

# Evolution of microbial ecology: A rare multidrug-resistant (*Enterobacter cloacae*) surgical wound infection after cesarean delivery: Our experience of 5946 cesarean deliveries

 Zeynep Bayramoglu<sup>1</sup>,  Erhan Okuyan<sup>2</sup>,  Hayrettin Tay<sup>2</sup>,  Adem Yoldas<sup>2</sup>

<sup>1</sup>Konya Education and Research Hospital, Clinic of Pathology, Konya, Turkey

<sup>2</sup>Batman Maternity and Child's Health Hospital, Clinic of Gynecology and Obstetrics, Batman, Turkey

Copyright © 2020 by authors and Annals of Medical Research Publishing Inc.

## Abstract

To demonstrate the rapidly changing multidrug-resistant microbial environment and its challenges from the viewpoint of microbiologists, pathologists, and obstetricians. In our research; upon our encounter with a rare multidrug resistance wound infection following a cesarean section; we retrospectively analyzed 5946 cesarean sections performed in our clinic between 2017-2019. Of the 5946 patients, 978 (16.44%) were literate and 4968 (83.56%) were illiterate. The average age of our patients is 23.44 and their average weight is 78.35 kg. The number of patients taken to emergency cesarean was 954, and 4992 of our patients were operated due to recurrent cesarean section. The number of patients operated under general anesthesia was 347, and 5599 patients received spinal anesthesia. In 2 years, 5946 patients had surgical site infection in 23 (0.39%) patients. Only one of our patients had multidrug-resistant *Enterobacter Cloacae*. None of our patients with surgical site infection had maternal mortality. Drug-resistant bacterial infection increases hospital stay, healthcare costs, and mortality, and for all nations, this problem is growing exponentially. Nowadays, understanding the multifactorial genetic basis of multidrug resistance should investigate genetic signatures in invasive infection.

**Keywords:** Evolution of microbial ecology; multidrug-resistant *Enterobacter Cloacae*; surgical wound infection

## INTRODUCTION

Cesarean section is the major surgical procedure that we use to manage complications during normal delivery. It is a major surgery that is very important for mother and baby health and can cause very important complications for both mother and newborn (1). Postoperative complications, which are more frequently observed in parallel with the increase in recurrent cesarean operations, contribute to maternal morbidity (2). In wound infections observed after cesarean section, one of the biggest concerns of obstetricians is personal hygiene factors and the other is obesity (3,4). Today, some examples of measures taken for postoperative wound infection include; sterile garments in the preoperative period, antiseptic procedures in the perioperative period, prophylactic antibiotic use in the postoperative period and surgical field care (5). Despite all these precautions, post-cesarean wound complications remain an economic and sociological problem all over the

world. Surgical wound infection is an infection that occurs in the area or organs that are operated within the first 30 days following surgery.

Surgical wound infection is standardized by centers for disease control and prevention and diagnostic criteria include; a-infection includes skin and subcutaneous tissues related to the incision line b-occurs within 30 days following the operation. c- in addition, at least one of the following factors must be accompanied. ; 1- Determinations of the microorganism in the culture of tissue and fluid were taken from the incision line under sterile conditions. 2- Purulent drainage from the incision line 3-Localized swelling, increased tenderness, redness and increased temperature accompanied by at least one of the findings 4-Surgeon suspected of infection (6,7). The contact of sterile amniotic fluid with the flora of the genital and gastrointestinal tract during the cesarean section is also a predisposing factor for infection in

**Received:** 21.12.2019 **Accepted:** 27.03.2020 **Available online:** 23.05.2020

**Corresponding Author:** Erhan Okuyan, Batman Maternity and Child's Health Hospital, Clinic of Gynecology and Obstetrics, Batman, Turkey **E-mail:** dreo06@hotmail.com

the pelvic organs (8). Bacterial infections are 5-20 times higher in pregnant women delivered by cesarean section when compared to normal vaginal delivery. *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus* species, Coagulase-negative staphylococcus are the most common pathogens detected in surgical wound infections (9,10). Multidrug resistance of bacteria isolated from surgical wound infection areas continues to increase with each passing day worldwide, therefore, It continues to increase maternal morbidity, hospital costs, and length of hospital stay and remains a very important and serious socio-economic problem.

It is observed that; the antibiotics that will be effective in the fight against multidrug resistance bacteria in surgical field infections in cesarean section patients are decreasing day by day (11). Risk factors of surgical wound infections after cesarean delivery is related to factors such as premature rupture of membranes, repeated cesarean section, prolonged labor, chorioamnionitis, gestational diabetes mellitus, obesity, and lack of preoperative personal hygiene. *Enterobacter* family is one of the most frequently isolated microorganisms in nosocomial infections, causing a wide spectrum of infections including genitourinary tract infections, respiratory system infections, and septicemia. As multidrug-resistant *Enterobacter* infections have become increasingly common in recent years, it has increased the interest of scientists on this microorganism. In a revolutionary article published by Annavajhala MK and colleagues in January 2019 reported that It is predicted that the multidrug-resistant *Enterobacter* family can be solved by genomic research in the coming years for the determination of unexplained factors among virulence factors, drug resistance development mechanisms and virulence factors (12). We wrote a common complication in obstetric practice cause of a rare pathogen, its results and our experience from the viewpoint of microbiologist, pathologist, and obstetrician.

## MATERIAL and METHODS

In our research; upon our encounter with a rare multidrug resistance wound infection following a cesarean section; we retrospectively analyzed 5946 cesarean sections performed in our clinic between 2017-2019. In the patient registration data kept in our clinic; literate status, age, weight, number of cesarean section and indications were achieved. Hospital stay, personal hygiene status, height, concomitant diseases, type of complications developed and antibiotic regimens applied could not be recorded.

## RESULTS

When we look at the cesarean indications and percentages in our research; it was observed that this operation was performed at the highest rate in the last 2 years due to the previous cesarean section. In our clinic, no maternal death was observed in pregnancy and the postpartum period between 2017-2019, and newborn records could not be reached.

Of the 5946 patients, 978 (16,44%) were literate and 4968 (%83,56) were illiterate. The average age of our patients is 23.44 and their average weight is 78.35 kg. The number of patients taken to emergency cesarean was 954, and 4992 of our patients were operated due to recurrent cesarean section. The number of patients operated under general anesthesia was 347, and 5599 patients received spinal anesthesia. In 2 years, 5946 patients had surgical site infection in 23 (0.39%) patients (Table 1). Our caesarean indications other than recurrent cesarean are summarized in Table 2. Only one of our patients had multidrug-resistant *Enterobacter Cloacae*. None of our patients with surgical site infection had maternal mortality (Table 3).

**Table 1. Accessible information of 5946 cesarean operations between 2017-2019**

Literate	978 (16.44%)
illiterate	4968 (%83.56)
Average Age (years)	23.44
Average weight (kg)	78.35
Emergency Cesarean section	954 (16.05%)
Repeated Cesarean section	4992 (83.95%)
Spinal anesthesia	5599
General anesthesia	347

**Table 2. Our caesarean indications other than recurrent cesarean**

Fetal Distress(worsening in fetal well-being)	%6.12
Cephalopelvic disproportion	%0.70
Brech presentation	%1.54
Twin pregnancies	%0.60
Hypertensive diseases(Preeclampsia)	%2.2
Macrosomic fetus	%1.04

When we examine our patient with *Enterobacter Cloacae* infection in detail, a 30-year-old patient with G9P8, 120 kilograms, had diet regulated gestational diabetes was admitted to our emergency unit due to premature rupture of membranes. In the ultrasonographic examination, the estimated fetal weight was measured as 4950 g and a cesarean decision was made. A single, live, 4950 gr, a male baby was delivered with first-minute APGAR score 9 and fifth-minute APGAR score 10. The patient was morbidly obese (Picture-1), preoperative 1 gram cefazolin prophylaxis was performed and maximum attention was paid to antisepsis rules. Perioperative subcutaneous tissue was washed with sterile saline and the patient was admitted to the gynecology service. The patient was discharged with full recovery at 48th hour with no early complication. The patient was admitted to the emergency department at 96th postoperative hour with the complaint of localized pain, swelling and redness and yellow discharge

in the incision line she had been feeling for about 4 hours. Her vital signs included a temperature of 37.5° C, a heart rate of 110/min, and a blood pressure of 85/47 mmHg. There was a malodorous, seropurulent discharge from the incision and dehiscence of approximately 3 centimeters was observed in the midline of the incision. The patient had a white blood cell count of 33K/mm<sup>3</sup> and C-reactive protein was 195 mg/L. The patient was admitted to the gynecology department with the diagnosis of surgical site infection after cesarean section. Skin sutures are fully opened due to very intense smelly seropurulent discharge. Before antibiotic prophylaxis was started, the infectious diseases specialist was consulted and wound samples were obtained by sterile culture bar, aspiration with a sterile needle from the seropurulent collection and tissue biopsies taken from the surgical infection area and sent to the laboratory (13,14). While waiting for wound culture results, abscess and exudate formations were evacuated 3 times a day and necrotic tissues were debrided with a scalpel. The necrotic tissues that were observed in the incision line, extending to a width of approximately 7 centimeters and a depth of 6 centimeters, were treated with wet to dry dressing six times a day, therefore, the wound was replaced with a sterile slightly moistened gauze and covered with sterile dry gauze (15). In the microscopic examination of the tissue, mixed type inflammation consisting of neutrophils, macrophages, plasma cells, and lymphocytes was observed in adipose tissue and fibrous tissue (Figure 1). Also, necrosis has been seen.

The infected wound line was left open for secondary healing. Wound culture was detected as multidrug-resistant *Enterobacter cloacae* at the 48th hour of hospitalization (Table 4).

Antibiotic sensitive	Antibiotic resistant	Antibiotic resistant
Daptomycin	Ciprofloxacin	Erythromycin
Amikacin	Levofloxacin	Fusidic acid
Linezolid	Gentamicin	Rifampicin
Antibiotic sensitive	Antibiotic resistant	Antibiotic resistant
Teicoplanin	Ampicillin	Clindamycin
Vancomycin	Amoxicillin/clavulanic acid	Tetracycline
	Cefoxitin,TMP/SMX	Oxacillin, Pen G

In consultation with infectious disease specialists, the antibiotic regimen was changed to Ceftriaxone 2 grams per day and vancomycin 2 grams per day. On the 6th postoperative day, the majority of the necrotic tissues recovered and the seropurulent discharge was not observed, so secondary suturing was decided (Figure 2). The patient was discharged from the hospital on the third day after reoperation with complete recovery in the laboratory findings and physical examination.

Cesarean Delivery number of last 3 years	Surgical site infection number of last 3 years	Rate	Maternal mortality
5946	23	0.39	None

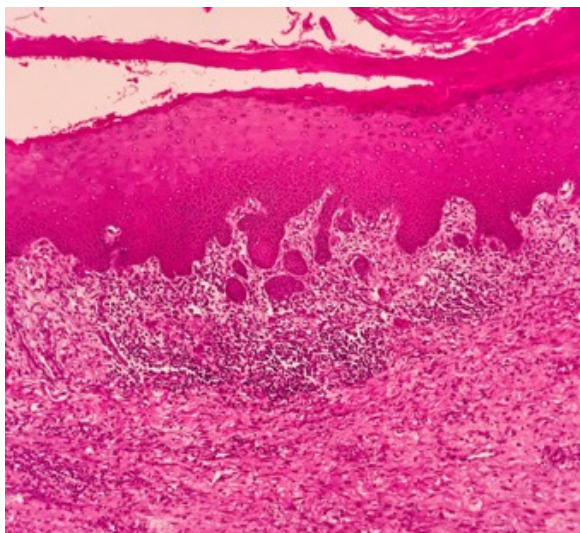


Figure 1. In the microscopic examination, mixed type inflammation under the skin (H&E 100X)



Figure 2. The appearance of the wound on the 6th day after the operation

**DISCUSSION**

Pathogenesis of surgical wound infection after cesarean section; continues to vary with each passing year due to the increasing use of antibiotics. Although there is a variable degree of infection prevention strategies proven in literature, To understand these complex mechanisms, we anticipate the need for future gene-level studies. Surgical wound infections after cesarean delivery increase parallel to the increase in obesity and primary cesarean rates all over the world and it is an iceberg that we still cannot find a definite solution. It is considered that at least 2 of the following factors which can be sorted as increased contact of cervicovaginal flora and amniotic fluid due



to prolonged labor, exogenous bacterial contamination, disruption of sterile surgical technique and emergency cesarean section should coexist for infection of the surgical incision line after cesarean section (16). We have not found a high-quality publication or review of a large number of case series related to a surgical site infection with the pathogen *E. Cloaca* after cesarean delivery.

According to a Cochrane review published in 2018, the author's listed high-quality evidence as follows: Prophylactic intravenous antibiotics administered before cesarean incision reduces surgical wound infections, use of adhesive drapes increases wound infections. (high-certainty evidence). Preoperative antibiotic use in breast cancer surgery reduces the risk of surgical site infection compared to placebo (17). In our case, the main component of our treatment was aggressive debridement of all necrotic tissues and repeated daily debridements accelerated the healing process and had a positive effect on survival. In the current literature, most clinicians have turned to research strategies to prevent surgical site infections, however, the number of effective drugs in our hands is gradually decreasing due to the increasing drug resistance surgical site infections.

The distribution of surgical wound infection pathogens in our clinic in the last 3 years is as follows; Coagulase-negative staphylococcus(6), Staphylococcus Aureus(5), *E. Aerogenes*(1), *Klebsiella pneumoniae*(2), *Streptococcus agalactiae*(1), *Escherichia coli*(3), *Proteus mirabilis*(1), *Enterococcus faecalis*(1), *Streptococcus spp.*(1) *Acinetobacter baumannii*(1), *Enterobacter cloacae*. (1).

Due to the unnecessary use of antibiotics, resistance to treatment increases and remains a huge problem affecting all countries, both economically and socioculturally. Postpartum infections are a major cause of prolonged hospital stay and comprise a large burden to our health care system (18). One study attributed the costs of an additional \$3700 for surgical wound infection in 2010 (19). We have not found any large-scale detailed study of the cost and mortality rates of surgical site infection to countries that have been found today (20,21).

In our study, we could not conclude the wound infection risks observed after the cesarean section between 2017-2019 due to the patients anamnesis were not recorded in detail. More importantly, we were unable to reach data that could compare neonatal infection rates and responsible microorganisms, neonatal mortality rates, and duration of stay in neonatal intensive care, with obstetric risk factors (Obesity, Health literacy, personal hygiene status, early rupture of membranes, diabetes mellitus). We think that the most important reason for this is the absence of a sufficient number of medical secretaries who can keep the information of the patients hospitalized in our clinic.

## CONCLUSION

Multidrug-resistant bacterial infection increases hospital stay, healthcare costs, and mortality, and for all nations,

this problem is growing exponentially. Nowadays, understanding the multifactorial genetic basis of multidrug resistance should investigate genetic signatures in invasive infection. Surveillance studies should be initiated by establishing a multinational multidisciplinary committee in order to reach standardized optimum treatment all over the world and to prevent mortality. In our opinion, there is a need for multinational large-scale, randomized controlled trials with a large number of cases based on genetic modeling and detailing clinical outcomes.

*Competing interests: The authors declare that they have no competing interest.*

*Financial Disclosure: There are no financial supports.*

## REFERENCES

1. Gregory KD, Jackson S, Korst L, et al. Cesarean versus vaginal delivery: whose risks? Whose benefits? *Am J Perinatol* 2012;29:7-18.
2. Creanga AA, Bateman BT, Butwick AJ, et al. Morbidity associated with cesarean delivery in the United States: Is placenta accreta an increasingly important contributor? *Am J Obstet Gynecol* 2015;213:384-11.
3. Newlin C, Kuehl TJ, Pickrel A, et al. Cesarean section incision complications and associated risk factors: A quality assurance project. *Open J Obstet Gynecol* 2015;789-94.
4. Conner S, Verticchio J, Tuuli M, et al. Maternal obesity and risk of postcesarean wound complications. *Am J Perinatol* 2013;31:299-304.
5. Ayres-de-Campos D. Obesity and the challenges of caesarean delivery: Prevention and management of wound complications. *Best Pract Res Clin Obstet Gynaecol* 2015;29:406-14.
6. Dessie W, Mulugeta G, Fentaw S, et al. Pattern of bacterial pathogens and their susceptibility isolated from surgical site infections at selected referral hospitals, Addis Ababa, Ethiopia. *Int J Microbiol* 2016.
7. Garner JS, Jarvis WR, Emori TG, et al. CDC definitions for nosocomial infections. *J Infect Control* 1988; 16:128-40.
8. Amatya J, Rijal M, Baidya R. "Bacteriological study of the postoperative wound samples and antibiotic susceptibility pattern of the isolates in BB hospital. *J Sex Med* 2015;3:1019.
9. Kabau DM, Wanjala S, Kagema F. Incidence and determinants of surgical site infection after Cesarean Delivery at Kenyatta National Hospital,"Incidence and determinants of surgical site infection after Cesarean Delivery at Kenyatta National Hospital, 2014:51.
10. Mitt P, Lang K, Peri A, et al. Surgical-site infections following cesarean section in an Estonian university hospital: postdischarge surveillance and analysis of risk factors. *Infection Control & Hospital Epidemiology* 2005;26:449-54.
11. Mulu W, Kibru G, Beyene G, et al. Postoperative nosocomial infections and antimicrobial resistance

- pattern of bacteria isolates among patients admitted at Felege Hiwot Referral Hospital, Bahirdar, Ethiopia. *Ethiop J Health Sci* 2012;22:7-18.
12. Annavajhala MK, Gomez-Simmonds A, Uhlemann AC. Multidrug-Resistant *Enterobacter cloacae* Complex Emerging as a Global, Diversifying Threat. *Front Microbiol* 2019;10:44.
  13. Gardner SE, Frantz RA, Saltzman CL, et al. Diagnostic validity of three swab techniques for identifying chronic wound infection. *Wound Repair Regen* 2006;14:548-57.
  14. Wayne PA. Clinical and laboratory standards institute. Performance standards for antimicrobial susceptibility testing; 2011.
  15. Ovington LGS. Hanging wet-to-dry dressings out to dry. *Home Healthc Nurse* 2001;19:477.
  16. Martens MG, Kolrud BL, Faro S, et al. Development of wound infection or separation after cesarean delivery. Prospective evaluation of 2,431 cases. Department of Obstetrics and Gynecology, Baylor College of Medicine, Houston, Texas, USA. *J Reprod Med* 1995 ;40:171-5.
  17. Liu Z, Dumville JC, Norman G, et al. Intraoperative interventions for preventing surgical site infection: an overview of Cochrane Reviews. *Cochrane Database Syst Rev* 2018;2:CD012653.
  18. Blumenfeld YJ, El-Sayed YY, Lyell DJ, et al. Risk factors for prolonged postpartum length of stay following cesarean delivery. *Am J Perinatol* 2015;32:825-32.
  19. Olsen MA, Butler AM, Willers DM, et al. Comparison of costs of surgical site infection and endometritis after cesarean delivery using claims and medical record data. *Infect Control Hosp Epidemiol* 2010;31:872-5.
  20. Goksever Celik H, Celik E, Dikmen S, et al. Surgical Site Infections in a Tertiary Referral Obstetric and Gynecologic Clinic Center in Istanbul and Review of the Literature. *Gynecol Obstet Reprod Med* 2018;24:37-41
  21. Yavuz E, Malatyalioglu E, Bildircin F. Vaginal Preparation with Povidone Iodine and Postcesarean Infectious Morbidity: A Retrospective Trial. *Gynecology Obstetrics & Reproductive Med* 2016;20:15-9.