breast Surgery*. https://www.breastsurgeons.org/about/statements/PDF_Statements/Antibiotics_SurgicalSiteInfection.pdf
- Bratzler, D. W., & Hunt, D. R. (2006). The surgical infection prevention and surgical care improvement projects: national initiatives to improve outcomes for patients having surgery. *Clin Infect Dis*, 43(3), 322–330. <https://doi.org/10.1086/505220>
- Bratzler, D. W., Dellinger, E. P., Olsen, K. M., Perl, T. M., Auwaerter, P. G., Bolon, M. K., Fish, D. N., Napolitano, L. M., Sawyer, R. G., Slain, D., Steinberg, J. P., & Weinstein, R. A. (2013). Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Surg Infect (Larchmt)*, 14(1), 73–156. <https://doi.org/10.1089/sur.2013.9999>
- Brook, R. H. (2011). The role of physicians in controlling medical care costs and reducing waste. *JAMA*, 306(6), 650–651. <https://doi.org/10.1001/jama.2011.1136>
- Burke, J. P. (2001). Maximizing appropriate antibiotic prophylaxis for surgical patients: an update from LDS Hospital, Salt Lake City. *Clin Infect Dis*, 33(s2), S78–S83. <https://doi.org/10.1086/321861>

- Çakmakçı, M. (2015). Antibiotic stewardship programmes and the surgeon's role. *J Hosp Infect*, 89(4), 264–266. <https://doi.org/10.1016/j.jhin.2015.01.006>
- Clarke-Pearson, D. L., & Geller, E. J. (2013). Complications of hysterectomy. *Obstet Gynecol*, 121(3), 654–673. <https://doi.org/10.1097/AOG.0b013e3182841594>
- Clifford, V., & Daley, A. (2012). Antibiotic prophylaxis in obstetric and gynaecological procedures: a review. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, 52(5), 412–419. <https://doi.org/10.1111/j.1479-828X.2012.01460.x>
- van Eyk, N., van Schalkwyk, J., & Infectious Diseases Committe. (2012). Antibiotic prophylaxis in gynaecologic procedures. *J Obstet Gynaecol Can*, 34(4), 382–391. [https://doi.org/10.1016/S1701-2163\(16\)35222-7](https://doi.org/10.1016/S1701-2163(16)35222-7)
- Jaiyeoba, O. (2012). Postoperative infections in obstetrics and gynecology. *Clinical Obstetrics and Gynecology*, 55(4), 904–913. <https://doi.org/10.1097/GRF.0b013e3182714734>
- Joyce, J. S., Langsjoen, J., Sharadin, C., Kuehl, T., & Larsen W. (2015). Non-Indicated Prophylactic Antibiotic use in Gynecologic Surgery. *J Minim Invasive Gynecol*, 22(3), S55–S56. <https://doi.org/10.1016/j.jmig.2014.12.113>
- Kamat, A. A., Brancazio, L., & Gibson M. (2000). Wound infection in gynecologic surgery. *Infect Dis Obstet Gynecol*, 8(5-6), 230-234. <https://doi.org/10.1155/S1064744900000338>
- van Kasteren, M. E. E., Kullberg, B. J., de Boer, A. S., Mintjes-de Groot, J., & Gyssens, I. C. (2003). Adherence to local hospital guidelines for surgical antimicrobial prophylaxis: a multicentre audit in Dutch hospitals. *J Antimicrob Chemother*, 51(6), 1389–1396. <https://doi.org/10.1093/jac/dkg264>
- Kirkland, K. B., Briggs, J. P., Trivette, S. L., Wilkinson, W. E., & Sexton, D. J. (1999). The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. *Infect Control Hosp Epidemiol*, 20(11), 725–730. <https://doi.org/10.1086/501572>
- Kremer, K. M., Foster, R. T., Drobnis, E. Z., Hyde, K. J., & Brennaman L. M. (2018). Non-indicated use of prophylactic antibiotics in gynaecological surgery at an academic tertiary medical centre. *J Obstet Gynaecol*, 38(4), 1-5. <https://doi.org/10.1080/01443615.2017.1371119>
- Leaper, D., Burman-Roy, S., Palanca, A., Cullen, K., Worster, D., Gautam-Aitken, E., & Whittle, M. (2008). Prevention and treatment of surgical site infection: summary of NICE guidance. *BMJ*, 337, a1924. <https://doi.org/10.1136/bmj.a1924>
- Morrill, M. Y., Schimpf, M. O., Abed, H., Carberry, C., Margulies, R. U., White, A. B., Lowenstein, I., Ward, R. M., Balk, E. M., Uhlig, K., & Sung, V. W. (2013). Antibiotic prophylaxis for selected gynecologic surgeries. *Int J Gynaecol Obstet*, 120(1), 10–15. <https://doi.org/10.1016/j.ijgo.2012.06.023>
- van Schalkwyk, J., van Eyk, N., & Infectious Diseases Committe. (2010). Antibiotic prophylaxis in obstetric procedures. *J Obstet Gynaecol Can*, 32(9), 878–884. [https://doi.org/10.1016/S1701-2163\(16\)34662-X](https://doi.org/10.1016/S1701-2163(16)34662-X)
- Schimpf, M. O., Morrill, M. Y., Margulies, R. U., Ward, R. M., Carberry, C. L., & Sung, V. W. (2012). Surgeon practice patterns for antibiotic prophylaxis in gynecologic surgery. *Female Pelvic Med Reconstr Surg*, 18(5), 281–285. <https://doi.org/10.1097/SPV.0b013e31826446ba>
- Stulberg, J. J., Delaney, C. P., Neuhauser, D. V., Aron, D. C., Fu, P., & Koroukian, S. M. (2010). Adherence to surgical care improvement project measures and the association with postoperative infections. *JAMA*, 303(24), 2479–2485. <https://doi.org/10.1001/jama.2010.841>
- Viamonte, R. K., & Cherres, J. P. E. (2016). Profilaxis antibiótica preoperatoria en pacientes con cirugías ginecológicas en el Hospital “Homero Castanier Crespo.” *Rev Cubana Obstet Ginecol*, 42(4), 543–556. <http://scielo.sld.cu/pdf/gin/v42n4/gin15416.pdf>
- Wright, J. D., Hassan, K., Ananth, C. V., Herzog, T. J., Lewin, S. N., Burke, W. M., Lu, Y., Neugut, A. I., & Hershman, D. L. (2013). Use of guideline-based antibiotic prophylaxis in women undergoing gynecologic surgery. *Obstet Gynecol*, 122(6), 1145–1153. <https://doi.org/10.1097/aog.0b013e3182a8a36a>
- World Health Organization. (2018). *Global guidelines for the prevention of surgical site infection* (2nd ed.). World Health Organization. <https://apps.who.int/iris/handle/10665/277399>
- World Health Organization Collaborating Centre for Drug Statistics Methodology. (2020). WHOCC - ATC/DDD Index. Whocc.no. https://www.whocc.no/atc_ddd_index/