JOURNAL OF SURGICAL RESEARCH • JANUARY 2020 (245) 338–343

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Relationship Between Preoperative 25-Hydroxy Vitamin D and Surgical Site Infection

Ali Ghorbani Abdehgah, MD,[a] *Amir Monshizadeh, MD,*[a,*] *Mohammadreza Mohajeri Tehrani, MD,*[b] *Shirin Afhami, MD,*[c] *Behnam Molavi, MD,*[a] *Mahdi Jafari, MS,*[a] *Shirzad Nasiri, MD,*[a] *and Ahmadreza Soroush, MD*[a]

[a] *Department of Surgery, Tehran University of Medical Sciences, Shariati Hospital, Tehran, Iran*

[b] *Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Shariati Hospital, Tehran, Iran*

[c] *Department of Infectious Disease, Shariati Hospital, Tehran University of Medical Sciences, Shariati Hospital, Tehran, Iran*

ARTICLE INFO

Article history:
Received 20 February 2019
Received in revised form
2 July 2019
Accepted 16 July 2019
Available online xxx

Keywords:
Surgical site infection
Vitamin D
SSI

ABSTRACT

Background: Surgical site infection (SSI) is one of the most important and costly complications of surgical operations. Vitamin D antimicrobial and wound healing effects have been recently shown in animal models and in laboratory settings. Furthermore, potential effects of vitamin D in mitigating nosocomial infections and SSIs have been examined at a limited scale. To our knowledge, no comprehensive study has been performed to show the relationship between preoperative level of vitamin D and incidence of SSI. The present study was designed and implemented to investigate this relationship.

Materials and methods: We performed a prospective cross-sectional study involving 300 adult patients who were admitted to undergo surgery in our tertiary care unit from January 2016 to January 2018. Cutoff point was considered at a level of 30 (ng/mL) in defining vitamin D deficiency. The presence of any SSI was investigated and recorded at the time of discharge and at postoperative visits up to 30 d after the surgery. Cross-tabulation and bivariate and multivariate logistic regression with unadjusted and adjusted odd ratio were used to determine the association between dependent and independent variables and to identify factors associated with SSIs.

Results: Overall, of 300 patients who were investigated, 39% had preoperative vitamin D deficiency and 11% developed SSI. In univariate logistic regressions, 20 predictors were selected to be included in the multivariate analysis. Finally preoperative level of 25-hydroxy vitamin D, history of recent infection, preoperative and postoperative hospital length of stay, and postoperative blood transfusions were confirmed as statistically significant independent predictors of SSI.

Conclusions: Preoperative 25-hydroxy vitamin D level has a strong effect on postoperative SSI. Prospective double-blinded randomized clinical trials are required to confirm such strong relationship and to settle preoperative vitamin D measurement as a standard

* *Corresponding author*. Department of Surgery, Tehran University of Medical Sciences, North Karegar Street, Jalal-Ale-Ahmad Street, Tehran, Iran, 23185. Tel.: +989126044955; fax: +982188633039.

E-mail address: amir_mz1@yahoo.com (A. Monshizadeh).

https://doi.org/10.1016/j.jss.2019.07.036

approach to reduce postoperative complications including SSI. Preoperative patient optimization, limiting hospital length of stay, and blood transfusion are other strategies to reduce SSI.

Introduction

Surgical site infection (SSI) is one of the most important and costly complications of surgical operations and a crucial index for evaluating surgeon and hospital performance in quality improvement programs.[1-3] In spite of knowing the pathogenesis of SSI, the advances occurring in surgical techniques, and extensive use of prophylactic antibiotics, SSI "with an incidence of 2%-15% in general surgery" claims the first rank among "health care–associated infections."[3-6] This results in increased morbidity and mortality among surgical patients.[6]

In recent studies, special attention has been paid to the remarkable effects of vitamin D including its antimicrobial effects. In laboratory settings and animal models, vitamin D has been proven effective in wound healing, immune regulation, cellular growth, keeping the integrity of intestinal mucus, and diabetic ulcers.[4,5,7-10] Although the potential effects of this vitamin in mitigating nosocomial infections and SSIs have been examined in some of the abovementioned studies, to our knowledge, no comprehensive study has been conducted on the relationship between the incidence of SSI in general surgical operations and vitamin D.[11]

Today, vitamin D deficiency is considered a major health problem.[12] Considering the high prevalence of vitamin D deficiency and the potential effects it can have on SSI, the present study was designed and implemented with the aim of investigating the relationship between preoperative levels of vitamin D and SSI.

Materials and methods

After obtaining approval from our institutional review board, this prospective cross-sectional study was conducted on adult patients who were admitted to undergo surgery (emergency or elective) in our tertiary care center between January 2016 and January 2018. Patients who did not consent to participate in the study or did not complete the 30-d period for follow-up and cases under the age of 18 y were excluded from our research. Moreover, cases with uncontrolled diabetes (Hemoglobin A1C > 8%), having received chemotherapy or radiotherapy in the past 8 wk or currently undergoing treatments with immunosuppressive (other than corticosteroids) agents, and patients with a clean classification of surgical wounds were also excluded from the study. After obtaining informed consent, samples were withdrawn to measure the preoperative 25-hydroxy vitamin D, as well as albumin, hemoglobin (Hgb), Hgb A1c, blood urea nitrogen, and creatinine.

A confidential database was created to record items; this database was adapted from the American College of Surgeons National Surgical Quality Improvement Program user guide in addition to the lab results (Table 1) by a team of well-trained nurses supervised by a principal investigator. We used the criteria of the National Surgical Quality Improvement Program user guide to define SSI.[13] The presence of any superficial, deep, and organ-space infection was recorded at the time of discharge and at postoperative visits up to 30 d after the surgery. A level of 30 (ng/mL) was considered as the cutoff point in defining vitamin D deficiency. Any type of infections within 1 mo before surgery was also documented as part of the individual's data. The cutoff point was marked at 7 d to investigate the effect of preoperative or postoperative hospital length of stay (LOS) on SSI. Cross-tabulation and bivariate and multivariate logistic regressions with unadjusted and adjusted odd ratios were used to determine the association between SSI and independent variables and identify factors associated with SSIs. All variables with a P-value at or below 0.2 in the univariate logistic regressions were included in the multivariate logistic analysis to adjust the results of the univariate analysis for confounding variables. A two-sided P-value of 0.05 or lower was considered to be statistically significant in all analysis except the univariate logistic analysis. All analyses were performed with STATA version 11.2 (StataCorp. 2009. Stata Statistical Software: Release 11. College Station, TX: StataCorp LP.).

Results

Overall, the records of 300 patients were studied. Varied types of gastrointestinal tract, hepatobiliary, thoracic, and vascular operations were recorded during the time frame. 35 patients were excluded from the study. The mean age was 47.4 y, and 44.7% of the patients were male. Overall, 11% of the patients had SSI, whereas 89% were free of infection. Moreover, 39% of patients had preoperative vitamin D deficiency. The mean vitamin D level was 54 $\pm$ 47.07 ng/mL. Other characteristics and variables are shown in Table 1. In the univariate logistic analysis, it was shown that body mass index, history of cancer, preoperative use of corticosteroids, recent infection, smoking, preoperative 25-hydroxy vitamin D level, Hgb level, preoperative albumin level, Hgb A1C, postoperative LOS, operation type (open/laparoscopy), surgery type (elective/emergency), drain usage, preoperative blood transfusion, postoperative blood transfusion, blood transfusion during surgery, preoperative LOS, ICU LOS, and American Society of Anesthesiologists classification 2 and 3 significantly affect SSIs (P- Values < 0.20 were entered in the model) (Table 2).

In univariate logistic regressions, 20 predictors were selected to be included in multivariate analysis which showed patients with deficient levels of preoperative 25-hydroxy vitamin D were 4.10 times more likely to develop SSIs than patients with sufficient levels (P-value = 0.013). In addition, it was shown patients with recent infection were 3 times (P-value = 0.045) and patients who experienced postoperative blood transfusion were 5.90 times (P-value = 0.010) more likely

Table 1 – Descriptive characteristics of patients based on SSI.

Variables	Surgical site infection	
	Positive	Negative
Total *n* (%)	33 (11)	267 (89)
25-Hydroxy vitamin D (ng/dL) (mean ± SD)	24 ± 2.67	57 ± 4.31
BMI (kg/m^2) (mean ± SD)	23 ± 1.40	27 ± 1.52
Albumin (g/dL) (mean ± SD)	3.68 ± 0.54	3.88 ± 0.60
Hgb A1c (%)(mean ± SD)	5.97 ± 0.91	5.66 ± 0.88
Anemia (Hgb ≤ 12) (*n*) (%)	7 (21.21)	52 (19.47)
HTN (*n*) (%)	4 (12.12)	42 (15.73)
Cancer (*n*) (%)	16 (48.48)	4 (1.49)
Cr (mg/dL) (mean ± SD)	0.855 ± 0.03	0.933 ± 0.03
Age (y) (mean ± SD)	46.83 ± 13.84	48.1 ± 16.30
Corticosteroids intake (*n*) (%)	11 (33.33)	2 (0.74)
Sex (*n*) (%)		
Male	13 (39.4)	115 (43.07)
Female	20 (60.6)	152 (56.93)
Smoking (*n*) (%)	9 (27.27)	45 (16.58)
Yes		
No	20 (60.6)	177 (66.29)
Intraoperative blood loss (cc) (Mean ± SD)	255 ± 34.11	195 ± 29.89
Fluid balance (L) (mean ± SD)	2.1 ± 0.90	1.9 ± 0.75
Blood transfusion (before) (*n*) (%)	2 (6.06)	11 (4.11)
Blood transfusion (after) (*n*) (%)	2 (6.60)	15 (6.61)
Blood product (nonpacked cell) transfusion (*n*) (%)	3 (9.09)	24 (8.98)
Type of surgery (*n*) (%)		
Open	28 (78.8)	144 (53.9)
Lap.	8 (15.10)	114 (42.7)
Both	2 (6.06)	4 (1.5)
Prophylactic ABX, 60 min before op. (*n*) (%)		
Positive	11 (33.3)	182 (68.16)
Negative	22 (66.7)	91 (31.84)
ASA classification (*n*) (%)		
1	7 (21.21)	114 (42.69)
2	10 (30.30)	79 (29.58)
3	16 (48.49)	68 (25.46)
Postoperative LOS (d) (mean ± SD)	15.42 (6.42)	4 (1.75)
Preoperative LOS (d) (mean ± SD)	2.84 (0.80)	2.97 (0.80)
Wound classification (*n*) (%)		
Dirty	9 (27.27)	11 (4.11)
Clean/contaminated	17 (51.51)	213 (79.77)
Contaminated	7 (21.22)	26 (9.73)
Preoperative vitamin D intake (*n*) (%)		
Yes	1 (3.03)	21 (7.86)
No	17 (51.51)	133 (49.81)

(continued)

Table 1 – (*continued*)

Variables	Surgical site infection	
	Positive	Negative
Elective/emergency (*n*) (%)		
Elective	21 (63.6)	212 (79.4)
Emergency	12 (36.4)	55 (20.6)

HTN = hypertension; Cr = creatinine; Lap. = laparascopy; ASA = American Society of Anesthesiologists.

to develop SSIs than others. In addition, this analysis revealed that longer preoperative and postoperative LOS is associated with increased chance of developing SSI (P-value = 0.001 and P-value = 0.001, respectively).

Discussion

SSI is one of the most important indices of quality improvement programs to supervise and improve the performance and outcomes of surgical operations.[1-3] Investigation of the factors affecting these infections and finding novel methods to improve this index is considered crucial. A few studies have investigated the potential effects of this vitamin in reducing nosocomial infections and surgical wounds.

Our analysis showed that preoperative level of 25-hydroxy vitamin D, history of infection within last month of surgery, preoperative and postoperative hospital LOS, and postoperative blood transfusions are independent predictors of SSIs. As mentioned, we found that patients who had higher preoperative vitamin D levels suffered less from SSI. These findings are consistent with the study by Youssef *et al.* that collected different reports in interpreting the role of vitamin D in reducing nosocomial infections such as bacteremia, blood infections resulting from central venous catheters, pneumonia, *Clostridium difficile* infection, catheter-related urinary tract infection, *Methicillin resistant Staphylococcus aureus*, and SSI. They have proposed that the serum level of vitamin D should be measured from the very beginning of hospital admission, and immediate measures should be taken to treat and address insufficient levels of this vitamin.[11]

In addition, the study by Quraishi *et al.*, limited to patients undergoing Roux en Y gastric bypass, reported that preoperative vitamin D deficiency increases the risk of nosocomial infections including SSI.[14] We did adjust the results for confounders such as age, sex, body mass index, physical status, and other illnesses to minimize this issue with observational research. However, blinded clinical trials are still warranted to see whether correcting low levels of vitamin D before the surgery can prevent infection.

The rate of SSI in our study population was 11%, which is higher than other studies.[15-18] This discordance may be explained by our method in excluding clean type wounds because of lower rate of infection in these wounds and our limitation in investigating larger population to have statistically appropriate size in study groups and also inclusion of emergency operations in the study. In our study, 39% of

Table 2 – Univariate and multivariate logistic regression model results.

Variables	Levels	Univariate		Multivariate	
		OR (CI %)	P-value	OR (CI %)	P-value
Age	Year	1.0 (0.97-1.02)	0.751		
Sex	Male	Ref.			
	Female	0.69 (0.32-1.46)	0.337		
BMI	Kg/m^2	1.9 (1.22-2.79)	0.034*	1.67 (0.91-2.13)	0.187
Intraoperative blood loss	(cc)	2.05 (0.91- 3.55)	0.285		
Fluid balance	(L)	1.77 (0.88-2.31)	0.450		
Diabetes	No	Ref.			
	Yes	1.48 (0.53-4.15)	0.451		
History of cancer	No	Ref.		Ref.	
	Yes	2.13 (1.17-5.69)	0.028*	1.90 (0.98-3.67)	0.090
Hypertension	No	Ref.			
	Yes	1.29 (0.51-3.29)	0.583		
Use of corticosteroids	No	Ref.		Ref.	
	Yes	1.60 (1.12-5.86)	0.042*	1.87 (0.71-4.11)	0.225
Recent infection	No	Ref.		Ref.	
	Yes	7.19 (2.45-21.5)	<0.001*	3.0 (1.67-5.32)	0.045†
Smoking	No	Ref.		Ref.	
	Yes	0.34 (0.08-1.52)	0.161*	0.67 (0.25-1.05)	0.342
Preoperative level of vitamin D	Normal	Ref.		Ref.	
	Abnormal	4.11 (1.84-9.2)	0.001*	4.10 (2.05-6.20)	0.013†
Preoperative antibiotic	No	Ref.			
	Yes	0.94 (0.35-2.52)	0.914		
Hgb	(g/dL)	1.53 (0.23-2.13)	0.080*	1.23 (0.7-1.92)	0.129
Creatinine	(mg/dL)	1.45 (1.10-2.06)	0.383		
Albumin	(g/dL)	0.53 (0.28-0.99)	0.050*	0.51 (0.15-1.12)	0.213
Hgb A1c	(%)	2.54 (1.40-4.01)	0.078*	2.30 (0.89-3.88)	0.090
Postoperative LOS	Days	5.10 (1.52-9.21)	<0.001*	7.18 (3.56-10.78)	0.001†
Operation type	Lap.	Ref.		Ref.	
	Open	4.60 (1.55-13.61)	0.006*	2.50 (1.20-7.32)	0.335
Surgery type	Emergency	Ref.		Ref.	
	Elective	2.56 (0.95-3.87)	0.093*	2.79 (0.80-4.05)	0.086
Drain usage	No	Ref.		Ref.	
	Yes	0.7 (0.225-0.93)	0.046*	0.72 (0.11-0.85)	0.125
Preoperative blood transfusion	No	Ref.		Ref.	
	Yes	2.16 (0.8-8.55)	0.111*	3.45 (0.9-6.10)	0.095
Postoperative blood transfusion	No	Ref.		Ref.	
	Yes	4 (1.29-12.14)	0.001*	5.90 (3.56-8.78)	0.010†
Other blood product transfusion	No	Ref.			
	Yes	1.10 (0.3-3.41)	0.862		
Blood transfusion during surgery	No	Ref.		Ref.	
	Yes	2.23 (0.70-7.17)	0.178*	1.60 (0.58-3.08)	0.455
Preoperative LOS	Days	1.25 (1.10-2.5)	0.001*	4.50 (2.11-6.75)	0.001†
ICU LOS	Days	1.20 (1.05-135)	0.038*	2.30 (0.94-4.11)	0.785
ASA classification	Class 1	Ref.		Ref.	
	Class 2	3.04 (0.9-10.39)	0.076*	3.45 (0.83-7.65)	0.321
	Class 3	14.20 (6.45-22.50)	<0.001*	9.58 (1.0-16.22)	0.075

ASA = American Society of Anesthesiologists.
*0.2 level of significance in univariate analysis.
†0.05 level of significance in multivariate analysis.

patients had abnormal vitamin D level which is in line with prevalence of vitamin D deficiency in other reports.[19-21]

We found that, preoperative and postoperative hospital stay for more than 7 d increases the risk of SSIs by 4.50 and 7.18 times, respectively, which is consistent with other studies.[18,22-25] For example, Banashankari *et al.* report preoperative/postoperative hospital stay for longer days expose the patient for contamination or colonization by infectious pathogens which will increase risk of SSIs.[25] This suggests that shortening the preoperative hospital stay reduces the incidence rate of SSIs.

We observed that patients with history of recent infection were more likely to develop SSIs than other patients. In addition, our finding regarding the increased risk of SSI in patients who received blood transfusion (odds ratio = 5.90) is consistent with multiple reports in the literature. For example, results in a meta-analysis by Kim j. *et al.* showed that the prevalence of SSI was 2.88% and 1.74% for transfusion and nontransfusion patients, respectively. Authors revealed that the blood transfusion group had a significantly higher frequency of SSI based on the pooled analysis and concluded that blood transfusion is a significant risk factor in increasing the SSI rate.[26]

Some of the variables such as smoking were considered as risk factors for SSI in other studies.[27] In our univariate logistic regression, smoking was one of the risk factors for SSI but multivariate analysis could not approve that. This may be due to different population of other studies and the limited number of cases of our study groups.

Controlling all the risk factors that contribute to SSIs and adjusting for the confounders just for evaluation of one variable is hard and needs a very large population. We were limited in the number of our cases. In addition, although we controlled for factors such as patient overall and nutritional status by controlling comorbidities, American Society of Anesthesiologists score, and albumin level, but these entities are multifactorial and too complex to be thoroughly covered by statistical methods. In addition, although we used a standard criterion such as a surgeon's diagnosis of SSI, we probably had measurement bias in our observations.

Conclusion

We conclude that preoperative 25-hydroxy vitamin D levels have a strong effect on SSI. However, prospective double-blinded randomized clinical trials are needed to confirm such strong relationship and to settle preoperative vitamin D measurements as a standard approach to reduce postoperative complications including SSI. Preoperative patient optimization, limiting hospital LOS, and blood transfusion are other strategies to reduce SSI.

Acknowledgment

Authors' contributions: A.G.A. contributed to the study design, data collection, and interpretation. A.M. contributed to the literature search, study design and data analysis, interpretation, and writing. M.M.T. contributed to the study design, data collection, interpretation, critical revision, and project implementation. M.J. contributed to the study design and data analysis. S.A., S.N., B.M., and A.S. contributed to the study design and interpretation.

Disclosure

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

REFERENCES

1. Now SH. *Prevent surgical site Infectionsâ€"Getting Started Kit. Safer Healthcare Now*. 2014.
2. Lawson EH, Hall BL, Ko CY. Risk factors for superficial vs deep/organ-space surgical site infections: implications for quality improvement initiatives. *JAMA Surg*. 2013;148:849–858.
3. Safety WP, Organization WH. *WHO guidelines for safe surgery: 2009: safe surgery saves lives*. Geneva: World Health Organization; 2009.
4. Zubair M, Malik A, Meerza D, Ahmad J. 25-Hydroxyvitamin D [25 (OH) D] levels and diabetic foot ulcer: is there any relationship? *Diabetes & Metabolic Syndrome. Clin Res Rev*. 2013;7:148–153.
5. Burkiewicz CJCC, Guadagnin FA, Skare TL, do Nascimento MM, Servin SCN, de Souza GD. Vitamina D e cicatrização de pele: estudo prospectivo, duplo-cego, placebo controlado na cicatrização de úlceras de perna. *Revista do ColÃ©gio Brasileiro de CirurgiÃµes*. 2012;39:401–407.
6. Control CfD. Prevention. Surgical site infection (SSI) event. www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf; 2017. Accessed 2018.
7. Schwalfenberg GK. A review of the critical role of vitamin D in the functioning of the immune system and the clinical implications of vitamin D deficiency. *Mol Nutr Food Res*. 2011;55:96–108.
8. Heilborn JD, Weber GN, Grönberg A, Dieterich C, Ståhle M. Topical treatment with the vitamin D analogue calcipotriol enhances the upregulation of the antimicrobial protein hCAP18/LL-37 during wounding in human skin in vivo. *Exp Dermatol*. 2010;19:332–338.
9. Oda Y, Tu C-L, Menendez A, Nguyen T, Bikle DD. Vitamin D and calcium regulation of epidermal wound healing. *J Steroid Biochem Mol Biol*. 2016;164:379–385.
10. Molinari C, Rizzi M, Squarzanti DF, Pittarella P, Vacca G, RenÃ F. 1Î±, 25-Dihydroxycholecalciferol (Vitamin D3) induces NO-dependent endothelial cell proliferation and migration in a three-dimensional matrix. *Cell Physiol Biochem*. 2013;31:815–822.
11. Youssef DA, Ranasinghe T, Grant WB, Peiris AN. Vitamin D's potential to reduce the risk of hospital-acquired infections. *Derm Endocrinol*. 2012;4:167–175.
12. Palacios C, Gonzalez L. Is vitamin D deficiency a major global public health problem? *J Steroid Biochem Mol Biol*. 2014;144:138–145.
13. User guide for the 2014 ACS NSQIP participant Use data file (PUF). American College of surgeons. https://www.facs.org/~/media/files/quality%20programs/nsqip/nsqip_puf_userguide_2014.ashx; 2015. Accessed October 28, 2018.
14. Quraishi SA, Bittner EA, Blum L, Hutter MM, Camargo CA. Association between preoperative 25-hydroxyvitamin D level and hospital-acquired infections following Roux-en-Y gastric bypass surgery. *JAMA Surg*. 2014;149:112–118.
15. Garey KW, Dao T, Chen H, et al. Timing of vancomycin prophylaxis for cardiac surgery patients and the risk of

surgical site infections. *J Antimicrob Chemother*. 2006;58:645–650.
16. Amutha BVT, Science I. A retrospective study on the pattern of pathogens Isolated from surgical site wound infection in tertiary care hospital in Coimbatore. *India Int Res J Med Sci*. 2014;2:1–6.
17. Elbur AI, Yousif M, ElSayed A, AbdelRahman M. Prevalence and predictors of wound infection in elective clean and clean/contaminated surgery in Khartoum Teaching Hospital, Sudan. *Int J Infect Control*. 2012;8:1–10.
18. Wassef M, Hussein A, El-Sherif R. A prospective surveillance of surgical site infections: study for efficacy of preoperative antibiotic prophylaxis. *Afr J Microbiol Res*. 2012;6:3072–3078.
19. Alipour S, Saberi A, Seifollahi A. Risk factors and prevalence of vitamin d deficiency among Iranian women attending two university hospitals. *Iran Red Crescent Med J*. 2014;16:e15461.
20. Hashemipour S, Larijani B, Adibi H, et al. Vitamin D deficiency and causative factors in the population of Tehran. *BMC Public health*. 2004;4:38.
21. Rahnavard Z, Eybpoosh S, Homami MR, et al. Vitamin D deficiency in healthy male population: results of the Iranian multi-center osteoporosis study. *Iranian J Public Health*. 2010;39:45.
22. Anjum W, Abrar N. *A study on surgical site infections (SSI) and associated factors in a tertiary care hospital in Tumkur, Karnataka*. 2017.
23. Afifi IK, Labah EA, Ayad KM. Surgical site infections after elective general surgery in Tanta University Hospital: rate, risk factors and microbiological profile. *Egypt J Med Microbiol*. 2009;182:61–72.
24. Asgari S, Mohaghegh P, Ghorbani-Abdehgah A, et al. Comparison of surgical site infections between laparoscopic and open cholecystectomy. *Govaresh*. 2018;22:266–270.
25. Banashankari GS, Rudresh HK, Harsha SS. An overview of surgical site infections: an insight into the prevalence, etiology and predisposing factors. *Valley Int J*. 2014;1:493–499.
26. Kim JL, Park J-H, Han S-B, Cho IY, Jang K-M. Allogeneic blood transfusion is a significant risk factor for surgical-site infection following total hip and knee arthroplasty: a meta-analysis. *J Arthroplasty*. 2017;32:320–325.
27. Nolan MB, Martin DP, Thompson R, Schroeder DR, Hanson AC, Warner DO. Association between smoking status, preoperative Exhaled Carbon Monoxide levels, and postoperative surgical site infection in patients undergoing elective surgery. *JAMA Surg*. 2017;152:476–483.