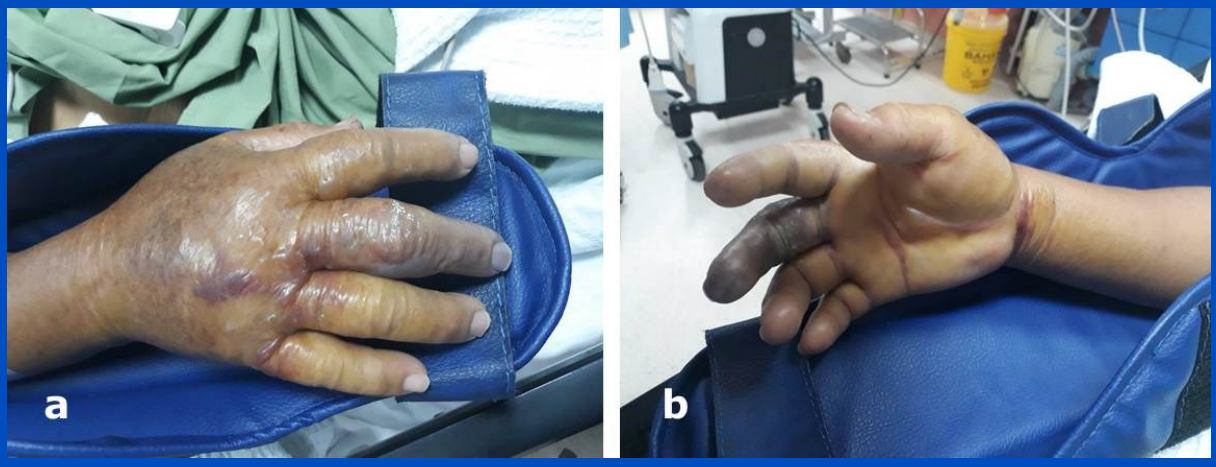
Brunei International Medical Journal

OFFICIAL PUBLICATION OF THE MINISTRY OF HEALTH, BRUNEI DARUSSALAM

Volume 14 12 December 2018 (4 Rabiulakhir 1440H)

NECROTISING FASCIITIS SECONDARY TO VIBRIO VULNIFICUS INFECTION: A CASE REPORT.

FOO KT, PANG GMH, FOO CH
Department of Orthopaedics, Queen Elizabeth Hospital, Kota Kinabalu, Sabah, Malaysia



ABSTRACT

Vibrio vulnificus is a bacterium that could cause severe to life-threatening infection. This is a case report of a woman with underlying myelodysplastic syndrome, presented with sudden onset of pain and swelling over her right middle finger, associated with bullae formation and high grade fever. Patient's condition deteriorated and she developed septic shock secondary to necrotizing fasciitis of right hand. Empirical intravenous antibiotic was started immediately and she was transferred to a tertiary hospital, where emergency wound debridement and ray amputation of her right middle finger was done. Her blood culture grew *V.vulnificus* and the antibiotic was escalated according to culture's sensitivity test. With proper wound care and intravenous antibiotics in the ward, the patient subsequently recovered and was discharged home well. Early establishment of diagnosis and prompt treatment is crucial in determining the patient's outcome.

Keywords: Amputation, Debridement, Necrotizing fasciitis,, Severe sepsis, *Vibrio vulnificus*.

Brunei Int Med J. *2018;14:167-171*

ISSN 1560 5876 Print
ISSN 2079 3146 Online

Online version of the journal is available at www.bimjonline.com

Brunei International Medical Journal (BIMJ)
Official Publication of the Ministry of Health, Brunei Darussalam

ISSN 1560-5876 Print
ISSN 2079-3146 Online

Aim and Scope of Brunei International Medical Journal

The Brunei International Medical Journal (BIMJ) is a six monthly peer reviewed official publication of the Ministry of Health under the auspices of the Clinical Research Unit, Ministry of Health, Brunei Darussalam.

The BIMJ publishes articles ranging from original research papers, review articles, medical practice papers, special reports, audits, case reports, images of interest, education and technical/innovation papers, editorials, commentaries and letters to the Editor. Topics of interest include all subjects that relate to clinical practice and research in all branches of medicine, basic and clinical including topics related to allied health care fields. The BIMJ welcomes manuscripts from contributors, but usually solicits reviews articles and special reports. Proposals for review papers can be sent to the Managing Editor directly. Please refer to the contact information of the Editorial Office.

Instruction to authors

Manuscript submissions

All manuscripts should be sent to the Managing Editor, BIMJ, Ministry of Health, Brunei Darussalam; e-mail: editor-in-chief@bimjonline.com. Subsequent correspondence between the BIMJ and authors will, as far as possible via should be conducted via email quoting the reference number.

Conditions

Submission of an article for consideration for publication implies the transfer of the copyright from the authors to the BIMJ upon acceptance. The final decision of acceptance rests with the Editor-in-Chief. All accepted papers become the permanent property of the BIMJ and may not be published elsewhere without written permission from the BIMJ.

Ethics

Ethical considerations will be taken into account in the assessment of papers that have experimental investigations of human or animal subjects. Authors should state clearly in the Materials and Methods section of the manuscript that institutional review board has approved the project. Those investigators without such review boards should ensure that the principles outlined in the Declaration of Helsinki have been followed.

Manuscript categories

Original articles

These include controlled trials, interventional studies, studies of screening and diagnostic tests, outcome studies, cost-effectiveness analyses, and large-scale epidemiological studies. Manuscript should include the following; introduction, materials and methods, results and conclusion. The objective should be stated clearly in the introduction. The text should not exceed 2500 words and references not more than 30.

Review articles

These are, in general, invited papers, but unsolicited reviews, if of good quality, may be considered. Reviews are systematic critical assessments of literature and data sources pertaining to clinical topics, emphasising factors such as cause, diagnosis, prognosis, therapy, or prevention. Reviews should be made relevant to our local setting and preferably supported by local data. The text should not exceed 3000 words and references not more than 40.

Special Reports

This section usually consist of invited reports that have significant impact on healthcare practice and usually cover disease outbreaks, management guidelines or policy statement paper.

Audits

Audits of relevant topics generally follow the same format as original article and the text should not exceed 1,500 words and references not more than 20.

Case reports

Case reports should highlight interesting rare cases or provide good learning points. The text should not exceed 1000 words; the number of tables, figures, or both should not be more than two, and references should not be more than 15.

Education section

This section includes papers (i.e. how to interpret ECG or chest radiography) with particular aim of broadening knowledge or serve as revision materials. Papers will usually be invited but well written paper on relevant topics may be accepted. The text should not exceed 1500 words and should include not more than 15 figures illustration and references should not be more than 15.

Images of interest

These are papers presenting unique clinical encounters that are illustrated by photographs, radiographs, or other figures. Image of interest should include a brief description of the case and discussion with educational aspects. Alternatively, a mini quiz can be presented and answers will be posted in a different section of the publication. A maximum of

three relevant references should be included. Only images of high quality (at least 300dpi) will be acceptable.

Technical innovations
This section include papers looking at novel or new techniques that have been developed or introduced to the local setting. The text should not exceed 1000 words and should include not more than 10 figures illustration and references should not be more than 10.

Letters to the Editor
Letters discussing a recent article published in the BIMJ are welcome and should be sent to the Editorial Office by e-mail. The text should not exceed 250 words; have no more than one figure or table, and five references.

Criteria for manuscripts
Manuscripts submitted to the BIMJ should meet the following criteria: the content is original; the writing is clear; the study methods are appropriate; the data are valid; the conclusions are reasonable and supported by the data; the information is important; and the topic has general medical interest. Manuscripts will be accepted only if both their contents and style meet the standards required by the BIMJ.

Authorship information
Designate one corresponding author and provide a complete address, telephone and fax numbers, and e-mail address. The number of authors of each paper should not be more than twelve; a greater number requires justification. Authors may add a publishable footnote explaining order of authorship.

Group authorship
If authorship is attributed to a group (either solely or in addition to one or more individual authors), all members of the group must meet the full criteria and requirements for authorship described in the following paragraphs. One or more authors may take responsibility 'for' a group, in which case the other group members are not authors, but may be listed in an acknowledgement.

Authorship requirement
When the BIMJ accepts a paper for publication, authors will be asked to sign statements on (1) financial disclosure, (2) conflict of interest and (3) copyright transfer. The correspondence author may sign on behalf of co-authors.

Authorship criteria and responsibility
All authors must meet the following criteria: to have participated sufficiently in the work to take public responsibility for the content; to have made substantial contributions to the conception and design, and the analysis and interpretation of the data (where applicable); to have made substantial contributions to the writing or revision of the manuscript; and to have reviewed the final version of the submitted manuscript and approved it for publication. Authors will be asked to certify that their contribution represents valid work and that neither the manuscript nor one with substantially similar content under their authorship has been published or is being considered for publication elsewhere, except as described in an attachment. If requested, authors shall provide the data on which the manuscript is based for examination by the editors or their assignees.

Financial disclosure or conflict of interest
Any affiliation with or involvement in any organisation or entity with a direct financial interest in the subject matter or materials discussed in the manuscript should be disclosed in an attachment. Any financial or material support should be identified in the manuscript.

Copyright transfer
In consideration of the action of the BIMJ in reviewing and editing a submission, the author/s will transfer, assign, or otherwise convey all copyright ownership to the Clinical Research Unit, RIPAS Hospital, Ministry of Health in the event that such work is published by the BIMJ.

Acknowledgements
Only persons who have made substantial contributions but who do not fulfill the authorship criteria should be acknowledged.

Accepted manuscripts
Authors will be informed of acceptances and accepted manuscripts will be sent for copyediting. During copyediting, there may be some changes made to accommodate the style of journal format. Attempts will be made to ensure that the overall meaning of the texts are not altered. Authors will be informed by email of the estimated time of publication. Authors may be requested to provide raw data, especially those presented in graph such as bar charts or figures so that presentations can be constructed following the format and style of the journal. Proofs will be sent to authors to check for any mistakes made during copyediting. Authors are usually given 72 hours to return the proof. No response will be taken as no further corrections required. Corrections should be kept to a minimum. Otherwise, it may cause delay in publication.

Offprint
Contributors will not be given any offprint of their published articles. Contributors can obtain an electronic reprint from the journal website.

NECROTISING FASCIITIS SECONDARY TO VIBRIO VULNIFICUS INFECTION: A CASE REPORT.

FOO KT, PANG GMH, FOO CH
Department of Orthopaedics, Queen Elizabeth Hospital, Kota Kinabalu, Sabah, Malaysia

ABSTRACT

Vibrio vulnificus is a bacterium that could cause severe to life-threatening infection. This is a case report of a woman with underlying myelodysplastic syndrome, presented with sudden onset of pain and swelling over her right middle finger, associated with bullae formation and high grade fever. Patient's condition deteriorated and she developed septic shock secondary to necrotizing fasciitis of right hand. Empirical intravenous antibiotic was started immediately and she was transferred to a tertiary hospital, where emergency wound debridement and ray amputation of her right middle finger was done. Her blood culture grew *V.vulnificus* and the antibiotic was escalated according to culture's sensitivity test. With proper wound care and intravenous antibiotics in the ward, the patient subsequently recovered and was discharged home well. Early establishment of diagnosis and prompt treatment is crucial in determining the patient's outcome.

Keywords: Amputation, Debridement, Necrotizing fasciitis, , Severe sepsis, *Vibrio vulnificus*.

INTRODUCTION

Vibrio vulnificus is a halophilic, motile, Gram-negative bacillus which belongs to the family *Vibrionaceae*, the same family as *Vibrio Cholera* and can cause severe to life-threatening infection. In most cases that have been reported, the infection were severe and generally fatal.[1] Those who survived usually required amputation of the affected limbs to control the infection.[2] Patients generally acquired the infection following ingestion of contaminated water, consumption of raw or undercooked seafood and exposure of broken skin to contaminated seawater or marine organisms.[1] *V.vulnificus* can be found worldwide, mostly in warm coastal environment where the water temperatures ranged from 9°C to 31°C.[1] Hence, most of the reported cases are near the tropical or subtropical regions. We reported a case of a 68 years old woman who developed septic shock after acquiring the infection while farming in a paddy field, with no prior history of ingestion of seafood or contact with seawater. She survived the infection after undergoing an emergency Ray amputation and debridement of the affected limb followed by appropriate intravenous antibiotics.

Correspondence: Dr. FOO Kuok Thong (MBBS), Department of Orthopaedics, Queen Elizabeth Hospital, 13a, Jalan Penampang 88200, Kota Kinabalu, Sabah, Malaysia.
Phone: +60124872220; Fax: +6088517555
Email: kuokthong@hotmail.com

CASE REPORT

A 68-year old female farmer presented to the Kudat Hospital, Sabah with pain and swelling over her right middle finger after doing some farming at the paddy field during the South-

west monsoon season. She was not aware of any cuts or bites on her hand prior to this. There was no significant history of seafood consumption or outdoor activities involving seawater recently. She has a background history of myelodysplastic syndrome and was taking oral Danazol 200mg twice daily. After a consultation in the outpatient clinic, she was discharged home with oral cloxacillin 500 milligrams, to be taken four times a day.

However, the pain and swelling worsened overnight, extending to her wrist and forearm, and was associated with high grade fever. She returned to the hospital the very next morning. Examination of her right upper limb revealed swelling and tenderness extending to mid-forearm. There was bluish discoloration of the skin over the middle finger, with small bullae seen at the dorsum of the right hand (Figure 1). Both ulnar and radial pulses were present in the right forearm. There was no gas shadow was seen on radiological imaging of the right hand and forearm.

She was admitted to the ward for further investigation but became hypotensive while on ward, and was resuscitated with intravenous fluids and inotropes. Blood investigations showed an elevated total white cell count (21.0 x 10^3/dL). Blood gases showed compensated metabolic acidosis. A diagnosis of necrotizing soft tissue infection complicated with septic shock was made and broad-spectrum intravenous antibiotic (ampicillin plus sulbactam) was administered after blood cultures was obtained. She was immediately referred to a tertiary hospital in Kota Kinabalu, Sabah for further management.

At the acute cubicle in orthopedic ward, her right middle finger was found to be cold and dusky. Emergency Ray amputation of the right middle finger was performed followed by judicious debridement of necrotic tissue over the dorsum of her hand on the same day. Post debridement, her wound was left open for daily dressing (Figure 2). Blood cultures taken from the Kudat hospital grew Gram-negative bacilli, *Vibrio vulnificus*, which was sensitive to piperacillin-tazobactam. (Figure 3). Thus, the antibiotic was escalated to intravenous piperacillin-tazobactam 4.5 gram six hourly with clindamycin 600 milligrams eight hourly accordingly.

During the first week, she developed multiple skin lesions over her left arm, right calf and right flank. These skin lesions were raised, firm and tender with erythematous surrounding skin; which were initially thought to be abscesses, but subsequently treated as cellulitis as no pus was drained when incision and drainage was performed under general

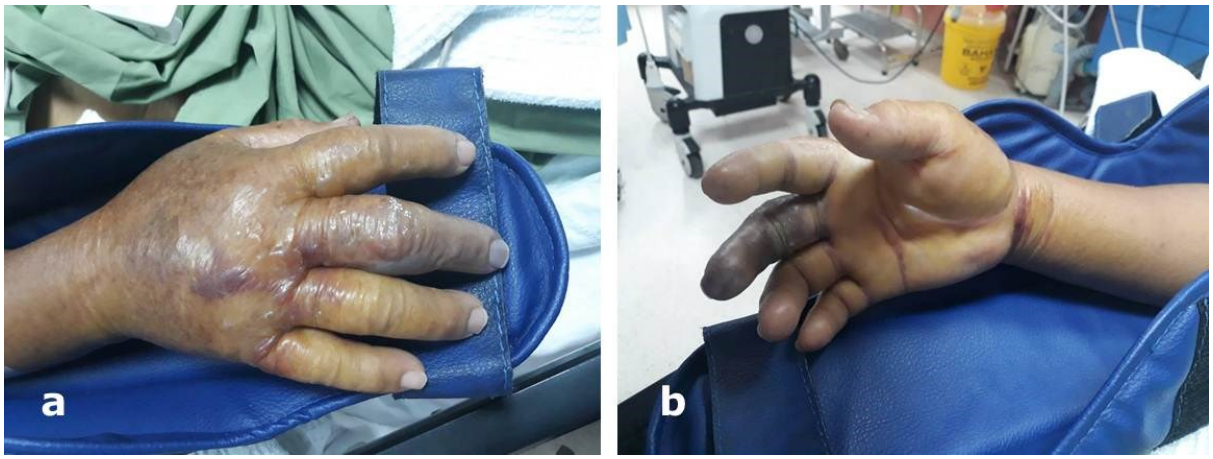


Figure 1: (a) bluish discolouration with small bullae on the dorsum of the right hand, (b) Palmar view of patient's right hand indicating the cyanotic and ischemic right middle finger, at time of presentation to Kudat Hospital.

Figure 2: Dorsal view of patient's hand one week post operation.

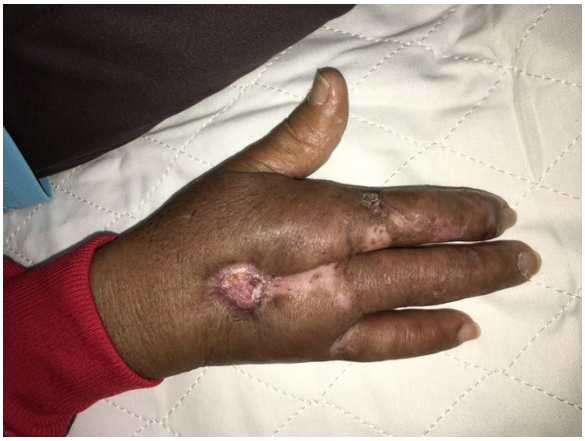


Figure 3: Dorsal view of patient's right hand two months post operation.

anaesthesia. She completed two weeks of intravenous piperacillin-tazobactam with clindamycin, followed by two weeks of oral ciprofloxacin 500mg twice daily. Her hand wound was dressed with Dermasyn[tm] solution and saline water, and covered with paraffin gauze dressing, sterile gauze and crepe bandage. The dressing was changed daily. She was discharged with continuation of wound care at Kudat hospital. Subsequent clinic review 2 months after surgery showed her wound healed and she was able to regain fair function of her right hand, although with limited flexion of the right index, ring and little finger (Figure 3). She was referred to physiotherapy for further rehabilitation to improve her right hand function.

DISCUSSION

Even though Malaysia is surrounded by sea, it is unusual to encounter *V.vulnificus* infection here, even in Borneo. There was only one reported death from infection in Kuala Lumpur in 2009.[3] The preferred habitat reported to be water temperature above 18°C with salinities between 15 and 25 parts per thousand.[4] Based on a study of sea water parameters in Sabah, Malaysia, the sea water condition is ideal for *V.vulnificus* to proliferate. [5] *V.vulnificus* has also been reported to be present in 13% of the seafood samples, (cockles *Anandara granosa* - 32%) and 23% of the seawater samples tested around Malaysia.[6,7] With such prevalence, it is inevitable that our population has a high likelihood of exposure to *V.vulnificus.*

V.vulnificus-related infections usually manifest as one of three clinical syndromes; primary sepsis, necrotizing soft tissue infection and gastroenteritis.[1] Primary septicemia is the most common presentation, characterized by bacteremia without obvious source of infection and is usually associated with fever, vomiting, diarrhea and pain in the extremities. Onset is usually within seven to 14 days after ingestion of the contaminated food. Secondary cutaneous lesion such as ecchymoses and bullae usually appear within 24 hours after the onset of illness. Positive tissue cultures obtained from debridement in patients without an open wound at the initial presentation should be included in this category. Primary septicemia has a high mortality rate (60-75%), especially those presented with septic shock.[1]

The second most common presentation is wound infection, which differs from primary septicemia by the presence of a cutaneous portal of entry. *V.vulnificus* can be inoculated into damaged exposed skin while performing activities in contaminated water or environment.[1] Traumatic injuries sustained while handling contaminated seafood will also

allow entry of the bacterium into the body.[8,9] The infection may manifest as cellulitis, bullae, ecchymosis or generalised macular or maculopapular eruptions, which should not be mistaken as abscesses, as seen in our case. Necrotizing soft tissue infection caused by *V.vulnificus* has a lower fatality rate compared to primary septicemia, ranging from 20 -30%, and up to 60% when concomitant bacteremia exists.[10]

A milder form of manifestation is gastroenteritis, where the patients will suffer from abdominal pain, diarrhea, nausea and vomiting, usually accompanied by fever and chills. Skin manifestation and death is rare in this subgroup.

As for our case, we could only hypothesized that the infection was possibly contracted via unnoticed direct injury to her hand by fresh water organism, such as fishes. Kudat province is at the tip of north Sabah and is surrounding by sea, so it is inevitable that this bacterium may have gotten into inland eco system. A similar situation occurred in Israel where several cases of soft-tissue infection resulting from handling fresh water fishes were reported.[11] Because of her compromised immune status (myelodysplastic syndrome, hemochromatosis and diabetes mellitus), she is more susceptible to develop septicemia when infected with *V.vulnificus*.

Early establishment of diagnosis and prompt treatment is crucial for optimal patient outcome. High index of suspicion is required, especially in the coastal areas. Regardless of the routes of inoculation, *V.vulnificus* infection usually responds well to antibiotic treatment.[1] United States of America's Center of Disease Control and Prevention (CDC) recommends doxycycline and ceftazidime as the antibiotics of choice in adults.[9] In children, the recommended treatment is trimethoprim-sulfamethoxazole and an aminoglycoside.[9]

Besides appropriate antibiotics based on culture sensitivity, wound debridement is essential in patients with severe soft tissue infection as antimicrobial therapy alone is usually ineffective in the necrotic tissue. Necrotic and infected tissues must be removed during surgical debridement, thus reducing the bacterial load in the patient. There has been reported cases in which despite prompt treatment with intensive care support, patients still succumbed to their infection.[3,12] CDC has published recommendations to prevent *V.vulnificus* infections with thorough cooking of seafood and avoid consumption of raw oysters or cockles, especially those harvested from warm sea or brackish water. In addition, one should wear protective footwear and clothing when wading in the warm sea or brackish water.[9]

CONCLUSION

V.vulnificus is capable of causing potentially fatal infection, especially in susceptible individuals. Prompt diagnosis and treatment are crucial to avoid fatal outcome. For patients who present with progressive skin lesion and sepsis, with a history of contact with sea water or consumption of undercooked seafood, *V.vulnificus* infection should also be considered, especially in those with predisposing factors. Patient should be treated with intravenous antibiotics such as doxycycline and ceftazidime as recommended by CDC. Antibiotics can be tailored accordingly to culture and sensitivity. Early aggressive debridement and amputation, if necessary, along with supportive therapy in the intensive care settings, will ensure a more promising prognosis in patient infected with this deadly bacterium.

Declaration of interest: The authors declare that they have no competing interests and that all authors have contributed equally to the manuscript. Consent was also obtained from the patient for publication.

REFERENCES

1: Heng SP, Letchumanan V, Deng CY, et al. *Vibrio vulnificus*: An Environmental and Clinical Burden. Front Microbiol. 2017;8:997. DOI:10.3389/fmicb.2017.00997 [Accessed on December 11, 2018]. Full article available at: https://www.frontiersin.org/articles/10.3389/fmicb.2017.00997/full

2: Park. J, Lee. C.S. Vibrio vulnificus Infection. N Engl J Med 2018; 379:375. DOI: 10.1056/NEJMicm1716464 [Accessed on December 11, 2018]. Available from: https://www.nejm.org/doi/pdf/10.1056/NEJMicm1716464

3: Zetti ZR, Norazlah B, Raha AR. A Fatal Case of Vibrio vulnificus Cellulitis with Septicaemia. Med J Malaysia. 2009;64:246-247.

4: Motes M., DePaola A., Cook D., et al. Influence of water temperature and salinity on *Vibrio vulnificus* in Northern Gulf and Atlantic Coast oysters (*Crassostrea virginica*). Appl Environ. Microbiol. 1998;64(4):1459–65. [Accessed on December 11, 2018]. Pdf available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC106170/pdf/am001459.pdf

5: Nor Balqis bt MD Zohri. Seawater Properties in Brunei Bay, Sabah. Marine Science Programme. School of Science & Technology, University Malaysia Sabah. March 2007. [Accessed on December 11, 2018]. Pdf available at http://eprints.ums.edu.my/7173/1/ae0000001393.pdf

6: Paydar M, Thong KL. Prevalence and genetic characterization of Vibrio Vulnificus in raw seafood and seawater in Malaysia. J Food Prot. 2013;(10):1797-800. DOI: 10.4315/0362-028X.JFP-13-141

7: Kurdial-Dulaimi M., Mutalib S.A., Ghani M.A. et al. Antibiotic susceptibility and plasmid profile of Vibrio vulnificus isolated from cockles (*Anadara granosa*) in Selangor Malaysia. Asian Journal of Microbiology, Biotechnology and Environmental Sciences. 2016;18(2):305-314.

8: Oliver JD. Wound infections caused by *Vibrio vulnificus* and other marine bacteria. Epidemiol Infect. 2005;133(3):383-391.

9: Horseman MA, Surani S. A comprehensive review of Vibrio vulnificus: an important cause of severe sepsis and skin and soft-tissue infection. Int J Infect Dis. 2011;15(3):157-166. DOI: 10.1016/j.ijid.2010.11.003. [Accessed on December 11, 2018]. Pdf available from: https://www.ijidonline.com/article/S1201-9712(10)02538-5/pdf

10: Pérez-Moreno MMO, Romera G, Pous G, et al. Bacteraemia caused by *Vibrio vulnificus* in a patient with a skin ulcer exposed to seawater. Enfermedades Infecciosas y Microbiología Clínica. 1996;14:512–514.

11: Zaidenstein R, Sadik C, Lerner L, et al. Clinical characteristics and molecular subtyping of Vibrio vulnificus illnesses, Israel. Emerg Infect Dis. 2008; 14(2):1875-1882. DOI: 10.320/eid1412.080499 [Accessed on December 11, 2018]. Pdf available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2634625/pdf/08-0499_finalRCME.pdf

12: L.Torres, S.Escobar, A.I.López, et al. Wound Infection due to Vibrio vulnificus in Spain. Eur J Clin Microbiol Infect Dis. 2002;21(7):537–538. DOI: 10.1007/s10096-002-0767-4 [Accessed on December 11, 2018]. Available from: https://link.springer.com/article/10.1007%2Fs10096-002-0767-4.