Effect on length of stay (LOS) and cost of hospitalization by using Vacuum-assisted Closure (VAC) therapy in chronic diabetic foot ulcers: Experience with limited resources in a developing country.

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Abstract
Background
Managing diabetic foot ulcers in developing countries is demanding. Sri Lankan literature on the use of Vacuum-assisted Closure (VAC) is scarce due to lack of overall guidelines and awareness. This prospective cohort study evaluates the effectiveness of VAC therapy, effect on length of hospital stay (LOS) and cost of hospitalization in chronic diabetic foot ulcers.
Methods
Prospective study was carried out from March 2018 to February 2019. Fifty patients were selected. Based on the patient preference and informed written consent, 28 patients were treated with VAC therapy and rest were managed with standard surgical protocols. Haematological, serological and bacterial cultures from wounds were done in all patients. The ulcers were classified by Wagner classification. All patients were treated with antibiotics until the systemic infection settles. VAC dressing was changed every 72 hours. Ethical approval was obtained from the education and research ethical committee of Nawaloka Hospital PLC.Student t-test, regression analysis and chi-square were used for data analysis.
Results
The most affected were in 50 to 60 years of age [(50%, mean age; 59±7.7 years)]with a male preponderance (64%).The commonest presentation was cellulitis with abscess formation (66%). Majority of the ulcers (54%) were Wagner Type 3 and in hind foot (60%). Average VAC applied days was 11±0.98. There was no statistically significant difference between age, sex and levels of inflammatory markers between the two groups (P>0.05). There were significant differencesobserved between VAC and non – VAC groups innumber of surgical debridement (3±0.74 vs 7.8±1.22, p= 0.001);duration of days antibiotic administration [Intra-venous antibiotics; 4.1±0.38 vs 8.23±1.76 (p=0.001) and oral antibiotics; 7.61±0.87 vs 11.5±2.1 (p=0.001)]; Length of stay [(LOS in days) 11.68±0.98 vs 19.86±2.64, (p=0.001)].Significant reduction of total hospital cost was seen in the VAC group [VAC; (LKR) 645,060±86,600 vs Non-VAC; (LKR) 1,049,800±97,487, (p=0.001)] whilst, having a 63% significant negative effect on final bill. Wounds of all VAC patients were healed.
Conclusions
Our study showed that VAC therapy reduced the number of surgical debridement, duration of antibiotic administration, LOS and hospital cost.Authors suggest a clinical trial will enhance the evidence of this study.
Keywords - Vacuum assisted closure, chronic diabetes wounds, Length of hospital stay and cost

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I.   Background
Among numerous debilitating complications of diabetes, foot ulceration is given a higher priority due to the risk of amputation. Among the diagnosed diabetes mellitus patients, the prevalence of foot ulcers is 4 % to 10 % [1, 2].Pathogenesis of diabetes foot ulcers is a complex process. Superadded bacterial infection, reduced immunity, tissue ischemia, and ongoing trauma results in non-healing wounds which can lead to amputation of the limb [2].There are several techniques of treating chronic wounds due to diabetes. The recent developments include use of negative pressure dressings [3-7]. In Sri Lankan setting, the literature on the use of VAC is scarce. The reason for the scarcity is probably due to lack of guidelines of in this context and also due to the lack of awareness and knowledge among patients and healthcare personnel. In general, patients with diabetic foot ulcers need long term hospital stay due to slow process of wound healing. In this process, they end up having considerable expenditure towards healthcare. This study evaluates the effectiveness of vacuum assisted closure (VAC) therapy and its effect on length of hospital stay (LOS) and cost for patients with chronic diabetic foot ulcers.

Methods
Study setting
Nawaloka Hospitals PLC, Colombo.
Study design
Prospective comparative study.
Study participants
Fifty patients with diabetes who presented with foot ulcers were enrolled in the study from March 2018 to February 2019.
Sample size calculation
Significance level =0.05, Power = 80, Ratio of sample size B: A = 1, assumed SD =0.5 and assumed difference to be detected = 0.5. Based on WINPEPI, minimum sample size required was 32.

Inclusion and exclusion criteria for VAC therapy
The study was conducted in a tertiary care private hospital in Sri Lanka. All patients in the study had chronic diabetic foot ulcers of Wagner's Classification grade 2 and above. The procedure was clearly explained to the patient by the principal investigator before recruiting them for VAC therapy. Patients were informed that VAC machine is not a mobile unit and need to kept at bed side (Portable VAC machines are not available in Sri Lanka). Therefore, patient's normal mobility may be restricted. They were also explained that initial cost that will be borne by the patient for VAC therapy. Out of fifty patients, 28 agreed on VAC treatment and others preferred Non-VAC conventional surgical protocols. Both groups were handled by same team of treating doctor and nurses.
Wound swab cultures and sensitivity were done prior to the initial wound debridement in both groups. In this study, most of the patients had resistance to antibiotics. This was due to incomplete healing or self-treatment of theses wounds for long time. Therefore, broad-spectrum carbapenem and metronidazole antibiotics were used. (Similar brand in both groups).

Treatment procedure for non-VAC group
Following wound assessment, surgical debridement was performed. The entire debridement procedures were performed under sterile conditions in operation theatre. After each debridement, wound was dressed with silver-coated antimicrobial barrier dressings. Each wound was assessed every three days or more frequently, depending on patient's condition. If there was presence of slough and necrotic tissue, an additional wound debridement was performed.
All patients had intra-venous antibiotics, monitored with sequential WBC and CRP counts for the systemic response. Discontinuation of intra-venous antibiotics were decided when WBC < 9000 and CRP < 20).

Treatment procedure for VAC group
An initial wound debridement was performed prior to the application of VAC therapy in all patients in this group. All necrotic material and infected tissue was excised. The entire debridement procedures was performed under sterile conditions in operation theatre. A negative pressure of -125mmHg was applied to the external wound continuously. But in certain patients, when the -125mmHg was tolerant enough, a pressure of -150mmHg was also used. Changing of the VAC dressing was done every 3 days.

In each wound inspection, variability of size, depth, presence of necrotic material and presence of granulation tissue were assessed. When there was presence of slough and necrotic tissue, an additional wound debridement was performed as done for non-VAC group. The decision to stop VAC therapy was taken when absence of necrotic material, presence of fresh granulation tissue and more than 50 percent reduction of the initial size and depth were seen in the wound by sequential measuring with a sterile marker tape. Thereafter, the wound was closed with either split skin grafting or secondary closure.

Data collection and analysis

Patients' general biographic data, diabetes history, presence of diabetes related complications and other co-morbidities were recorded. Description of the ulcer included the site, size, depth, extent of the exposure of the deep tissues, presence of necrotic material and presence of granulation tissue were recorded before the treatment. The investigations performed prior to the use of VAC included full blood count, C- reactive protein, wound swab culture and HbA1c. The duration of VAC therapy, pressure settings and number of VAC applications were documented.

Data collection was carried out by the trained medical officers with regular supervision of the PI. Data were entered into EXCEL worksheets, checked manually and logically, and corrected where necessary. Descriptive statistics were derived and expressed as measures of central tendency and frequencies. Student t-test and ANOVA was used to compare averages. Data were analyzed using the Statistical Package for Social Sciences 16 (SPSS) (SPSS 16.0, Chicago, Illinois, USA) and STATA version 12 (12.0, Texas, USA). P values of <0.05 were considered significant.

Ethical approval

Ethical approval for this study was obtained from the Ethics Review Committee, Nawaloka hospitals PLC Colombo. All patients gave informed consent for their data to be included in the study.

II. Results

Table one shows the socio-demographic characteristics of the study participants. Male were dominant (64%). The commonest age group was 50 to 60 years (n=25; 50%). Cellulitis with abscess was the common presentation of diabetic foot ulcers of the study sample (66%). 60% of the ulcers were found on hind foot. 56% of the study population consented for VAC therapy.

Association between prognostic factors and VAC therapy (unadjusted) were shown in the table 2. There was significant difference between number of surgical debridement among VAC and non VAC groups. (3 ± 0.74 vs 7.8 ± 1.22, p= 0.001). Number of day's intra-venous and oral antibiotic administered had significant difference between VAC and non-VAC groups [Intra-venous antibiotic; 4.1 ± 0.38 vs 8.23 ± 1.76 (p=0.001) and oral antibiotics; 7.61 ± 0.87 vs 11.5 ± 2.1 (p=0.001)].LOS (days) had significant difference between the two groups [VAC; 11.68 ± 0.98 vs Non VAC; 19.86 ± 2.64 , (p=0.001)].Total hospital cost had significant difference between VAC and Non VAC group [VAC; (LKR) $645,060\pm86,600$ vs Non VAC; (LKR) $1,049,800\pm97,487$, (p=0.001)].

Predictors which associated with final bill during the hospital stay (Adjusted) were demonstrated in table three. Application of VAC has a 63% significant negative effect on final bill. Each additional day of intra venous and oral antibiotic has respectively 71% and 45% significant effect on increasing final bill. (Table 3)

Table four shows the final outcome of the treatment. All the wound were healed. 50% had undergone split skin graft.30% had secondary closure and 20 % underwent both procedures. There was no significant association between final outcome procedures between two groups.

III. Discussion

Chronic diabetic foot ulcers can present in a wide variety. These could range from confiding to the superficial skin loss to involvement of deep soft tissues including vessels, nerves, bones and internalorgans [8].

Use of sub-atmospheric pressure to promote debridement and healing was described by Fleischmann in 1993[9]. However, a specialized device for administrating negative pressure in wounds were first described by Argenta and Morykwas in 1997[10]. Since then there has been a lot of research done in the area of use of VAC in chronic wounds. Maintaining Controlled levels of negative pressure provides a good wound debridement with accelerated healing of various types of wounds [11].It has been proven that 125mmHg of pressure below the ambient, is optimum negative pressure for wound healing with usage of in cyclical manner in pressure for five minutes and off pressure for three minutes. [11]It is a noninvasive method. In Sri Lankan setting, the literature on the use of VAC and its effect on LOS and cost of hospital stay has not been done. The reason for the scarcity is probably due to lack of awareness among patients and healthcare personnel.

In our study, only 28 patients agreed to go through VAC procedure. This is mainly due to non-availability of portable VAC machines. The machines which are available in Sri Lanka has to be kept at bed side and it restricts patient movements. Apart from that, patients were not much convinced about the initial expenditure they have to bear on VAC treatment. Lack of knowledge on long term benefits were also added reasons for the refusal of VAC treatment by the patients.

The mechanism of wound healing by VAC therapy involves multiple factors [12]. In particular, increased blood flow due to low pressure, removal of interstitial fluid causing a decrease in tissue bacterial levels, increased production of protein and matrix molecules and enhanced angiogenesis [13] due to mechanical deformation and stress within the tissue has been noted. The ability to provide a sterile, moist environment which increases the rate of granulation tissue is also a known factor [14].

VAC therapy has shown a better reduction in the size of the wound compared to conventional dressings [15]. We were able to show the clinical improvement of the wound bed and observational reduction in the wound area was noted in all VAC therapy patients. In healing of wounds, presence of granulation tissue is of utmost importance which indicates healthy wound healing [16]. One of the mechanisms by which the wound healing is enhanced in VAC is by increased proliferation of granulation tissue [13].

In our study, secondary surgical treatment was performed when fresh granulation tissue was achieved by the use of VAC. The average time of achievement of fresh granulation tissue was 11.5 days in our study. This was shorter than some studies which achieved the same with 23.3 days [17], 32.9 days [18], and 57.4 days [19]. To our knowledge we believed that this may be due to the use of broad spectrum intravenous antibiotics and the meticulous debridement of ulcers at the initial presentation. The mean time of VAC treatment of our study was 11±0.98 days. According to literature, average period of the application of vacuum-assisted wound closure was 11.6 days (7–15 days) [20].

Our study outside country clearly shows that VAC treatment reduce duration of hospital stay, number of days intra venous and oral antibiotic usage and significant reduction of hospital cost. This clearly highlighted that VAC therapy is cost effective intervention on treating diabetic foot ulcers. A study conducted in Pakistan shows that availability of portable VAC machines will further reduce hospital cost [21]. Furthermore, study conducted in India has demonstrated that VAC treatment is a promising alternative method of reducing financial constraints of patient's especially in lower middle-income counties [22]. Lack of dedicated wound care staff, a wound clinicto treat and follow up these patients and lack of finical support for patients to render the cost of VAC therapy made us tolimitour sample size to 50 patients. Therefore a small sample size was a limitation of our study. Further studies with large cohort of patients are recommended to justify this findings to general population.

IV. Conclusion
Our study showed that the VAC therapy is useful in the treatment of chronic diabetic wounds bysignificantly reducing the frequency of surgical debridement, duration of antibiotic administration, length ofstay and hospital cost. We would like to suggest that a clinical trial will be immensely useful to generalize this study finding to general population.

List of abbreviations
VAC- Vacuum Assisted Closure
LOS – Length of stay

Declarations
Ethics approval and consent to participate
Informed written consent was obtained to write the case report and the approval of Nawaloka Hospital Ethical Review Committee was obtained.

Consent for publication
Informed written consent was obtained for publication.

Availability of data and material
Laboratory reports and necessary clinical data were obtained from Bed Head Ticket.

Competing interests

No conflict of interest

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Variable	Number	%
Sex		
Male	32	64
Female	18	34
Age(Year)		
Less than 50	8	16
50-60	25	50
More than 60	17	34
Wound diagnosis		
Cellulitis/abscess	33	66
Cellulitis/foot ulcer	17	34
Wagner classification		
Type 2	14	28
Type3	27	54
Type4	9	18
Site		
Hind foot	30	60
Mid foot	11	22
Fore foot	9	18
Vacuum assisted closure(VAC) therapy		
Applied		
Not applied	28	56
	22	44
Length of VAC treatment days		
10		
11	17	62.1
	11	37.9
Wound characteristics		
Widest with (cm)	38	76
Less than 6	12	24
More than 6		
Maximum depth (cm)	38	76
Less than 1.5	12	24
More than 1.5		

Table 1: Socio demographic characteristics

Table 2: Association between prognostic factors and VAC therapy (unadjusted)

Variable	VAC group (n=28)	Non-VAC group (n=22)	P- Value*
Age(Years)	58.86±7.7	59.23±7.8	0.868
HbA1C	8.87±1.0	9.10±0.98	0.426
WBC	16.27±1.15	16.02±1.47	0.512
CRP	66.25±13.82	73.32±15.24	0.093
Number of surgical debridement	3.0±0.74	7.8±1.22	0.001
No of days of I.V. antibiotics	4.1±0.38	8.23±1.76	0.001
No of days of oral antibiotics	7.61±0.87	11.5±2.1	0.001
Length of hospital stay	11.68±0.98	19.86±2.64	0.001
Total hospital bill	645,060±86,600	1,049,800±97,487	0.002

*Student t-test

[USD 1= 180 LKR]

Table 3: Predictors which associated with final bill during the hospital stay (Adjusted)

Variable	B-coefficient	Standard error	Beta	P-Value*
VAC applied	-462,099.75	276,050.41	-0.629	0.01
Number of days I.V. antibiotics administered	109,317.36	33,267.3	0.71	0.002
Number of days oral antibiotics administered	66,972.86	25,425.5	0.45	0.012
Number of surgical debridement	31,756.71	40,654.28	0.22	0.44

Table 4: Final outcome of the treatment

Procedure	VAC group (n=28)	Non-VAC group (n=22)	Significant*
Split skin graft [n=25]	12	13	
Secondary closure [n=15]	10	5	X^2=1.407 df=2 p=0.49
Split skin graft and Secondary closure[n=10]	6	4	

*Chi-square test