

# Detection of Toxic Shock Syndrome Toxin-1 among Children Undergoing Surgical Operations

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## Abstract:

**Background:** Toxic-shock syndrome (TSS) is an acute onset; multiorgan disease caused mainly by Toxic-shock syndrome toxin-1 (TSST-1) producing *Staphylococcus aureus* strains. Testing for TSST-1 or anti-TSST-1 antibodies in the clinical setting may help to predict and prevent the appearance of TSS caused by nosocomial *S. aureus* infection.

**Objectives:** Detection of TSST-1 in the sera of children patients arranged to undergo surgical operations, and its relevance with certain demographic factors.

**Patients and methods:** This cross-sectional study was conducted in the Baquba General Teaching Hospital-Diyala province for the period from August 2015 to April 2016. Eighty eight patients from those undergoing surgical operations were enrolled. The age range was 1-14 years. Thirty one (35.2%) were males and fifty seven (64.8%) were females. Human privacy was respected by taking patient's consensus. Venous blood samples were collected aseptically; the sera were separated and kept frozen till use. Serum samples were investigated for the presence of TSST-1 using ELISA technique. Statistical analyses were done using SPSS version 18. P value less than 0.05 was considered significant.

**Results:** The results showed that the overall detection rate of TSST-1 among children undergoing surgeries was 44.3%. It was insignificantly higher among younger age group, females, and ruralizes. According to the type of surgery, the detection rate was higher among those patients with fractures (10.2%), followed by patients with burns (9.1%), but it failed to reach the levels of statistical significant.

**Conclusion:** About one half of children patients undergoing surgical operations are infected with TSST-1 producing *S. aureus*.

**Keywords:** Toxic-shock syndrome, Toxic-shock syndrome toxin-1, *S. aureus*.

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## Introduction:

Infectious diseases caused by *Staphylococcus aureus* constitute a significant clinical and public health problem. It causes some of the most severe hospital-associated and community-acquired illnesses [1]. Toxic-shock syndrome (TSS) is an acute onset; multiorgan illness caused by TSS toxin-1 (TSST-1) producing *S. aureus* strains. The gene coding for TSST-1 is found in more than 20% of *S. aureus* isolates [2,3]. TSST-1 is the prototypical superantigen that binds to major histocompatibility complex molecule-II (MHC-II), yielding T cell

Stimulation, which promotes the protean manifestations of TSS [4,5]. One-third of all TSS cases have been found in men possibly due to surgical wounds or any skin wound. TSST-1 is the cause of 50% of non-menstrual and 100% of all menstrual TSS cases [6,7]. Additionally, the rate of neonatal TSS caused by Methicillin resistant *S.aureus* (MRSA) is increasing [8,9]. Clinically, TSS is associated with fever, shock and multisystem involvement, including a desquamative skin rash, making its

diagnosis difficult because, in the early stages, its signs and symptoms resemble those of other common illnesses such as scarlet fever [10,11]. As *S. aureus* is ubiquitous pathogen, the risk for preoperative or postoperative nosocomial infections has been markedly increased particularly among immunocompromised hosts mainly due to MRSA that consequently may develop TSS [12,13]. In this context, it has been reported that 40 million patients undergo surgery each year in the United States, 20% of them developed postoperative nosocomial infection most commonly by *S. aureus*, and carriage of *S. aureus* in the anterior nares has been identified as a riskfactor for these infections [14]. Furthermore, it has been found that MRSA is the major cause of surgical site infections, with a higher mortality and longer duration of care recommended that preoperative MRSA surveillance allows the selection of appropriate and effective bundle of interventions of decolonization and prophylaxis protocols and provides needed data for epidemiological studies [15,16]. Several studies had asserted that high prevalence of TSS was reported among patients with absence or low levels of anti-TSST-1 antibodies, suggesting that testing for TSST-1 antibody

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in the clinical setting may help to predict and prevent the appearance of TSS caused by nosocomial *S. aureus* infection [17,18,19,20]. Similarly, detection of TSST-1 is among a bundled intervention of decolonization and prophylaxis to decrease *S. aureus* surgical site infections [21,16,22].

**Patients and methods:**

This cross-sectional study was conducted in the Baquba General Teaching Hospital- Diyala province for the period from August 2015 to April 2016. 88 patients were enrolled, all of them were arranged to undergo surgical operations. The age range was 1-14 years. Thirty one (35.2%) were males and fifty seven (64.8%) were females.. All subjects were interviewed by means of a structured questionnaire for general demographic factors gender, age, residence, educational levels. Human privacy was respected by taken patient’s consensus. Five milliliters of venous blood sample was drawn aseptically; the sera were separated and kept frozen till use. Serum samples were investigated for the presence of TSST-1 using ELISA technique, (MYBio Source, USA) kit. Statistical analyses were done using SPSS version 18. Chi-square was used for paired comparison, and P value less than 0.05 was considered significant.

**Results:**

Eighty Eight child patients from those arranged to undergo surgical operation were included in this study. The age range was 1-14 years. The mean age was  $8.26 \pm 3.33$  years. Thirty one (35.2%) were males and fifty seven (64.8%) were females. Twenty one (23.9%) were urban and sixty seven (76.1%) were rural. The type of surgeries include 12(13.6%) ENT surgeries, 8(9.1%) were extraction of foreign bodies, 10 (22.4%) hernias, 6(6.8%) UT surgeries, 13 (14.8%) fractures, 19(21.6%) burns, 8 (9.1%) cardiovascular surgeries, 4(4.5%) neurosurgeries, 4(4.5%) cosmetic surgeries, and 4(4.5%) appendectomy, table (1) showed distribution of patients according to age, sex, and residence. The distribution of TSST-1 according to age, sex, residence of patients was showed in table (2). The TSST-1 detection rate was slightly higher in the 1-7 years compared to 8-14 years age group (31.8% vs 28.4%). The detection rate was also slightly higher among female compared to males (23.9 % vs 20.5%). It was also higher in rural than in urban (30.7% vs 13.6 %). In all these three relationships, the difference was failed to reach the levels of statistical significant. According to the type of surgery, the detection rate of TSST-1 was highest among those patients with fractures (10.2%) followed by patients with burns (9.1%); however, the difference in both cases was insignificant.

**Table (1): Distribution of patients according to their age, sex, and residence.**

Variables	No.	%	95% Confidence interval	
Age (Ys)				
1-7	35	39.8	29.8	51.1
8-14	53	60.2	48.9	70.2
Total	88	100		
Sex				
Male	31	35.2		
Female	57	64.8	24.4	43.2
Total	88	100	56.8	75.6
Residence				
Urban	21	23.9		
Rural	67	76.1	14.8	33.0
Total	88	100	67.0	85.2

**Table (2): Distribution of TSST-1 according to the age, sex, residence.**

Variable	TSST-1		Total (%)	P value
	Positive (%)	Negative (%)		
Age				Chi-Square= 0.439 P=0.329[NS]
1-7	28(31.8)	21(23.9)	49(55.7)	
8-14	25(28.4)	14(15.9)	39(44.3)	
Total (%)	53(60.2)	35(39.8)	88(100)	
Sex				Chi-Square=3.66 P=0.073[NS]
Male	18(20.5)	13(14.8)	31(35.2)	
Female	21(23.9)	36(40.9)	57(64.8)	
Total	39(44.3)	49(55.7)	88(100)	
Residence				Chi-Square= 1.83 P= 0.212[NS]
Urban	12(13.6)	9(10.2)	21(23.9)	
Rural	27(30.7)	40(45.5)	67(70.1)	
Total	39(44.3)	49(55.7)	88(100)	

**Table (3): Distribution of TSST-1 according to the type of surgery.**

Type of surgical operation	TSST-1		Total (%)	P value
	Positive (%)	Negative (%)		
ENT surgeries	4(4.5)	8(9.1)	12(13.6)	Chi-Square= 11.4 P= 0. 249 [NS]
Foreign bodies	4(4.5)	4(4.5)	8(9.1)	
Hernias	5(5.7)	5(5.7)	10(11.4)	
Urosurgeries	1(1.1)	5(5.7)	6(6.8)	
Fractures	9(10.2)	4(4.5)	13(14.8)	
Burns	8(9.1)	11(12.5)	19(21.6)	
Cardiovascular surgeries	4(4.5)	4(4.5)	8(9.1)	
Neurosurgeries	1(1.1)	3(3.4)	4(4.5)	
Cosmetic surgeries	0(0)	4(4.5)	4(4.5)	
Appendicitis	3(3.4)	1(1.1)	4(4.5)	
Total	39(44.3)	49(55.7)	88(100)	

**Discussion:**

Since more than decade ago, *S. aureus*, particularly MRSA strains had been identified as one of the most prevalent nosocomial pathogen that were responsible for a wide range of postoperative infections leading to significant patient

morbidity and mortality [21,13,4,] Undoubtedly the source of these strains could be either endogenously from healthcare workers carries these germs in their anterior narse or on their skin, or exogenously from admitted infected or carrier patients [23,24]. It is worth to remember here the results of our previous study in which the rate of nasal carriage of *S. aureus* among general population in Diyala province was 26.3% and higher rate was found among HCWs 30.5%, and in the healthcare settings including surgical theaters, hospital wards, and kitchens (27.2%, 22.0% and 18.6%) respectively [25]. So unsurprisingly, both hospital-acquired and community-acquired MRSA (CA-MRSA) strains had increased in frequency in the last few years, reaching epidemic dimensions [13]. Therefore, medical authorities and researchers were in continuous searching for an accurate detection and effective intervention to reduce the rate of nosocomial infections due to *S. aureus* [21,15,22]. A part from hospital admitters, surgical and burn patients were under a particular risk for acquiring *S. aureus* nosocomial infections for well documented reasons [14,25,16]. For these reasons, the present study was arranged to detect the TSST-1 which surely indicate the presence of TSST-1 *S. aureus* producing strains among surgical and burn patients in Diyala province. The present study found that the overall detection rate of TSST-1 among surgical patients was 44.3%. Similar higher results had been previously reported among burn and surgical patients [21,26]. Parsonnet and his workers reported that *S. aureus* was isolated from at least one site in 52% of women in Tokyo, and of these 9% were TSST-1 positive [2]. Furthermore, children with burns had greater risk of developing toxic shock syndrome than adults probably due to insufficient antibody titers. However, infants below 6 months and children more than 4 years were found to have protective levels of anti-TSST-1 antibodies [17,19]. Therefore, burned patients with negative titers of anti-TSST-1 antibody may be susceptible to TSS, suggesting that testing for TSST-1 antibody in the clinical setting may help to predict and prevent the appearance of TSS caused by nosocomial MRSA infection [27,20]. The higher rate of detection of TSST-1 among patients from rural areas compared to those from urban may indirectly indicate a higher carrier rate of *S. aureus* among rurals probably due to microbial, patient or environmental factors [2]. Given the importance of *S. aureus* nosocomial infections, as revealed by our findings, along with related results of previous studies, suggest the urgent need for the establishment of an effective bundled intervention with surgical site infections among patients undergoing surgeries including Preoperative decolonization and prophylaxis is one potential strategy to decrease or eliminate *S. aureus* nasal carriage among certain patient populations or in certain healthcare settings [21,15,28]. Routine screening of surgical or burn patients for the detection of antibodies to TSST-1

producing *S. aureus* stains using a rapid laboratory assay is the least recommended intervention [29]. Gustinet al. [30]. Indicates that surveillance data on surgical site infections may be an interesting epidemiological source for planning for the development of anti-staphylococcal vaccines is a priority to prevent surgical site infections. Additionally, surveillance data are very important to determine the local stains of *S. aureus* and to decide effective interventions [16, 22,24]. More precisely, it is essential that all pediatric and emergency departments accepting children with burns are aware of the symptoms, signs and early management of TSS [31].

#### **Conclusion:**

About one half of children patients undergoing surgical operations are infected with TSST-1 producing *S. aureus*. Preoperative screening of patients for TSST-1 or anti-TSST-1 antibodies is recommended to reduce the postoperative nosocomial infections.

#### **Author Contributions:**

AsmaaHaseebHwaid initiated the project and searched the databases for potentially eligible articles based on their titles and abstracts (study conception and study design). Abdulrazak SH. Hasan reviewed the articles, performed the statistical analysis and interpreted the results and wrote the manuscript. Zaienb M. criticalrevision. All the authors reviewed the final version of the manuscript prior to submission for publication.

#### **References:**

1. Ryan, K.J.; Ray C.G.; Ahmad, N.; Drew, W.L. and Plorde, J.J. *Staphylococci*. In: *Sherris Medical Microbiology*. 5th. Ed. 2010. McGraw Hill. PP 429-42.
2. Parsonnet, J.; Goering, R.V.; Hansmann, M.A.; Jones, M.B.; Ohtagaki, K.; Davis, C.C. and Totsuka, K. Prevalence of toxic shock syndrome toxin 1 (TSST-1)-producing strains of *Staphylococcus aureus* and antibody to TSST-1 among healthy Japanese women. *J.Clin. Microbiol.* 2008;46(8):2731-8. [IVSL].
3. Zarei, K.R.; Mahmoodzadeh, H. H.; Mehdizadeh, A. E.; Ghorbani, T.S. and Imani, F. A. Distribution of *tsst-1* and *mecA* Genes in *Staphylococcus aureus* Isolated From Clinical Specimens. *Jundishapur J. Microbiol.* 2016;9(3):e29057.
4. Kulhankova, K.; King, J. and Salgado-Pabon, W. *Staphylococcal toxic shock syndrome: superantigen-mediated enhancement of endotoxin shock and adaptive immune suppression*. *Immunol. Res.* 2014; 59(1-3):182-7.
5. Kang, D.; Lin, C.H.; Chen, G.; Guo, S.G.; Wu, Y.S.; Zheng, Z.P.; Shi, C.H.; Chen, G.L. and Ji, X. Interaction of toxin-1 and T lymphocytes in toxic shock syndrome. *Front Biosci. (Landmark Ed.)* 2014;19:571-7.
6. Fluer, F.S. *Staphylococcal toxin of toxic shock syndrome*.

- ZhMikrobiol. Epidemiol. Immunobiol. 2007; (5): 106-14.
7. McCormick, J.K.; Tripp, T.J.; et al. Functional Analysis of the TCR Binding Domain of Toxic Shock Syndrome Toxin-1 Predicts Further Diversity in MHC Class II/Superantigen/TCR Ternary Complexes. *J. Immunol.* 2012; 171:185-92.
  8. Takahashi, N. Neonatal toxic shock syndrome-like exanthematous disease (NTED). *Pediatr. Int.* 2003;45(2):233-7. [IVSL].
  9. Takahashi, N.; Imanishi, K. and Uchiyama, T. Overall picture of an emerging neonatal infectious disease induced by a superantigenic exotoxin mainly produced by methicillin-resistant *Staphylococcus aureus*. *Microbiol. Immunol.* 2013;57(11):737-45.
  10. Nhan, T.X.; Leclercq, R. and Cattoir, V. Prevalence of toxin genes in consecutive clinical isolates of *Staphylococcus aureus* and clinical impact. *Eur. J. Clin. Microbiol. Infect. Dis.* 2011;30(6):719-25.
  11. Pereira, N.; Edlind, T.D.; Schlievert, P.M. and Nyirjesy, P. Vaginal toxic shock reaction triggering desquamative inflammatory vaginitis. *J. Low. Genit. Tract. Dis.* 2013;17(1):88-91.
  12. Shirakusa, T. Postoperative immunocompromised host infection in patients with thoracic disease. *Nihon GekaGakkaiZasshi* 2002;103(12):861-4.
  13. Rubinstein, E. *Staphylococcus aureus* bacteraemia with known sources. *Int. J. Antimicrob. Agents*, 2008 ;32Suppl 1:S18-20.
  14. Fang, S.; Skeete, D. and Cullen, J.J. Preoperative risk factors for postoperative *Staphylococcus aureus* nosocomial infections. *Surg. Technol. Int.* 2004;13:35-8.
  15. Chen, A.F.; Heyl, A.E.; Xu, P.Z.; Rao, N. and Klatt, B.A. Preoperative decolonization effective at reducing staphylococcal colonization in total joint arthroplasty patients. *Arthroplasty* 2013;28(8 Suppl):18-20.
  16. Kavanagh, K.T.; Calderon, L.E.; Saman, D.M. and Abusalem, S.K. The use of surveillance and preventative measures for methicillin-resistant *Staphylococcus aureus* infections in surgical patients. *Antimicrob. Resist. Infect. Control* 2014;3:18.
  17. Childs, C.; Edwards-Jones, V.; Heathcote, D.M.; Dawson, M.; Davenport, P.J.. Patterns of *Staphylococcus aureus* colonization, toxin production, immunity and illness in burned children. *Burns.* 1994; 20:514-21.
  18. JavidKhojasteh, V.; Rogan, M.T.; Edwards-Jones, V. and Foster, H.A. Detection of antibodies to *Staphylococcus aureus* Toxic Shock Syndrome Toxin-1 using a competitive agglutination inhibition assay. *Letters in Applied Microbiology* .2003;36, 372-376.
  19. Quan, L.; Mortia, R. and Kawa Kami. Toxic Shock syndrome toxin-1 (TSST-1) antibody levels in Japanese children. *Burn.* 2010;36:716-721.
  20. Matsushima, A.; Kuroki, .Y.; Nakajima, S.; Sakai, T; Kojima, H.; Ueyama, M.. Low Level of TSST-1 Antibody in Burn Patients with Toxic Shock Syndrome Caused by Methicillin-Resistant *Staphylococcus aureus* .Osong. *Public. Health. Res. Perspect.* 2014; 5(2):96-100. doi: 10.1016/j.phrp.2014.03.002
  21. Perl, T.M. Prevention of *Staphylococcus aureus* infections among surgical patients: beyond traditional perioperative prophylaxis. *Surgery*, 2003;134(5 Suppl):S10-7.
  22. Schweizer, M.L.; Chiang, H.Y.; Septimus, E.; Moody, J.; Braun, B.; Hafner, J.; Ward, M.A.; Hickok, J.; Perencevich, E.N.; Diekema, D.J.; Richards, C.L.; Cavanaugh, J.E.; Perlin, J.B. and Herwaldt, L.A. Association of a bundled intervention with surgical site infections among patients undergoing cardiac, hip, or knee surgery. *JAMA.* 2015;313(21):2162-71.
  23. Iwatsuki, K.; Yamasaki, O.; Morizane, S. and Oono, T. Staphylococcal cutaneous infections: invasion, evasion and aggression. *J. Dermatol. Sci.* 2006; 42(3):203-14.
  24. Marimuthu, K.; Eisenring, M.C.; Harbarth, S. and Troillet, N. Epidemiology of *Staphylococcus aureus* Surgical Site Infections. *Surg. Infect. (Larchmt)*. 2016 ;17(2):229-35.
  25. Hasan, A. SH.; Al-Ammar, N.GH. and Al-Zuhairi, E.A. *Staphylococcus aureus* isolation rates among normal population and hospital settings in Baquba-Diyala province. *Diyala J. Appl. Res.* 2008; 4 (1): 30-37.
  26. Prindeze, N.J.; Amundsen, B.M.; Pavlovich, A.R.; Paul, D.W.; Carney, B.C.; Moffatt, L.T. and Shupp, J.W. Staphylococcal superantigens and toxins are detectable in the serum of adult burn patients. *Diagn. Microbiol. Infect. Dis.* 2014;79(3):303-7.
  27. Park, J.Y.; Kim, J.S. and Woo, H. Prevalence of antibody to toxic shock syndrome toxin-1 in burn patients. *Ann. Lab. Med.* 2015;35(1):89-93.
  28. Schweizer, M.; Perencevich, E.; McDanel, J.; Carson, J.; Formanek, M.; Hafner, J.; Braun, B. and Herwaldt, L. Effectiveness of a bundled intervention of decolonization and prophylaxis to decrease Gram positive surgical site infections after cardiac or orthopedic surgery: systematic review and meta-analysis. *Brit. Med. J.* 2013;346:f2743.
  29. Claassen-Weitz, S.; Shittu, O.A.; Ngwara, R.M. et al. Fecal Carriage of *Staphylococcus aureus* in the Hospital and Community Setting: A Systematic Review. *Front. Microbiol.*, 10 May 2016 | <http://dx.doi.org/10.3389/fmicb.2016.00449>.
  30. Gustin, M.P.; Giard, M.; Benet, T. and Vanhems, P. Use of surveillance data to identify target populations for *Staphylococcus aureus* vaccines and prevent surgical site infections: a pilot study. *Hum Vaccine Immunother.* 2014;10(12):3517-21.
  31. Young, A. E. and Thornton, K. L. Toxic shock syndrome in burns: diagnosis and management. *Arch. Dis. Child. Educ. Pract. Ed.* 2007;92:4 ep97-ep100.