



Review Article

The burden of aerobic bacterial nosocomial infections, associated risk factors and antibiotic susceptibility patterns in a surgical site in Ethiopia: A systematic review

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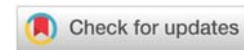
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Abstract

Nosocomial infection is an infection that acquired after exposure of patients to hospital for 48-72 hrs, but not present during admission. Surgical site infection is among the leading nosocomial infection that acquired after operation or admission. This review aims to determine the burden of NI in surgical site infection in Ethiopia systematically. Among a 167 mean of clinically suspected patients samples 9-92% were culture-confirmed with a mean of 70.125 and median 67. Seven studies identified 49.3-100% of culture-confirmed infection as SSI; two studies reported BSI 2.2 & 20.8 percent and one study declare UTI as 29.8 percent among 77 cultures confirmed and one study not reported about infection identified. Ward type, type of operation, wound type, being a male, site of a wound, age \geq 51, diabetes mellitus, anaemia, antibiotic usage after surgery, 11-15 days preoperative hospital stay, postoperative hospital stay; surgical procedure, urinary catheter, mechanical vent, IV catheter, longer duration from admission to discharge, longer duration of preoperative and preoperative prophylaxis identified as potential risk factors. *S. aureus* and CoNS is among the leading gram-positive bacterial isolate and *E. coli*, *Klebsiella spp*, *Proteus spp* and *P. aeruginosa* are among gram-negative organisms that isolated from eight studies in Ethiopia.

Introduction

Nosocomial Infection (NI) is an infection that acquired after the admission of patients to a hospital within 48-72 hrs, but not present during admission [1,2]. It is a major public health problem that causes morbidity, mortality and increased health care cost for hospitalization worldwide and remains significant now a day's [3,4]. Surgical Site Infections (SSI) are among these nosocomial an infection that occurs after an operation in the part of the body where the surgery took place. Most SSIs only involves the skin surrounding the incision; others may be deeper and more serious [5].

During the 1950s, a severe epidemic of NI occurred in surgical units in Europe and America, but thanks to the beginning of antiseptic surgery and antibiotics as prophylaxis, the problem

reduced a lot [6]. Despite the technological advances that have been made in surgery and wound management, wound infection has been regarded as the most common NI currently [7]. Surgical site infections are a major problem in developed countries, where it affects from 0.5% to 15% of hospitalized patients and as many as 50% or more of patients in Intensive Care Units (ICUs). The prevalence of NI in some developed countries, in the USA (15%), German and France (<3%) [8,9] and Brazil (16.9%) [10] were reported. In developing countries, the magnitude of the problem remains underestimated or even unknown largely because NI diagnosis is complex and surveillance activities to guide interventions require expertise and resources. A study conducted in Tanzania among patients undergoing major surgery reported 26% SSI [11]. In Ethiopia, different studies reported that the prevalence of post-surgical

wound infection ranges from 14.8–60% [12–15]. The variation in prevalence might be due to the difference in the type of operation (obstetrics & gynaecology, general surgery and orthopaedic) and the underlying status of patients as well as the infection control practices of the hospital environment and the type of etiologic agent [9,16,17].

The most predominant bacteria in SSIs are *S. aureus*, *Enterococcus spp.*, *P. aeruginosa*, *E. coli*, and other *Enterobacteriales*. Even though isolation of single bacterial species is common, 9–27% of polymicrobial, isolation from different surgical sites were reported [10,11,16,18]. These infections pose therapeutic challenges and are associated with substantially longer duration of hospital stay, increased hospital cost, higher morbidity and mortality [8,19], particularly when the agents are Methicillin-Resistant *S. aureus* (MRSA), Extended-Spectrum Beta-Lactamase (ESBL) producing *Enterobacteriales* and/or other agents collectively referred to as Multidrug-Resistant (MDR) [18,20,21].

Studies from developing countries have shown high rates of resistance (ranging from 50–100%) to the commonly used antibiotics like ampicillin, trimethoprim-sulphamethoxazole, gentamicin, chloramphenicol and third-generation cephalosporins among *S. aureus*, *E. coli*, and *P. aeruginosa* [11,22] as opposed to low rates of resistance ranging from 0–50% in developed countries [23]. However, in both settings, substantial rates of resistance to oxacillin, erythromycin and clindamycin to *S. aureus*, (ranged from 10–60%) were reported [11,16,22,24] whereas, vancomycin resistance (for *S. aureus* and other Gram-positive bacteria), amikacin, piperacillin, tazobactam and Imipenem resistance (for *E. coli*, *P. aeruginosa* and other Gram-negative bacteria) showed resistant rates less than 25% [23,25].

Factors underlying for NI after surgery are multiple and include the type of surgical procedure, the skills of the surgeon, the duration of surgery and the underlying disease of the host [26]. Both infection and wound healing are adversely influenced by poorly controlled diabetes mellitus. Age is considered an important factor, neonates and the elderly are particularly at risk of infection. Lifestyle can also impinge on immuno-competency especially stress, alcohol and drug abuse, smoking and lack of exercise or sleep [27].

In Ethiopia, there are few studies conducted on SSI [15,22,28–33]. This review provides a general overview of the burden of aerobic bacterial nosocomial infections, associated risk factors and antibiotic susceptibility patterns in a surgical site in Ethiopia based on the information available in the scientific literature.

Literature search strategy

A literature search was performed with English language restriction but without time restriction to retrieve publications on the burden of NI in the surgical site in 2017. PubMed was searched using a combination of the following keywords, including “nosocomial infection in the surgical site, postoperative infection,” together with the country name

“Ethiopia”. Reference lists of retrieved articles were hand-searched for additional studies that are not on PubMed sited but its Portable Document Format (PDF) is freely accessible from Google. Studies that are done on either prevalence and antibiotics susceptibility or prevalence and risk factors were selected and included in the review. There is no communication, which made and no permission found from authors.

Result

The PubMed search yielded 29 papers. Of these, 5 met the illegibility criteria and 3 studies from Google scholar added (Figure 1).

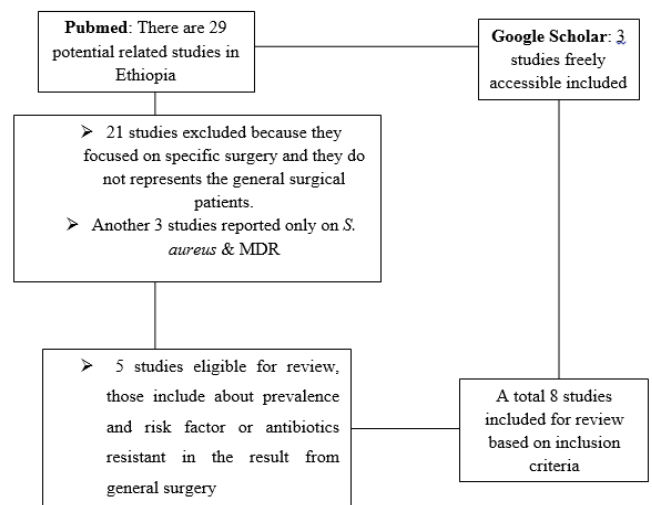


Figure 1: The flow diagram shows a systematic review of the burden of aerobic bacterial nosocomial infections, associated risk factors and antibiotic susceptibility patterns in a surgical site in Ethiopia.

Characteristics of studies and prevalence of SSI

Eight studies from five different regions of Ethiopia with prospective cross-sectional study design were included: Four studies from Amhara region; Two, from Southern Nation, Nationalities and People Representatives (SNNPR); one, from Addis Ababa and one from Tigray [15,22,28–33]. Authors name, year of publication/ study period and study area; study design, sample size, number and percent of clinically suspected SSI; number, percent and type of specimen taken; number and percent of culture-confirmed positive; number, percent and type of infection; significant risk factors $p < 0.05$ and total, list and percent of isolate manipulated from the result part of all studies.

All studies based on prospective cross-sectional studies. Almost all studies reported both clinical and microbiological data except one study from Bahir Dar not reported isolated organisms [30]. The mean of sample size is 435 with a range of 100–854 [15,22,28–33]. Six studies reported the mean age of patients with a mean of mean 20.7 yrs with a range of 26–38.2 years [15,22,28,30,32]. Age range reported in five studies which vary from 6 month– 100 years [15,28,30–32] but not in the



other three studies [22,29,33]. The mean is 169 for clinically suspected NI in SSI with a median of 166 cases with (8.2–100%) sampled patients [15,22,28–33]. All researchers used a swabbed sample from the wound site [15,22,28–33] however, three studies also used blood for Bloodstream Infection (BSI) [15,29,30] and one study used urine for Urinary Tract Infection (UTI) [15]. Among clinically suspected patients was confirmed culture positive with a mean of 70.125 and median 67 with 9–92 percent [15,22,28–33]. Seven studies identified 49.3–100 percent of culture-confirmed infection as SSI; two studies reported BSI 2.2 & 20.8 percent and one study declare UTI as 29.8 percent among 77 cultures confirmed and 1 study not reported about infection identified (Table1).

Risk factors and potential bacteria

Potential risk factors for acquiring NI in surgical site infections presented in table 2. *S. aureus*, *E. coli*, *CoNS*, *Klebsiella spp* and *Proteus spp* and *P. aeruginosa* are the most frequently isolated bacteria in descending order after calculated the average of the isolates from seven studies. Isolated organism not reported in a study from Bahir Dar which only focused on risk factors [30] (Table 2).

Antibiotic resistance rate

Antibiotics resistance among gram positive and gram-negative bacteria occurred with different rates of resistance. Total percent of antibiotics resistance for gram positive and negative bacteria that isolated from each sample for specific drug calculated and rates of resistance determined. Bacteria that showed resistance < 60% are low rates of resistance, 60–80% intermediate rates resistance, 81–99 % high rates of resistance and 100% fully resistance (Table 3).

Discussion

The small number of papers retrieved is evidence that little information is available on the burden of NI in the surgical site in Ethiopia. The review has shown that published studies were conducted in certain regions of the country and the majority of them are from the same hospitals. Besides, the scope of the studies is limited, since all were conducted in single hospitals. This review tried to include the prevalence SSI, types of bacteria, risk factors and antibiotics resistance is evaluated which is the strength of our study. The limitation of our review is only based on limited databases that may have an impact on the interpretation of the result.

Our review showed great variability in the reported prevalence of NI in the surgical site that ranges from 7.25 – 92%. Taking the average percentage of SSI in our study is 28.3 %, this finding is consistent with the prevalence reported from Vietnam (8.3–43.3%) [34], systematic review from Africa (2.5–30.9%) [35], Uganda 28.4% [36] and higher than reported from Nigeria (20.3%) [7], Saudi Arabia (11.4%) [37], Turkey (2.18%) [38]. The high prevalence of NI in surgical sites in Ethiopia may be due to lack of proper infection prevention, insufficient health personnel, overcrowded beds and a longer hospital stay before and after surgery.

In this review, different risk factors were identified age \geq 51 is one factor for acquiring of SSI [30] in one study, but a prospective study from China showed that patients aged over 75 years (5.6%) were more likely to develop SSI than those under the age of 75 years (3.0%), but the association is not significant with $P > 0.05$. There was no relationship observed between gender and development of SSI in the study from Nigeria with ($P < 0.98$, OR 0.99, 95% CI 0.47–2.09) [7]. Ward

Table 1: General Characteristics of papers retrieved in a systematic review of the literature on the burden of aerobic bacterial nosocomial infections, associated risk factors and antibiotic susceptibility patterns in a surgical site in Ethiopia.

Authors, year of publication, town	Study design	Sample size	Mean & range of age	No.(%) clinically suspected NI	No.(%) of the sample taken	No.(%) of culture-confirmed positive	No.(%) types of infection
Nigatu E, 2008, Addis Ababa [15]	Cross-sectional	854	38.2, (17-79)	215 (21.5)	88(40.9) puss 84 (39.1) urine 43 (20) blood	77 (9)	38(49.3) SSI 23(29.8) UTI 16(20.8) BSI
Lopiso D, 2009, Hawassa	Cross-sectional	194	28, (6 M –100)	194(100)	194(100) puss	138 (71.1)	138 (71.1) SSI
Bemnet A, et al. 2011, Gonder [22]	Cross-sectional	770	26, (15-40)	88(11.4)	88 (100) Swab	57 (7.4)	57 (7.4) SSI
Wondemagegn M, et al. 2012, Bahir Dar [29]	Cross-sectional	294	32.2, (NR*)	294(100)	Swab & blood (NR*)	32 (10.9)	30(93.8) SSI 7 (2.2) BSI
Wondemagegn M. et al. 2013, Bahir Dar [30]	Cross-sectional	294	32.2 (NR*)	294(100)	Swab & blood (NR*)	32 (10.9)	NR*
Aschalew G, et al. 2014, Gonder [31]	Cross-sectional	510	NR*, (4-77)	42(8.2)	37 (100) swab	37 (7.25)	37 (88.1) SSI
Reiye E, et al. 2014, Mekelle [32]	Cross-sectional	610	35.95, (15-79)	128(20.98)	128(100) swab	96(15.7)	96 (95) SSI
Meseret G, et al. 2014, Hawassa [33]	Cross-sectional	100	NR*	100(100)	100(100) swab	92(92)	92 (92) SSI

Keys: NI: Nosocomial Infection; BSI: Bloodstream Infection; UTI: Urinary Tract Infection; SSI: Surgical Site Infection; NR*: Not Reported



Table 2: Shows authors, publication year, significant risk factors and total, list and percent of an isolate of a systematic review the burden of aerobic bacterial nosocomial infections, associated risk factors and antibiotic susceptibility patterns in a surgical site in Ethiopia.

Authors, publication year	Significant risk factors, p -value < 0.05	Total, list, and % of isolates
Nigatu E, 2008 [15]	Surgical procedure (p < 0.000), urinary catheter (p < 0.000), mechanical vent (p < 0.000) and IV catheter (p < 0.000)	84: E. coli, 19; S. aureus, 16.7; Klebsiella Spp 16.7; P. aeruginosa, 14.3; CoNS, 11.9; P. vulgaris & E. cloacae, 7.1; S. pneumoniae & Citrobacter spp., 2.4; Serratia spp & M. morgani, 1.2
Lopiso D, 2009	Being a male (p < 0.001) and site of the wound (p < 0.034)	177: S. aureus, 37.5, E. coli, 25.4, Klebsiella Spp, 13.6, Proteus Spp, 10.2 and P. aeruginosa, 10.2, CoNS, 3.4
Bemnet A, et al. 2011 [22]	Ward type (p < 0.001) and emergency surgery (p < 0.001)	111: E. coli, 24.3; S. aureus, 23.4; CoNS 19.8; Enterobacter spp., 9.9
Wondemagegn M, et al. 2012 [29]	Wound type (P < 0.04)	42: S. aureus, 26.2; E. coli, 21.4; CoNS, 21.4; P. aeruginosa, 11.9; p. mirabilis, 9.5 Klebsiella spp, 4.8; E. aerogens, 4.8
Wondemagegn M, et al. 2013 [30]	Age ≥ 51 (p < 0.033); diabetes mellitus (p < 0.018), anemia (p < 0.007); antibiotic usage after surgery (p < 0.02), 11-15 preoperative hospital stay (p < 0.03), post-operative hospital stay, 5-10 (p < 0.004), 11-15(p < 0.000), >15 (p < 0.001)	NR*
Aschalew G. et al. 2014 [31]	NR*	49: S. aureus, 22.4; CoNS, 8.2; Klebsiella spp, 20.4; Proteus spp., 18.4; E. coli, 12.2; Enterobacter spp, 8.2; P. aeruginosa, 6.1; Citrobacter spp, 4.1
Reiye E, et al. 2014 [32]	Longer duration from admission to discharge (p < 0.008), longer duration of preoperative (p < 0.014); wound type (p < 0.029), ward type (p < 0.012); type of operation(p < 0.038) and preoperative prophylaxis (p < 0.021)	123: S. aureus ,34.2; Klebsiella spp, 24.8; CoNS , 15.4; Proteus spp, 12.8; P. aeruginosa, 9.4; E. coli, 5.1; Citrobacter spp, 3.4
Meseret G, et al. 2014 [33]	Ward type(p < 0.05)	177: S. aureus, 25.4; Klebsiella spp, 18.1; E. coli, 16.9; CoNS, 14.7; P. aeruginosa, 9.0; Proteus spp, 6.8; Streptococcus spp, 5.1; Citrobacter spp, 2.3; Enterobacter spp, 1.7

Table 3: Shows author's name, year of publication and overall rates of antibiotics resistance bacteria for a systematic review the burden of aerobic bacterial nosocomial infections, associated risk factors and antibiotic susceptibility patterns in a surgical site in Ethiopia.

Authors, Year	Antibiotics Resistance Rate							
	GRAM POSITIVE				GRAM-NEGATIVE			
	< 60%	60-80%	81 – 99 %	100%	<60%	60-80%	81-99 %	100%
Nigatu E, 2008 [15]	CRO, NOR, CIP	-	AMC, CN, C, MET, AML, DO	P, AMPCAF, TAT, SXT	NA, NOR, CRO, CIP, FM	CN	AMP, AMC, CAF, DO	AML, TAT, SXT
Lopiso D, 2009	SXT, CN, CAF, AMC, E, CIP	VAN	AMP, CRO	P	CN, CIP, AMC	CRO, CAF, SXT	AMP	-
Bemnet A, et al. 2011 [22]	DA, VAN, TAT	A, E, MET, CIP, CRO, CN, K	AMP, AML, DO, SXT, CAF	-	CIP, CRO, CN, TAT	A, K, SXT, C	AMP	AM
Wondemagegn M, et al. 2012 [29]	DO, TAT, CIP, CRO, E, CN	CAF, NOR, SXT, P, AM	-	AMP	DO, K, FM, TAT, NOR, CAF, CIP, CN	SXT, NA	CRO, AMP, AM	-
Wondemagegn M, et al. 2013 [30]	ND	-	-	-	-	-	-	-
Aschalew G, et al, 2014 [31]	ND	-	-	-	-	-	-	-
Reiye E, et al. 2014 [32]	E, CN	AMP, CRO, AMC	TAT, AML, C	-	E, CN, CIP	AMC	CRO, TAT, AMP, AML	-
Meseret G, et al. 2014 [33]	CRO, NOR, CN, VAN, P	AMP	-	-	CRO, NOR, CN	VAN	P, AMP	-

Key: AMK: Amikacin; AMP: Ampicillin; AMC: Amoxicillin /clavulanic acid; AML: Amoxicillin; C: Cloxacillin; CRO: Ceftriaxone; CIP: Ciprofloxacin; CN: Gentamicin; CAF: Chloraphinicol; Do: Doxycycline; DA: Clindamycin; E: Erythromycin; FM: Nitrofurantoin; K: Kanamycin; MET: Methicillin; NA: Nalidixic Acid; NOR: Norfloxacin; P: Penicillin; SXT: Cotrimoxazole; TAT: Tetracycline; VAN: Vancomycin

type is among significant factors for the development of SSI with p = 0.001, 0.012 & 0.05 in studies from Gonder, Tigray & Hawassa respectively [22,32,33]. A study from Saudi Arabia assessed acquiring infection is significant in different wards with p< 0.0001 [39].

In these review type of operation is identified as a significant risk factor with p<0.001 in emergency surgery only [22] and p<0.038 in all type of operation [32]. Type of operation also was assessed a study from China with the significant association in emergency surgery with p<0.000 which agreed with this review. Lower rate of SSI reported in emergency operation

compared to elective from Vietnam as opposed to the finding of this review [34]. Acquiring infection in emergency operation is due to low preoperative operation and use of antiseptics before surgery [40].

The indwelling device is considered as associated risk factors for different NI. Among 8 reviewed articles one study identified this device as risk factors: Urinary catheter (p < 0.000), Mechanical vent (p<0.000) and IV catheter (p<0.000) for the formation of infection other than surgical site infection such as BSI, UTI and Respiratory infection [15]. Similarly, a study from Vojvodina agreed as significantly associated risk factors



for the formation of NI [3]. Preoperative hospital stay for 11–15 Days ($p < 0.03$) & Hospital stay after operation for 5–10 days ($p < 0.004$), 11–15 days ($p < 0.000$) and > 15 days ($p < 0.001$) was one of the main risk factors for acquiring infection after surgery from a study from Bahir Dar [30]. A study from Saudi Arabia showed the length of hospital stay had a significant association for the development of NI between days of 8–13 and above with $p < 0.0001$ [39], but not good predictor from Vietnam [34]. Diabetics Mellitus (DM) and anaemia among the risks factors that assessed in one study from Bahir Dar by Wondimagegn, et al. with a p -value less than 0.018 & 0.007, respectively. Patients who were diabetic had six times increased risk of surgical site infection than those who were not diabetic. Anaemia patients have three and half times the risk for postoperative infection when compared with those without anaemia in a study from Nigeria [7], which support the study from Bahir Dar but the other 7 studies failed to assess about DM and anaemia. Antibiotic used before and after surgery determined as risk factors; from Mekelle and Bahir Dar with $p < 0.012$ & 0.02 respectively. According to a study from China by Cheng k, et al. only giving prophylaxis not a guaranty for prevention of SSI infection rather coordinated infection prevention needed from management to all personal that involved in the surgical ward. Also in one systematic review, a statistically significant association between antibiotic prophylaxis and increased risk of SSI observed in one study lacks biologic plausibility as a causal relationship given well-documented evidence regarding a protective effect of antibiotics for SSI [41].

According to this review, *S. aureus* [18.5%] and *E. coli* [17.8%] were the predominant bacterial isolate followed by *Klebsiella spp* [16.4%], CoNS [13.5%], *Proteus spp* [10.8%], *P. Aeruginosa* [10.2%], *Enterobacter spp* [6.34%] and *Citrobacter spp* [3.05%] [15,22,28–33]. In a study from Nepal [42] *S. aureus* and *E. coli* was the most frequently isolated bacteria from postoperative wound infection with 37.5% and 25%, respectively. Similarly, a study from Uganda [43], Gabon [44] and Nigeria [45] agreed with this review, but a study from Tanzania reported *P. aeruginosa* as the most frequently isolated bacteria followed with *S. aureus* and *K. pneumoniae* [46].

For this review antibiotics, resistance classified as those $< 60\%$ resistance for a specific drug as low-rates resistant, 60–80 % intermediate rate of resistant, 81%–99% high rates of resistant and 100% completely resistant. A drug that has a low rate of resistant in one area may have a high level of resistant in another area for both grams positive and gram-negative bacteria as tried to show Table 3.

Conclusion

Nosocomial infection in SSI due to the resistant organism is the most serious challenge for both physicians and patients to cure on time and spending more money on treatments. According to this review, the resulted infection rate or prevalence, which ranges from 7.25–92% was comparatively the highest report from Africa. A wide range of risk factors identified for SSI in this review (age, sex, indwelling device, anaemia, diabetes mellitus, wound type, type of operation, sites of the wound, longer pre- and post-operative hospital stay, pre

and post-operative antibiotics usage and ward type. *S. aureus* and CoNS are the most frequently isolated organism among gram positive and *E. coli*, *Klebsiella spp*, *Proteus spp* is frequently isolated gram-negative bacteria followed by *Enterobacter spp* and *Citrobacter spp*. In this review, different rates of resistance observed, a drug that is resistant to one area have low rates of resistance in another area, so empirical treatment should be avoided to reduce further cost and life loss. High rates of resistance (100%) occurred among gram-positive bacteria for P, AMP, TAT, SXT, CAF and SXT, AML and TAT among gram-negative bacteria, so ordering this drugs has no value in those areas.

Author contribution

TA conceived the idea, reviewed available data and prepared the manuscript.

Availability of data and material

Can be obtained from the corresponding author.

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