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Assessing the impact of enhanced hygiene precautions during the COVID-19 pandemic on surgical site infection risk in abdominal surgeries

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Abstract

Background A surgical site infection (SSI) is a postoperative infection that occurs at or near the surgical incision. SSIs significantly increase morbidity, mortality, length of hospital stay, and healthcare costs. The World Health Organization (WHO) has established hospital hygiene precaution guidelines for the prevention of SSIs, which were enhanced during the COVID-19 pandemic. The current study aims to explore the effect of the COVID-19 pandemic on SSI incidence among initially uninfected postoperative patients. We hypothesize that these enhanced precautions would reduce the incidence of SSIs.

Materials and methods A retrospective study comparing surgical outcomes before and during the pandemic. Patients who had abdominal surgery between June and December 2019 (Non-COVID-19) or between February and June 2020 (COVID-19) were included. The two groups were matched in a 1:1 ratio based on age, Sex, acuity (elective or emergent), surgical approach, and comorbidities. Electronic medical records were reviewed to identify SSIs and hospital readmissions within 30 days after surgery. Pearson's chi-square test and Fisher's exact test were used.

Results Data was collected and analyzed from 976 patients who had surgery before the COVID-19 pandemic (non-COVID group) and 377 patients who had surgery during the pandemic (COVID group). After matching, there were 377 patients in each group. In our study, we found 23 surgical site infections (SSIs) in both laparoscopic and open surgeries. The incidence of SSIs was significantly higher in the non-COVID period compared to the COVID period [17 cases (4.5%) vs. 6 cases (1.6%), respectively, $p = 0.032$], especially in non-COVID open surgeries. The incidence of SSIs in laparoscopic surgeries was also higher during the non-COVID period, but not statistically significant.

Conclusions Enhanced hygiene precautions during the COVID -19 pandemic may have reduced SSIs rates following abdominal surgery.

Keywords Hygiene Precautions, Covid-19 Pandemic, Surgical Site Infection, Abdominal surgery

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Introduction

A surgical site infection (SSI) is an infection associated with a surgical operation that occurs at or near the surgical incision, within 30 days following the procedure or within 90 days if a prosthetic was implanted during surgery [1]. SSIs, accounting for up to 5% of in-hospital acquired infections, significantly elevate morbidity, mortality, hospital stays, and healthcare costs [2, 3]. The primary culprits behind SSI are Staphylococcus aureus, coagulase-negative Staphylococcus, and Escherichia coli [4]. Most cases of SSI occur in patients undergoing abdominal surgery [5–7]. Notably, nasal colonization of methicillin resistant Staphylococcus aureus (MRSA) in patients undergoing surgery has been found to be associated with increased risk of SSI [8, 9].

The emergence of the COVID-19 pandemic in late 2019 overwhelmed hospitals globally, leading to a surge in death rates among hospitalized patients. A 2021 study found that COVID-19 infection in postoperative patients is highly associated with increased blood transfusions, renal failure, sepsis, reintervention, readmission, and death [10]. Furthermore, the incidence of SSI significantly rises in patients infected with COVID-19 during an operation.

While standard surgical antiseptic and sterile techniques have been commonplace for decades, the pandemic prompted organizations such as the World Health Organization (WHO) and the Surgical Infection Society to recommend enhanced hygiene precautionary guidelines. These guidelines included hand hygiene with soap or alcohol-based hand rub. Additionally, personal protective equipment (PPE), such as clean nonsterile gloves, masks, eye protection, or face shields, were advised. Education of health workers, patients, and visitors was also deemed important [11]. Such efforts were intended to reduce adverse events, as COVID-19 infection greatly increases postoperative morbidity and mortality [10, 12]. Studies have shown conflicting results on changes in SSI rates during the pandemic [13–16]. Additional hygiene precautions established during the pandemic include ensuring that all staff in the operating room wear full protective gear. Anesthesia induction often involved minimal staff presence due to incomplete COVID-19 testing for many surgical cases. Enhanced cleaning protocols were implemented in the operating room. Patients were educated on the significance of hand hygiene, mask-wearing, and maintaining social distance. Routine wound inspections were conducted with full protective gear and usually by a single physician. Overall, direct contact between healthcare workers and patients has been minimized [16].

The current study aims to contribute to the literature on this topic, hypothesizing that these enhanced hygiene precautions during the pandemic may have led to reduced incidence of SSIs in non-infected patients. However, our study focuses on specific types of surgeries, particularly abdominal surgeries, for which this topic is not extensively discussed in the literature.

Methods

This was a retrospective record review of patients operated on before or during the COVID-19 pandemic. The study was approved by the Medical Ethical Committee of Galilee Medical Center, Naharia, Israel. Patients who underwent abdominal surgery before or during the COVID-19 pandemic were eligible for inclusion. The inclusion criteria encompassed patients over 18 years old who underwent elective or urgent abdominal surgery, excluding those undergoing oncology treatment with chemotherapy and/or radiation, as well as patients who had COVID-19 or developed it during admission.

All patients received the same preoperative antiseptic preparation, which included using an electric hair clipper, soap scrub, and a combination of chlorhexidine gluconate and alcohol-based skin preparation. Diabetic patients received perioperative glycemic control. Normothermia was maintained by employing active warming methods including warmed intravenous fluids and skin warming. All patients received prophylactic antibiotics based on surgery type. Anesthesia method in both groups was identical, including the mode of induction and maintenance with the same drugs.

Data collection occurred for two distinct periods: pre-COVID-19 (June to December 2019) and during the pandemic (February to June 2020). Collected information included demographic details (age, Sex, risk factors for SSI), past surgical history, and operative data (surgery approach, acuity, and duration). Follow-up involved routine office visits for 30 days, with re-admissions to the emergency room also monitored.

We identified 1,353 patients who underwent abdominal surgery, including 976 in the pre-COVID-19 group and 377 in the COVID-19 group. To minimize bias risk stemming from heterogeneity between the two groups in terms of comorbidities, surgical acuity, and approach, a 1:1 propensity matching strategy was employed. The two groups were matched in a 1:1 ratio based on age, Sex, acuity (elective or emergent), surgical approach (laparoscopic or open), and comorbidities (diabetes, smoking, and obesity).

SSI type was categorized per Centers for Disease Control and Prevention (CDC) definitions as follows: 1. Superficial – infection developed within 30 days post-surgery that involved skin and subcutaneous tissue; 2. Deep – infection developed after 30 days or within one year if a foreign body was implanted and involved fascia and muscles; 3. Organ or body cavity infection in close proximity to the surgical site – developed within 30 days or one year if a foreign body was implanted [1].

Statistical analysis focused on patients developing infections between the COVID-19 (2020) and control groups in 2019.

Propensity score matching was conducted in R version 3.3. Pearson Chi-square and Fisher exact tests were used to assess categorical differences, while T-tests were used to assess quantitative parameters. A receiver operating characteristic (ROC) model was used identified the best surgery duration cutoff for infection, and a multivariate logistic regression model determined the impact of independent parameters on infection. SPSS version 28 was used for statistical analysis, with a significance level set at $P < 0.05$.

Results

Data were collected from 1,353 patients who underwent abdominal surgery, with 976 in the pre-COVID-19 group and 377 in the COVID-19 group. Following 1:1 propensity matching, 377 patients were retained in each group (Table 1). The study found no significant differences between the two groups in terms of age, gender, hospitalization duration, type of surgery (including elective, urgent, open, and laparoscopic), and comorbidities (diabetes, smoking, and obesity). These results indicate a successful matching process, rendering the groups well-balanced and comparable in these variables and enhancing the internal validity of the study (Table 1).

A total of 23 SSIs were identified across various surgical procedures encompassing both laparoscopic and open surgeries. Laparoscopic surgeries included procedures such as bariatric surgery, inguinal hernia repair, cholecystectomy, and diagnostic laparoscopy. Open surgeries included procedures such as inguinal hernia repair, umbilical and ventral hernia repair, incisional hernia repair, elective colectomy, and emergent laparotomy with small or large bowel resection.

The incidence of SSI was significantly higher in the non-COVID period compared to the COVID period [17 cases (4.5%) and six cases (1.6%), respectively, $p = 0.032$]. Furthermore, there were more cases of SSI in non-COVID open surgeries compared to COVID open surgeries, with

Table 1 Summary of demographics and results

	COVID19; $n = 377$	**Non COVID19 $n = 377$**	**p**
Age	48.03 ± 17.9	48.3 ± 18.3	$P = 0.84$
Sex			$P = 0.51$
Male	174 (46%)	164 (43.5%)	
Female	203 (54%)	213 (56.5%)	
Time of hospitalization	3 [2-4]	3 [2–5]	$P = 0.14$
Past surgery	149 (39.5%)	156 (42%)	$P = 0.55$
Elective surgery	254 (67%)	263 (70%)	$P = 0.53$
Urgent surgery	123 (32.62%)	114 (30.23%)	$P = 0.53$
Open surgery	96 (25.5%)	105 (27.9%)	$P = 0.51$
Laparoscopy surgery	281 (74.5%)	272 (72.14%)	$P = 0.46$
Duration of surgery (min)	0:40 [0:25–60:00]	0:50 [0:33–70]	**< 0.001**
Diabetes	54 (14.3%)	59 (15.6%)	$P = 0.68$
Smoke	90 (23.9%)	82 (21.8%)	$P = 0.54$
Obesity	142 (37.7%)	145 (38.5%)	$P = 0.88$
Surgical site infection (SSI)	6 (1.6%)	17 (4.5%)	$\mathbf{P = 0.032}$
Superficial SSI	5(83.3%)	12(70.58%)	$P = 1.00$
Deep SSI	1(16.6%)	3(17.6)%	$P = 1.00$
Organ space	0 (0%)	2(11.76%)	$P = 1.00$
Laparoscopic SSI	1/281 (0.35%)	3/272 (1.1%)	$p = 0.36$
Open SSI	5 (5.2%)	14 (13.3%)	$\mathbf{P = 0.05}$
Superficial SSI (open surgery)	5 (100%)	9 (64.28%)	$p = 0.26$
Deep SSI (open surgery)	0 (0%)	3 (21.42%)	$p = 0.53$
Organ space SSI (open surgery)	0 (0%)	2 (14.28%)	$P = 1.00$
Open clean surgery SSI (diversity type of hernia)	3/58 (5.1%)	5/56 (8.92%)	$P = 0.48$
Open Contaminated surgery SSI (emergent laparotomies, with intestinal resection)	1/16 (6.3%)	9/39 (23.1%)	$P = 0.25$
Other types of open surgeries SSI (hepatectomy, splenectomy, gastrectomy, elective colectomy with pre-operative preparation)	1/16 (6.25%)	0/16(0%)	
Treatment with antibiotic	58 (15.4%)	96 (25.5%)	**< 0.001**

a significant difference [14 cases (13.3%) and five cases (5.2%), respectively, $p=0.05$] (Fig. 1). When comparing laparoscopic surgeries between the two periods, there were also more cases of SSI in the non-COVID period compared to the COVID period without statistical significance, likely due to low number of SSI in laparoscopy [three cases (1.1%) vs. one case (0.35%), $p=0.36$] (Fig. 1).

In order to investigate the characteristics of the patients who developed SSI in both groups, we compared the parameters of patients who developed SSI in both time periods. We found no significant differences in patient parameters, the acuity of surgery, or the patients' comorbidities. This suggests that the variation in SSI rates between the two periods was possibly due to the precautions taken during the pandemic rather than patient-related factors (Table 2).

In the context of contaminated open surgeries, which included urgent laparotomies with colon or small bowel resection due to trauma or perforation, we noted 39 surgeries in the non-COVID period compared to 16 surgeries during the COVID period. SSI was found in nine out of 39 patients in the non-COVID period, and in one out of 16 patients during the COVID period (23.1% vs. 6.3%, respectively, $p=0.25$). Although statistical significance was not achieved, a clinically significant difference is evident (Fig. 1).

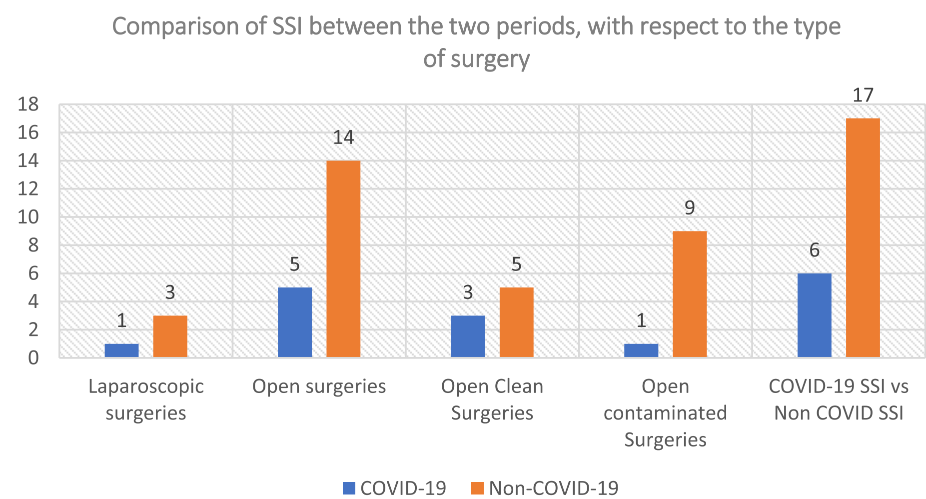

Fig. 1 In this diagram we observe that the number of SSI during the COVID-19 period is lower compared to the number of SSI in the pre-COVID-19 period

Table 2 comparison of parameters between SSI groups before and during the COVID-19 pandemic

	Non COVID19; SSI ($n=17$)	COVID19; SSI ($n=6$)	p
Age (Years)	57.8 ± 18.7	53.8 ± 16.3	$P=0.65$
Gender			$P=1.00$
Male	9 (53%)	3 (50%)	
Female	8 (47%)	3 (50%)	
Time of hospitalization (Days)	14 [6.5–32.5]	3 [2.8–13]	$\mathbf{P=0.044}$
Past surgery	11 (65%)	4 (67%)	$P=1.00$
Elective surgery	7 (41.2%)	4 (66.7%)	$P=0.37$
Urgent surgery	10 (58.8%)	2 (33.2%)	$P=0.37$
Open surgery	14 (82.4%)	5 (83.3%)	$P=1.00$
Laparoscopy surgery	3 (17.6%)	1 (16.7%)	
Duration of surgery (Hours)	02:24 ± 01:29	01:02 ± 00:33	$\mathbf{P=0.043}$
Diabetes	3 (17.6%)	1 (16.7%)	$P=1.00$
Smoke	5 (29.4%)	3 (5%)	$P=0.62$
Obesity	2 (11.8%)	3 (50%)	$P=0.089$

Among all the surgical site infections identified in the two periods, the types of infections according to CDC criteria differed. During the COVID period, there was one case of deep SSI out of six total cases, while in the non-COVID period, three cases of deep SSI occurred out of 17 total cases (16.6% and 17.6%, respectively, $p=1.00$). Conversely, during the COVID period, there were five cases of superficial SSI out of six total cases, whereas in the non-COVID period, there were 12 cases of superficial SSI out of 17 total cases (83.3% and 70.5%, respectively, $p=1.00$). Additionally, we identified organ space infections in two cases out of 17 patients in the non-COVID period, while no cases of organ space infections were found during the COVID period (11.76% and 0%, respectively, $p=1.00$) (Fig. 2).

Regarding the operative time, we observed that it is significantly longer in the non-Covid -19 group, which could be attributed to various reasons. Firstly, early in the pandemic, many elective and non-essential surgeries were postponed or canceled. This enabled surgical teams to become more focused, streamlined, and effective due to the reduced surgical volume. Additionally, surgeons had to adjust certain techniques and approaches to minimize aerosolization and the risk of viral transmission, even attempting to expedite the surgery in order to reduce the exposure time with patients. These modifications occasionally resulted in more efficient surgical workflows.

Discussion

The COVID-19 pandemic, which outbroke at the beginning of 2020, was found to be highly transmissible through respiratory droplets and close contact [17]. Therefore, the WHO published guidelines for the protection of health care workers during the pandemic COVID-19 patients, and to protect the patients themselves, recommending contact and droplet precautions [18]. The CDC then called for the use of a face mask when in a patient's environment [19]. At our institution we also limited patient visitation hours and placed a strong emphasis on hand hygiene. It should be mentioned that the issue of using intensive preventing and restricting personal means to reduce the spread and the side effects of the COVID-19 pandemic and particularly those related to wound care were evolved in China, where this pandemic started [20]. Apart from the extensive measures to prevent the spread of the disease, massive measures were taken to improve wound care [20].

The addition of these enhanced precautions led us to speculate that SSI incidence would decrease among patients operated on during the pandemic. Thus, in the current study we analyzed SSI incidence among patients with surgeries conducted prior to compared to during the COVID-19 pandemic.

The incidence of SSIs in our study was statistically significantly higher among patients who underwent surgery before the pandemic. The SSI rate after open surgeries was particularly higher in the non-COVID group, also to a statistically significant degree. We observed that contaminated surgeries, including emergent laparotomy with gastrointestinal intervention, had a higher incidence of SSI in the non-COVID period group. However, this result was not statistically significant, likely due to the low number of patients in this subgroup. Still, there may be clinical significance to this result and larger future studies may be indicated to confirm this. A higher incidence of deep and organ space SSI was found during the non-COVID period, although not to a statistically significant degree, again likely due to the low number of such SSI

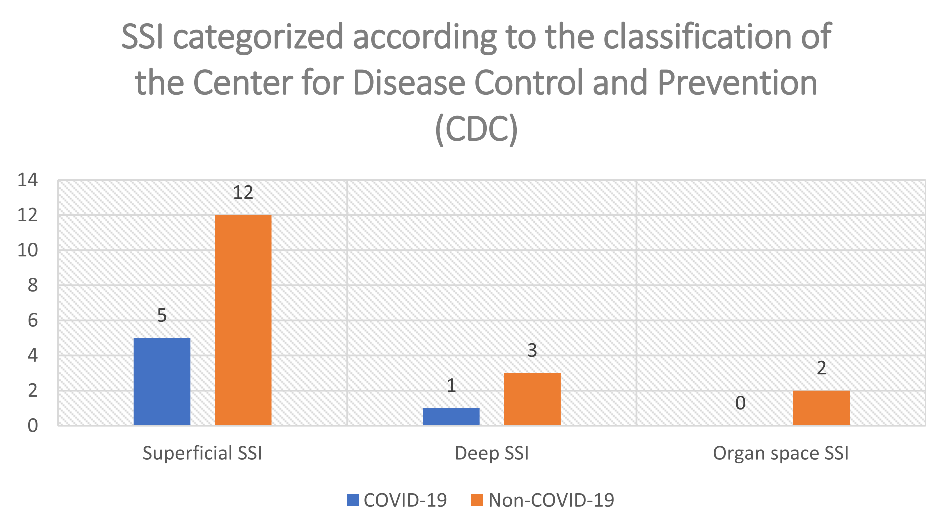

Fig. 2 In this diagram we observe a higher incidence of each type of SSI in the non-COVID era

events (Table 1). Our findings present a contrast to those reported in other studies. Baldwin et al. (2021), in a retrospective cohort study focusing on patients undergoing surgery for hand and wrist trauma before and during the COVID-19 pandemic, observed no difference in surgical site infection (SSI) incidence among their 556-patient cohort [21]. Similarly, Unterfrauner et al. (2021), in retrospective study on orthopedic surgery during the COVID-19 pandemic, found that the risk for SSI, wound healing, and other complications was not influenced by heightened public health measures. [22]. Another retrospective study by Smith et al. (2022) comparing SSI before and during the COVID-19 pandemic found no significant differences in SSI following colorectal surgery, hysterectomy, and knee prosthesis surgery [23]. Humphrey T et al. (2022) conducted a multicenter retrospective study including a total of 14,844 patients who underwent total joint arthroplasty (TJA) before COVID-19 and 5,453 TJAs during the COVID-19 pandemic. There was no statistically significant difference in the surgical site infection (SSI) rate between the pre-COVID-19 (0.35%) and COVID-19 era (0.26%) groups ($P = 0.303$) [24]. A study by Mimura T et al. (2024) examined the monthly incidences of total SSIs, specifically deep or organ/space SSIs, and SSIs caused by MRSA following orthopedic surgeries. They concluded that the hygiene measures implemented during the COVID-19 period did not significantly affect the SSI rate [25].

The lack of significant differences in the SSI rate for orthopedic surgeries between the periods could be explained by the lower rate of general SSIs in clean orthopedic elective surgeries [26]. Therefore, there is a need for more studies focused on abdominal surgeries to obtain more reliable results and better understand the impact of restrictions during this period.

Losurdo et al. (2020) conducted a retrospective study involving 198 patients before the pandemic and 123 during the COVID-19 period [27]. Their investigation focused on the impact of enhanced hygiene and contact precautions on SSI incidence in the general surgery department. While they found no significant difference when comparing the periods before and during the COVID-19 pandemic, multivariate analysis revealed that the additional precautions during the pandemic were independently associated with a reduction in SSI development. Notably, the incidence of both superficial and deep SSIs decreased during the COVID-19 pandemic compared to the pre-pandemic period.

Our study aligns with the outcomes of a retrospective analysis by Hussain et al. (2020), which investigated sternal wound infections in 2,600 patients undergoing cardiac surgery [28]. They observed a notable reduction in the incidence from 3.0% before the pandemic to 0.8% during the pandemic ($p = 0.006$). Similarly, Chacón-Quesada et al. [16] explored SSIs following primary neurosurgery in 1,278 patients [16]. The SSI rate decreased from 2.9% before the COVID-19 pandemic to 1.4% during the pandemic ($p = 0.003$). Another retrospective study by D'Oria et al. (2023), involving 194 patients undergoing vascular groin surgery, found that patients operated on during the COVID-19 era were less likely to develop SSIs compared to the non-COVID era (10% vs. 28%, $p = 0.008$) [29]. This encompassed both deep and superficial infections. When specifically comparing our study with theirs, no statistically significant difference was noted in the subgroup of clean surgeries, including inguinal hernia, umbilical hernia, and incisional hernia. However, there was a trend towards a higher SSI incidence during the non-COVID period (8.92% vs. 5.17% during the COVID period). The lack of statistical significance might be attributed to the low number of SSIs in the clean surgery group (Fig. 1). Notably, we observed a diversity of SSI types during the non-COVID period for clean surgeries, including 20% deep SSI, 20% organ space, and 60% superficial infections. During the COVID period, all SSIs were superficial. However, when comparing all types of open surgeries, we observed that during the COVID period, all surgical site infections (SSI) were predominantly superficial (100%), compared to the non-COVID period. Specifically, we found that 64.2% of the SSIs were superficial, 21.42% were deep, and 14.28% were categorized as organ space infections, although statistical significance was not achieved, a clinically significant difference is evident (Fig. 3).

It should be emphasized that although the findings in our work indicate that strict adherence to hygiene principles during the COVID-19 period may reduce postoperative infections, it can also be inferred that adherence to enhanced sterility principles in the surgical environment, regardless of the context of COVID-19, can lead to similar results. Future studies, particularly retrospective investigations focusing on abdominal surgeries, are essential to strengthen the reliability of our results. Moreover, conducting prospective studies using the precautions implemented during the COVID-19 era would offer valuable insights into the SSI status in specific patient types and subgroups. This collaborative effort will enhance our understanding and guide effective strategies for preventing SSIs in the evolving landscape of healthcare.

We believe that propensity matching method provided us with more accurate and reliable results because comparing patients with different comorbidities and parameters could lead to unreliable results. None of the studies mentioned utilized the propensity matching method, and some of them exhibited variances in certain parameters,

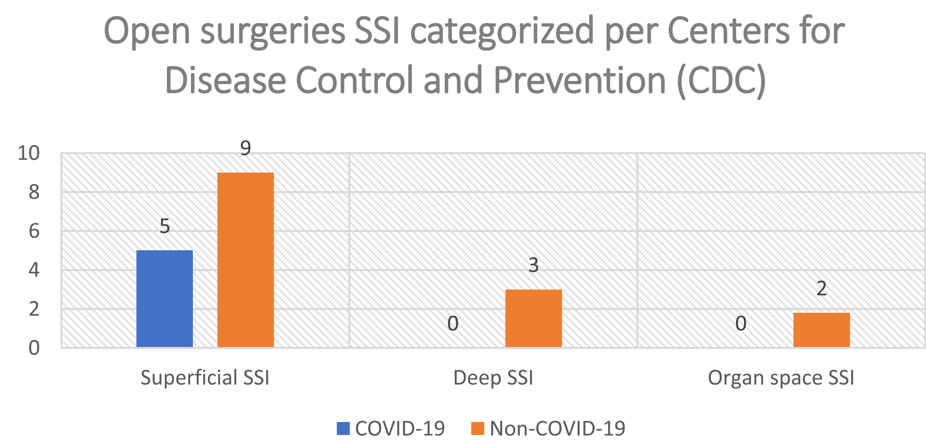

Fig. 3 In this diagram, we compare the types of SSI for all open surgeries in both time periods, we observe a higher incidence of each type of SSI in the non-COVID -19 era

which may be considered a limitation. Furthermore, most studies involved patients with Covid-19 infections, which could significantly impact the occurrence of surgical site infections (SSI). However, not all studies discussed the exact precautions taken during the Covid era. Variations in sterilization methods could potentially explain why differences in SSI cases persist. Therefore, a more stringent sterilization approach may be necessary to observe and justify these differences accurately. Moreover, in those studies in which we did not find any difference in the SSI rate, it could have been due to already high-quality perioperative hygiene awareness in some countries, regardless of the pandemic. Therefore, the increases in hygiene restrictions during the pandemic may not have a significant impact on the SSI rate.

While we find that this study provides valuable insights into SSI incidence during the COVID-19 pandemic, it does have limitations. A key limitation is the absence of a formal sample size calculation. Due to the retrospective nature of our analysis and the availability of eligible patients within the study period, a convenience sampling approach was employed. This approach may negatively impact the generalizability of our findings. The relatively low number of patients with SSI and the limited representation of subgroups, particularly open contaminated surgeries, may also impact generalizability and statistical power. Additionally, the majority of our SSI cases were superficial. We typically send cultures in cases of extensive erythema and deeper infections; however, since most SSI cases in our study were superficial, there is a significant lack of cultures for superficial SSIs (Table 3), making it difficult to verify if there are any differences in the types of pathogens involved over specific time periods.

Despite these limitations, we took measures to enhance the internal validity of our study, such as propensity score matching. Future studies with larger, more diverse samples are encouraged to validate and extend our findings. It's worth mentioning that since the eruption of the

Table 3 Pathogens involved in Surgical Site Infections (SSI) across the two study periods by SSI Type

SSI	*Covid-19*	*Non-Covid 19*
Superficial	***1/5:*** *STAPHYLOCOCCUS AUREUS / P. AURUGONOSA / ENTEROCOCCUS FAECALIS*	***7/12:*** *-STAPHYLOCOCCUS AUREUS* *-ESCHCERIA COLI, CANDIDA SPP* *-KLEBSIELLA PNEUMONIAE* *-ESCHERICHIA COLI, ENTEROCOCCUS FAECALIS* *-STAPH. EPIDERMIDIS* *-E. COLI / ENTEROCOCCUS FAECALIS* *-E. COLI / STAPHYLOCOCCUS AUREUS*
Deep	***1/1:*** *ESCHCERIA COLI*	***3/3***: *-CANDIDA SPP / Eschceria coli* *-ESCHERICHIA COLI/ ENTEROCOCCUS FAECALIS* *- STAPH. EPIDERMIDIS*
Organ Space	***0***	***2/2*** *- KLEBSIELLA PNEUMONIAE / CITROBACTER AMALONATICUS* *-KLEBSIELLA PNEUMONIAE / ENTEROCOCCUS FAECALIS*

Covid-19 pandemic, our department has been working to limit the number of visitors per day. The majority of medical staff continue to wear masks during visits and rounds. We have noticed that staff are using alcohol hand rub more frequently throughout the day. However, the results will need to be further examined in the coming years. We believe this could lead to a positive change with potential benefits in reducing SSI rates.

Conclusion

Our data, along with the published studies, demonstrate a low incidence of SSI during the COVID-19 pandemic. However, there is a clinically significant difference regarding the types of SSIs. During the COVID era, the predominant type of SSI is superficial. On the other hand, in the non-COVID era, we also observe a higher incidence of deep and organ space infections. Notably, the literature lacks sufficient studies, both in general and specifically for abdominal surgery, necessitating further research in this area. The implementation of restricted precautions such as practicing good hand hygiene using soap or alcohol-based hand rub, and using personal protective equipment like fresh nonsterile gloves, masks, eye protection, or face shields may have been crucial during the COVID-19 pandemic to prevent the development of SSI. Limiting visitors during the day may have also been a contributing factor. However, the presence of studies with contrasting results underscores a level of controversy on this topic. While our study contributes a robust foundation based on available data, it also calls for additional research.

Abbreviations

SSI	Surgical Site Infection
CDC	Centers for Disease Control and Prevention
MRSA	Methicillin resistant Staphylococcus aureus
WHO	World Health Organization
PPE	Personal protective equipment

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Not applicable.

Authors' contributions
SG - Made substantial contribution to conception, design, analysis and interpretation of data, participated in drafting of the article and gave final approval of the version to be published. TS – Made substanitial contribution to conception, design. Participated in drafting of the manuscript and gave final approval of the version to be published. RA - Made substantial contribution to conception and design and analysis and interpretation of data and gave final approval of the version to be published. AB- Made substantial contribution to the article, and participated in revised it critically, gave final approval of the version to be published. AK – made data collection, contributed to design and analysis, gave final approval of the version to be published. RL- made substantial contribution to conception, worked on data analysis and interpretation of data. EK- Made substantial contribution to the article, and participated in revised it critically, gave final approval of the version to be published.

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Availability of data and materials
All data generated or analyzed during this study are included in this published article [and its supplementary information files]. In case someone would like to request the data, they should contact the corresponding author (see the Title page).

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study and all relevant methods were approved by the Institutional Ethics Committee (Helsinki) of the Galilee Medical Center, 0092–20-NHR. The requirement for informed consent was waived by the ethics committee (Helsinki). Helsinki has granted us permission to access the patients' data, subject to their approval.

Competing interests
The authors declare no competing interests.

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