




Surgical Site Infections in Post-Living Donor Liver Transplantation: Surveillance and Evaluation of Care Bundle Approach

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Abstract

Edited by: Slavica Hristomanova-Mitkovska
Citation: Wassef M, Yousef RHA, Hussien MM, El-Shazly MA, Ghaith DM. Surgical Site Infections in Post-Living Donor Liver Transplantation: Surveillance and Evaluation of Care Bundle Approach. Open-Access Maced J Med Sci. 2022 Aug 05; 10(A):1411-1416. <https://doi.org/10.3889/oamjms.2022.10155>
Keywords: Surgical site infection; Liver transplantation; Care bundle
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Received: 17-May-2022
Revised: 08-Jun-2022
Accepted: 26-Jul-2022
Copyright: © 2022 Mona Wassef, Reham H. A. Yousef, Marwa Mahmoud Hussien, Mostafa A. El-Shazly, Doaa M. Ghaith
Funding: This research did not receive any financial support.
Competing Interest: The authors have declared that no competing interest exists
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BACKGROUND: Although implantation of a care bundle approach is well established in intensive care units, its impact on reducing surgical site infections (SSI) among post-living donor liver transplantation (LDLT) patients has not been established.

AIM: This study aims to evaluate the impact of a care bundle on reducing SSI and to detect the pattern of antibiotic resistance in LDLT.

MATERIALS AND METHODS: This before and after comparative study was conducted at El Manial Specialized Tertiary Hospital, Cairo University, over 3 years (January 2016–December 2018) including 57 LDLT patients. We introduced a care bundle comprising a group of evidence-based practices implemented together. The study was divided into three phases. All bacterial identification and antibiotic sensitivity testing were done by a Vitek 2 Compact system.

RESULTS: SSIs rates were reduced significantly by 30.4% from the pre-implementation to the post-implementation phase (from 13/24, 54.2–5/21, 23.8%, OR 0.21, CI 95%: 1.137–0.039). This reduction went hand in hand with an increase in hand hygiene compliance from 57.3% to 78%, then remained sustained with a median rate of 78% in the last 6 months. *Klebsiella pneumoniae* was 11/25 (44% of SSIs), *Acinetobacter baumannii* 8/25 (32% of SSIs), *Escherichia coli* 5/25 (20%), *Pseudomonas aeruginosa* 5/25 (20%) and methicillin resistance Staph aureus (MRSA) was 4/25 (16%).

CONCLUSION: SSIs in LDLT mandate the strict implementation of comprehensive evidence-based care bundles for a better patient outcome.

Introduction

Over 50% of post-liver transplantation (LT) patients struggle with nosocomial infections, of which 70% are caused by bacteria mostly occurring early after the operation followed by viral and fungal infections [1]. Surgical site infections (SSIs) are the most prevalent among hospital-acquired infections (HAIs) occurring in the first 30 days after operation in patients undergoing LT. They are the leading cause of longer hospital stays, higher mortality rates, and high health care costs [2].

At present, extensively drug-resistant (XDR) organisms are a common cause of HAI in post-living donor LT (LDLT) [3]. The first LDLT in Egypt was done in 2001 [4]. The care bundle approach which comprises a group of evidence-based practices together to offer a systematic method to reduce infection has been well implemented in intensive care unit (ICU) settings, but its impact on reducing SSI among LDLT patients has not been yet established [5]. We conducted this study to evaluate the impact of a care bundle on reducing SSI and to detect the pattern of resistance in LDLT in Egypt.

Materials and Methods

This before and after the comparative study was conducted at El Manial Specialized Hospital, Cairo University. It is a tertiary care teaching hospital with eight ICUs and 328 beds. The study was done over 3 years (January 2016–December 2018) including 57 LDLT patients. We introduced a care bundle comprised a group of evidence-based practices implemented together. The study had three distinct stages: Pre-implementation phase (15 months, 24 patients), implementation phase (6 months, 12 patients), and post-implementation phase (15 months, 21 patients).

During the pre-implementation phase (January 2016–March 2017), the baseline SSI rates for all the patients undergoing LDLT were calculated according to the CDCs NHSN, definitions 2017. Moreover, the antibiogram was conducted [6].

Through the implementation phase (April 2017–September 2017), bundle care forms for SSI were made according to the CDC guidelines. Subsequently, the forms were issued, and the infection control nurses of the LT ICUs were instructed (by lectures and on-the-job

training) about the importance of applying the elements of the bundle together and about the importance of compliance to hand hygiene. The components of the SSI care bundle included the following:

1. Perioperative antibacterial prophylaxis consists of piperacillin/tazobactam 4.5/8 h interrupted after 48 h unless signs of infections appeared, for example, elevated CRP, elevated TLC, and fever depending on the risk factors. Results of microbiologic cultures and clinical factors dictate modifications to the antibiotic therapy given after LT operation.
2. Pre-operative skin preparation with betadine and shaving
3. Betadine shampoo for skin pre-operative bath
4. Normothermia 36.1–37.1
5. Maintain low blood glucose <180 mg/dl.

Monitoring of hand hygiene (HH) compliance rate was done, as shown in Figure 1. The SSIs rates of the LDLT were calculated during routine surveillance of the LT ICU.

During the post-implementation phase (October 2017–December 2018), the bundle care and HH forms continued to be used; the active surveillance of SSI rates was carried out to assess the effect of the implementation of bundle components altogether. The antibiogram was conducted all through the three phases of the study.

Clinically

Case definition of SSI patients according to the CDC/NHSN 2017: SSI was classified as superficial incisional which involves only the skin or subcutaneous tissue, while deep incisional involves the fascia and/or muscular layers. If the infection reaches any area related to the operation apart from the skin incision, fascia, or muscle layers, it is considered organ-space SSI occurring within 30 days after the operative procedure. All SSI cases had pus draining from the deep incision in addition to one or more of the following criteria: (1) A deep incision that impulsively dehiscd or is purposely opened by a surgeon and was culture positive. (2) One of the following signs or symptoms: Fever (>38°C), localized pain, or tenderness [6], [7].

Laboratory

Identification

Pus was collected by sterile swabs and transported immediately to the clinical microbiology lab for further processing. All swabs were cultured on conventional blood, chocolate, MacConkey, and mannitol agar (Oxoid, England). They were incubated at 35°C for 24 h. Identification of bacterial species was performed by a Vitek 2 Compact (Biomerieux, France) automated system. The procedure was done, according to the manufacturer's recommendations.

Antibiotic susceptibility testing

It was done by a Vitek 2 Compact system (Biomerieux, France). Multidrug resistance (MDR) was defined as isolates acquiring non-susceptibility to at least one antibiotic in three or more classes, XDR was defined as bacterial isolates remain susceptible to at least one antibiotic in only one or two classes [8]. Confirmation of acquiring extended-spectrum beta-lactamase (ESBL) phenotype was performed by an approximation test according to the [9], whereas acquiring methicillin-resistant *Staphylococcus aureus* (MRSA) phenotype was confirmed by a ceftioxin susceptibility test according to the CLSI, 2017 [8], [9].

Statistical analysis

Data were statistically defined in terms of mean \pm standard deviation (\pm SD), median and range, or frequencies (number of cases) and percentages when suitable. A comparison of numerical variables between the study groups was done using the Kruskal–Wallis test. Odds ratio (OR) with the 95% confidence interval (95% CI) was assessed for infections between the pre-implementation phase and each of the implementation and post-implementation phases. For comparing categorical data, Chi-square (χ^2) test was done. The exact test was used instead when the expected frequency was <5. Within the group, comparisons were done using the McNemar test. Two-sided $p < 0.05$ were considered statistically significant. All statistical calculations were done by IBM (Statistical Package for the Social Sciences;

day	Date	Type of Contact according WHO 5 moments	Health Care Professional	Name Initials	Gender	Hand Hygiene done or not	Technique Adequate or not	Used product for hand-rub (alcohol or soap)	Used towel (paper or cloth)
1									
2									

Figure 1: Form for monitoring hand hygiene compliance

IBM Corp., Armonk, NY, USA) release 22 for Microsoft Windows.

Results

Our study included 57 LDLT patients, the mean age groups of recipients in the implementation and post-implementation phases were ± 49.75 and ± 34.62 years, respectively, the average donor's mean age was ± 32.08 and ± 30.1 years in the implementation and post-implementation phase, respectively. Demographic data, underlying morbidity with pre-operative viral screening, underlying chronic diseases, and causes of mortality, are shown in Table 1. SSI rates, types, and causative organisms are shown in Tables 2 and 3, respectively.

Regarding patterns of resistance of the isolated organisms among SSI, XDR Gram-negative bacteria were the most prevalent pattern 14/25 (56%), followed by ESBL of Gram-negative bacteria 6/25 (24%), then MRSA 4/25 (16%).

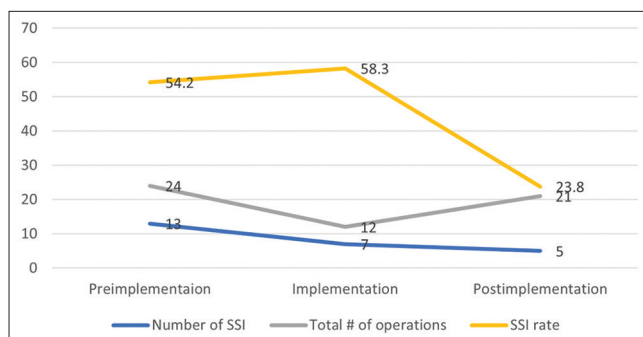


Figure 2: SSI rates before and after implementation of bundle

The effect of implementing the bundle on rates of SSI is shown in Figure 2. The odds ratio was calculated for logistic regression of SSIs between pre- and post-implementation phase (ORs ratio, 0.21 [95% significant confidence interval, 1.137–0.039]).

We increased the hand hygiene compliance rate and contact precautions during the implementation of the bundle, from 57.3% before to 78% after, then compliance remains sustained with a median rate of 78% in the past 6 months, as shown in Figure 3.

Discussion

Although implantation of a care bundle approach is well established in ICUs settings, its impact on reducing SSI among LDLT patients has not been established [5]. In 2008, García Prado *et al.* studied the effect of unifactorial antibiotic perioperative prophylaxis on reducing the incidence of SSI and concluded that an integral perspective of SSI besides a multifactorial approach is needed to prevent SSIs [10]. In our study, we evaluated the effect of a care bundle approach on the reduction of SSI rates, and we found that the SSIs rates were reduced significantly by 30.4% from pre-implementation to post-implementation (from 13 to 24, 54.2% to 5/21, 23.8%, OR 0.21, CI 95%: 1.137–0.039). This reduction went hand in hand with an increase in hand hygiene compliance from 57.3% to 78%, then remained sustained with a median rate of 78% in the past 6 months.

SSI occurs in 10–37% of recipients in systematic reviews [11]. This high incidence of SSIs in LT may be multifactorial due to; the complexity of surgery in a clean-contaminated space, or even contaminated space if the failing liver is infected at the time of transplantation, preexisting comorbidities, moreover the immunocompromised state of the host [12].

All over our study, we reported a high SSI rate of 25 events 25/57 (43.9%) (total SSI rate = several SSI/total number of operations performed). Given that the incidence of SSI after LT is hard to assess, with institutional reports ranging from 12% to 30%. For

Table 1: Demographic data, underlying morbidity with pre-operative viral screening, underlying chronic diseases and causes of mortality

Parameters	Pre-implementation Total 24		Implementation Total 12		Post-implementation Total 21		Total/average Total 57		p value
	N	%	N	%	N	%	N	%	
Male	19/24	79.2	12/12	100	19/21	90.5	50	87.7	0.017
Female	5/24	20.8	0	0	2/21	9.5	7	12.3	
Underling morbidity									0.026
HCC	13	54.2	5	41.7	14	66.7	32	56.1	
Liver cirrhosis	5	20.8	7	58.3	1	4.5	13	22.8	
Budd-Chiari syndrome	5	20.8	0	0	4	19	9	15.8	
Autoimmune hepatitis	1	4.2	0	0	2	9.5	3	5.3	
Pre-operative viral screening									0.21
HCV	18	75	9	75	11	52.4	38	66.7	
HBV	1	4.2	1	8.3	1	4.8	3	5.3	
CMV	0	0	0	0	1	4.8	1	1.7	
HIV	0	0	0	0					
EBV	0	0	0	0					
Underling chronic disease									0.60
DM	6	25	1	8.3	3	14.2	10	17.5	
HTN	5	20.8	3	25	1	4.7	9	15.7	0.25
Causes of mortality									0.32
Hematemesis	1	4.1	2	16.6	2	9.5	11	19.3	
Infection	2	8.3	1	8.3	1	4.7			
Others	0	0	1	8.3	1	4.7			

HCC: Hepatocellular carcinoma; HCV: Hepatitis C virus; HBV: Hepatitis B virus; CMV: Cytomegalovirus; DM: Diabetes mellitus; HTN: Hypertension; HIV: Human Immunodeficiency virus; EBV: Epstein-Barr virus.

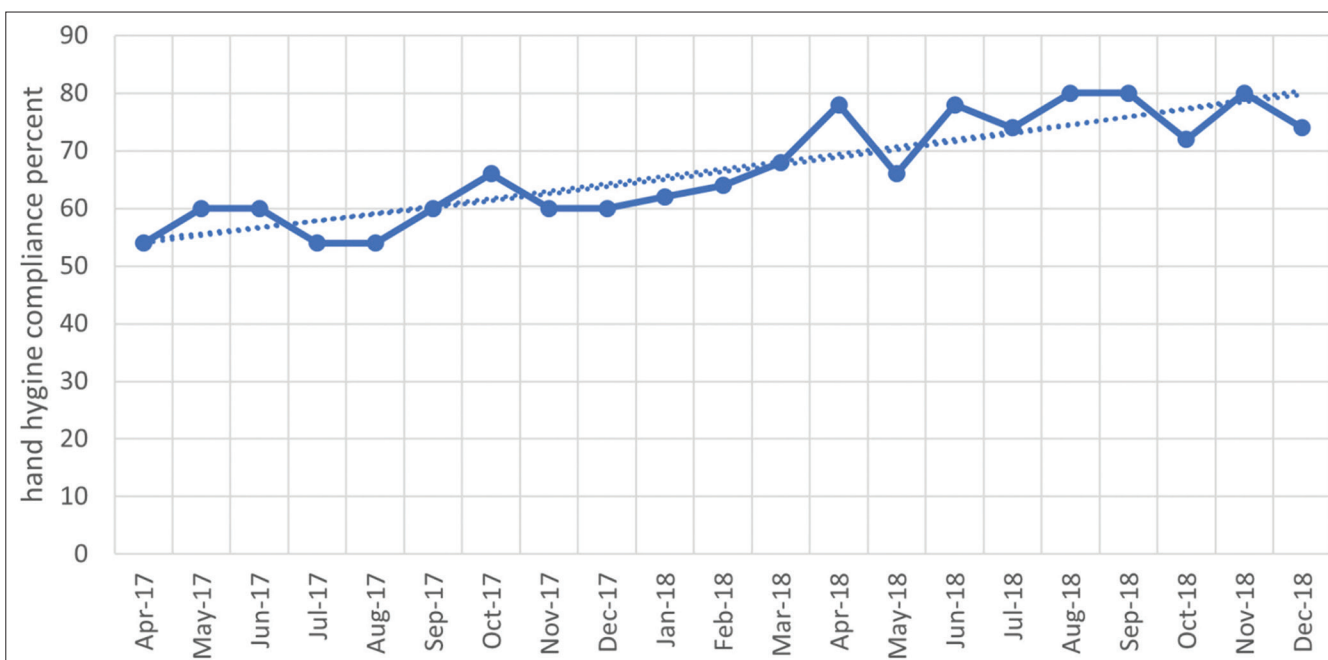


Figure 3: Hand hygiene compliance during and after implementation of care bundle approach

example, Freire *et al.* found SSI after LT to be 24% and 30% in different periods in Brazil [2], while Parekh and colleagues found impressive variation in SSI after LT (0–29%) across 29 participating sites in the USA [13]. On the other hand, a cohort study by Natori *et al.* assessed SSIs after LTs in Canada where they recorded 17.2% of SSIs post-liver transplants, which is extremely analogous to the rate stated by Viehman *et al.*, 2016 (18%) [14], [15], whereas Moreno *et al.* estimated the occurrence of SSIs after LT in Spain to be ~10%. On the other hand, Yamamoto *et al.* evaluated SSIs in adult living donor liver transplants and found the rates of 30.3% and 41.3% in two different periods [16], [17].

Table 2: SSI rates and types before and after the bundle care approach

phase	SSI rate		SSI rate (%)	SSI type	
	Events of SSI N	Total N of operations		Superficial incisional n (%)	Organ space n (%)
Pre-implementation	13	24	54.2	4 (30.7)	9 (69.3)
Implementation	7	12	58.3	2 (28.5)	5 (71.5)
Post-implementation	5	21	23.8	2 (40)	3 (60)
Total/average	25	57	43.9	8 (32)	17 (68)

SSI rate = Number of SSI/total number of operations performed.

This wide difference range in rates may be due to the usage of different definitions of SSIs, which determine the incidence over different periods during which many changes in practice may take place and impact the incidence [13].

Table 3: Causative organisms and pattern of resistance

Types of organisms	SSI causative organisms						Total SSI events n 25(%)
	Pre-implementation n (24)		Implementation n (12)		Post-implementation n (21)		
<i>Klebsiella pneumoniae</i>	7	29.2	2	16.7	2	9.5	11 (44)
<i>Acinetobacter baumannii</i>	5	20.8	2	16.7	1	4.8	8 (32)
<i>Escherichia coli</i>	2	8.3	2	16.7	1	4.8	5 (20)
<i>Pseudomonas aeruginosa</i>	2	8.3	2	16.7	1	4.8	5 (20)
Methicillin resistance <i>Staphylococcus aureus</i> (MRSA)	1	4.2	1	8.3	2	9.5	4 (16)

Regarding types of SSIs, shallow wound infections are classically more common in the general surgical patient, unlike the liver recipients who developed higher rates of deep infections such as abscesses (3% vs. 15% in one study) [14]. In concordance with other studies, we found that the organ-space SSIs were 17/25 (68%), while the superficial incisional wounds were 8/25 (32%).

Similarly, Natori *et al.*, 2017, in Canada found that among 47 SSIs, 33 (70.2%) were organ-space SSIs, 9 (19.1%) were superficial SSIs, and 5 (10.6%) were deep SSIs [15].

Furthermore, Softness and colleagues in the USA found 24 events of SSI out of 252 LT (9.5%) in (superficial 8/24, 33%, deep 4/24, 17%, and organ-space 12/24, 50%) [18].

Regarding types of organisms causing SSIs, Gram-negative bacteria are taking the upper hand in all HAIs including SSIs [19].

In our study, the causative organisms of SSIs were predominated by *Klebsiella pneumoniae* 11/25 (44% of SSIs), *Acinetobacter baumannii* 8/25 (32% of SSIs), *Escherichia coli* 5/25 (20%), *Pseudomonas aeruginosa* 5/25 (20%), and MRSA 4/25 (16%). Some SSI events showed coinfections, so the total number of isolated organisms was 33. However, most of the

published studies were concerned with the type of organisms causing infections in LT patients, fewer reports were focusing on the distribution of organisms among SSI events. In an Egyptian multicenter study by Mukhtar *et al.* and his colleagues in 2014, they found that organisms causing infections in post-LDLT were dominated by *P. aeruginosa* (110 episodes [26%]), followed by *Klebsiella* species (79 episodes [19%]), *E. coli* (69 episodes [16%]), *A. baumannii* (33 episodes [8%]), and methicillin-resistant *S. aureus* (32 episodes [7.7%]) [3].

Furthermore, Pouldfar *et al.*, 2019, reported predominance of Gram negative rods (n = 55; 51%) with wide range of different organisms; *Acinetobacter* spp. (n = 18; 16.7%), *Klebsiella* spp. (n = 13; 12%), *Pseudomonas* spp. (n = 10; 9.2%), *E. coli* (n = 10; 9.2%), *Stenotrophomonas maltophilia* (n = 3; 2.8%), and *Citrobacter* spp. (n = 1; 0.9%) with the median isolation time of 15 days post-LT. Gram positive bacteria comprised 53 isolates (49.1%), the most common strains of which were *Enterococcus* spp. (n = 39; 36.1%) including 32 strains of VRE (82%), *Staphylococcus* spp. (n = 12; 11.1%), and *Streptococcus* spp. (n = 2; 1.8%) [1]. On the other hand, Viehman *et al.*, 2016, noticed high incidence of *Enterobacteriaceae* (42%), *Enterococcus* spp. (24%), and *Candida* spp. (15%) [14].

As a fact, the emergence of drug-resistant pathogens is affected by the rate of resistant pathogens in the nearby areas, unfortunately, the rates of MDR bacteria, especially CRE, are obviously at Cairo University Hospitals [20], [21], [22]. According to the antibiogram of the LT unit in El Manial Specialized Tertiary Care Hospital, XDR Gram-negative bacteria were the most prevalent pattern 14/25 (56%), followed by ESBL of Gram-negative bacteria 6/25 (24%), then MRSA 4/25 (16%).

In Mukhtar *et al.*, 2014, the overall, 75% of Gram-negative isolates were MDR, including 90% (30 of 33) of *A. baumannii* isolates, 76% (84 of 110) of *P. aeruginosa* isolates, 57% (46 of 79) of *Klebsiella* species isolates, and 53% (37 of 69) of *E. coli* isolates [3].

Worldwide, in 2008, Prado *et al.* noticed that *E. coli* caused 21.25% of SSIs among which 47% were ESBL producers. More recently, Viehman *et al.*, 2016, reported overall 53% of MDR bacteria, including 95% of *Enterococcus faecium* and 55% of *Enterobacteriaceae*; 82% of deep SSIs were caused by bacteria resistant to antimicrobials used for prophylaxis, and 58% of patients were treated with an inactive empiric regimen [14].

In our study, usage of piperacillin/tazobactam as a pre-operative prophylactic antibiotic depended on the annual antibiogram of the transplantation unit showing sensitivity percent to Gram-negative organisms as the followings: 2016 (*K. pneumoniae* 40%, *P. aeruginosa* 60%, *A. baumannii* 16.6%, and *E. coli* 75%), 2017 (*K. pneumoniae* 33.3%, *P. aeruginosa* 40%, *A. baumannii* 11.1%, and *E. coli* 60%), and 2018 (*K. pneumoniae*

42.8%, *P. aeruginosa* 28.5%, *A. baumannii* 50%, and *E. coli* 40%).

Conclusion

SSIs in LT are complicated by many factors. A fact mandates the strict implementation of comprehensive evidence-based care bundles with close monitoring and follow-up for reduction of incidences and better patient outcomes.

The single-center experience may be a limitation concerning the total number of patients that can be analyzed, however, in our study, it is a strong point due to the uniform protocol and consistent team of LT ICU staff. Furthermore, evaluation the elements of the bundle was reviewed by a single investigator guaranteeing that all the data were analyzed in the same comprehensive manner.

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