Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 810–814

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Meta-analysis for assessing the healing process of ulcers among diabetic patients: Cases of HbA1c, lipid, S. Creatinine, Adiponectin, Cat D, HSP70, HSP47, 25-hydroxy vitamin D

Mohammad Zubair [a, *], Jamal Ahmad [b]

[a] Department of Medical Microbiology, Faculty of Medicine, University of Tabuk, Tabuk, 71491, Saudi Arabia
[b] Rajiv Gandhi Centre for Diabetes and Endocrinology, J N. Medical College, Aligarh Muslim University, Aligarh 202002, India

ARTICLE INFO

Article history:
Received 19 November 2018
Accepted 7 December 2018

Keywords:
Adiponectin
Cat-D
Diabetic patients
Vitamin D
S. Creatinine
Ulcer grades

ABSTRACT

Background: The study aims to investigate the significance of predictors including HbA1c, Lipid, S. Creatinine, Adiponectin, Cat D, HSP70, HSP47, and 25-hydroxy vitamin D and to evaluate the rate of healing of ulcers among the diabetic foot patients.
Methods: A retrospective method is used to quantitatively assess the role of HbA1c, Lipid, S. Creatinine, Adiponectin, Cat D, HSP70, HSP47, and 25-hydroxy vitamin D in the healing process of ulcer among diabetic patients. A total of 192 diabetic patients were included, who underwent ulcer healing diagnosis.
Results: The results have shown a positive and significant correlation between Adiponectin and Cat D with group 2. The findings have shown higher prevalence of Cad D among patients with group 1, HSP70 among patients with group 2, HSP47 among patients with group 2, and 25-hydroxy vitamin D among patients with group 1.
Conclusion: The study concluded that insignificant predictors should be assessed more comprehensively to reveal its efficacy on healing of ulcers with different grades.

1. Background

Diabetic foot ulcer is prevalent amongst 4–10% of people, suffering from diabetes mellitus. Diabetic patients, who have a high risk of getting foot ulcerations, need preventive involvement of a combination of medications, intensive podiatric care, smoking reduction, cessation or surgery [1]. The increased rates of diabetes and its associated complications are considered as serious public health concerns across the globe. A major problem is faced by the developing countries as a result of increased prevalence of diabetes [2]. Macrovascular symptoms of diabetes cause cardiovascular diseases; like atherosclerosis, and microvascular symptoms; including neuropathy, retinopathy and nephropathy. It is identified that there is a strong and positive association between glycemic blood levels and risk of developing diabetic complications. Moreover, there is reduction in micro vascular and macro vascular diabetic complications, if glycemic levels are tightly controlled [3]. The identification of modifiable factors that help in the process of healing is performed through the optimization of wound healing process.

There is an association between lipid peroxidation, blood glucose, and high oxidative stress among diabetic patients [4]. HbA1c is the glycosylated hemoglobin in the blood, and it classifies the average plasma glucose concentration. The normal range of hemoglobin A1c level is between 4% and 5.6% in people without diabetes. People, having borderline diabetes or who are pre-diabetic, have a hemoglobin A1c level between 5.7% and 6.4% and above that, which is determined by a blood test, is categorized as the diagnosis of diabetes. Statins not only play an important role in lowering lipid levels in cardiovascular disorders but may also be helpful in reducing the acceleration of microvascular symptoms among diabetic patients. Statins can prevent diabetic peripheral neuropathy by maintaining the circulation of blood around the sciatic nerve [5].

The serum creatinine level tends to represent the renal functions; therefore, proper care is needed among the diabetic patients, suffering from renal impairment and ulcers. A study conducted clearly stated that serum creatinine levels are known as a significant predictor risk factors among the diabetic patients [6]. There is increased risk of delay in the cutaneous wound, healing among the

* Corresponding author.
E-mail address: mohammad_zubair@yahoo.co.in (M. Zubair).

https://doi.org/10.1016/j.dsx.2018.12.004
1871-4021/

diabetic patients. Adiponectin plays a crucial role in depicting the pathogenesis of diabetes; however, its role in wound healing is still unknown [7].

Proteins called adipokines are released by the adipose tissue. Adiponectin, a kind of adipokine, is closely related to lipid and glucose metabolism and is essential for the normal functioning of the body. Low levels of adiponectin are linked to attention deficit disorder, diabetes, rheumatoid arthritis, obesity, and cardiovascular diseases. Adiponectin levels can become normal through life-style changes like diet control and exercise. Additionally, the use of thiazolidinedione, which is used to reduce insulin resistance, can help to increase the adiponectin level [8].

Vitamin D is converted into 25-hydroxy vitamin D by the liver. Normal levels of calcidiol are between 20 and 40 ng/ml. Vitamin D levels between 21 and 29 ng/ml indicates Vitamin D deficiency. Vitamin D supplements not only reduces systolic blood pressure, but also improves endothelial activity in diabetic patients [9]. HSP70 commonly known as the heat-shock protein 70 defends against oxygen free radicals and is an anti-oxidant. People suffering from diabetes have lower levels of antioxidants and more free radicals in their body. HSP70 levels are higher in the mononuclear cells of diabetic patients, indicating high oxidative stress [10].

Heat shock protein (HSP) 47 is a collagen binding protein. It also plays an important role in the processing of procollagen molecules. High plasma levels of heat shock protein 47 have been found in patients with diabetic foot ulcers [11]. Normal levels of HbA1c, Lipid, S. Creatinine, Adiponectin, Cat D, HSP70, HSP47, and 25-hydroxy vitamin D play an imperative role in the healing process of ulcers in diabetic patients.

The management of diabetic foot ulcers is similar all across the world; the only difference is observed among the outcome of its clinical management. In order to ensure best outcome, it is important to manage the diabetic foot complications carefully. Previous studies have not investigated the cases of HbA1c, Lipid, S. Creatinine, Adiponectin, Cat D, HSP70, HSP47, and 25-hydroxy vitamin D as a standard measure within the healing process of ulcers among the diabetic patients. Therefore, the present study will assess the process of healing in the light of above mentioned factors. HbA1c, Lipid, S. Creatinine, Adiponectin, Cat D, HSP70, HSP47, and 25-hydroxy vitamin D are important biomarkers to predict the rate of wound healing in diabetic patients. Therefore, this study intends to find the association among the level of these predictors in the process of wound healing. Therefore, the study has investigated the significance of predictors including HbA1c, Lipid, S. Creatinine, Adiponectin, Cat D, HSP70, HSP47, and 25-hydroxy vitamin D to evaluate the rate of healing of ulcer among the diabetic patients.

2. Methods

The study has incorporated prospective cohort approach to assess the role of significant predictors, including HbA1c, Lipid, S. Creatinine, Adiponectin, Cat D, HSP70, HSP47, and 25-hydroxy vitamin D in the healing process of ulcer among the diabetic patients. The rationale for using prospective cohort approach is to identify and achieve the anticipated outcomes by using different specimens and sample groups. Previous studies have used prospective cohort approach to assess the role of significant predictors in the healing process among diabetic patients [3,6,12]. A total of 192 diabetic patients (group 1) admitted in the Rajiv Gandhi Centre for Diabetes and Endocrinology, of Jawaharlal Nehru Medical College Hospital, Aligarh Muslim University, Aligarh, India were included in this study. We also included 192 diabetic patients without foot ulceration (Group 2) admitted to our endocrine wards for other causes between 2014 and 2016. Patients with inflammatory or infectious diseases, autoimmune and rheumatic diseases, cancer, haematological diseases, severe renal or liver failure, as well as those who were under treatment with anti-inflammatory drugs, were excluded. Each recruited participant gave informed consent to be recruited in the study. Declaration of Helsinki as revised in 2001 was properly followed by the researchers. The data including age, gender, weight, BMI, blood pressure, HbA1c, and lipid profile of all the participants was obtained. Blood pressure, serum glucose, serum cholesterol, triglyceride, LDL-cholesterol, HDL-cholesterol levels, and urinary albumin excretion (UAE) values of all the patients were measured on first day of hospital admission. Duration of ulcer, site, and size of ulcer, history of smoking, history of previous amputation, and clinical outcome were noted in every patient. Swelling, exudates, surrounding cellulitis, odour, tissue necrosis, crepitation and pyrexia were certain signs of infection, which were classified and determined. The data was analyzed using Statistical Package of Social Sciences (SPSS) version 20.0.

3. Results

The results have shown demographic and baseline characteristics for age, sex, S. creatinine, Adiponectin, HbA1c, Cat D, HSP70, HSP47, 25-hydroxy vitamin D, and lipid profile based on ulcer healing rate. The results have analyzed these variables using descriptive analysis and diagnosed the prevalence of S. creatinine (1.12 ± 0.054) among patients with improved ulcer healing (Table 1). Moreover, CAD (521.66 ± 172.48) was found among patients with group 1 and HbA1c (9.68 ± 2.06) was identified among patients with group 1. Similarly, BMI (20.18 ± 4.10) was used among patients with group 1. Furthermore, results have shown high prevalence of total cholesterol (137.01 ± 14.12) among patients with group 1.

Table 1 has illustrated the percentage of ulcer outcomes (Impaired, Improved and Healed) among diabetic patients with respect to lipid profile. The results have shown that mostly diabetic patients were healed with intact skin (Male = 33, Female = 53), improved ulcer healing (Male = 34, Female = 54), and impaired ulcer healing (Male = 3, Female = 12). The results have analyzed these variables using descriptive analysis and diagnosed the prevalence of S. creatinine (1.09 ± 0.323) among patients with improved ulcer healing (Table 2). Moreover, CAD (521.4 ± 173.3) was found among patients with group 1 and HbA1c (7.929 ± 0.8613) was identified among patients with group 1. Similarly, BMI (20.20 ± 4.10) was used among patients with group 1. Furthermore, results have shown high prevalence of total cholesterol (137.02 ± 14.19) among patients with group 1.

In terms of TG, results have shown that diabetic patients mostly improve their ulcer healing (168.07 ± 101.63). In terms of HDL, results have shown that diabetic patients were mostly categorized with impaired ulcer healing (44.14 ± 7.551). In terms of LDL, results have shown that diabetic patients mostly improve ulcer healing (107.17 ± 38.62). In terms of HDL, results have shown that diabetic patients were mostly categorized with impaired ulcer healing (43.67 ± 47.76) (Fig. 1).

Table 3 has shown correlation between ulcer healing and data. The results have shown that there is a positive correlation for ABI, TBI, HSP-70, 2(OH)-D, serum albumin (SA) and serum globulin (SG) with adiponectin. Moreover, findings have indicated there is a positive correlation for ABI, HSP-70, 2(OH)-D, serum albumin (SA) and serum globulin (SG) with cathepsin D. The results have shown that there is a positive correlation for HSP-70, HSP-47, cathepsin D,

Table 1
General and demographic variables in cases and controls.

Factors	Patients with Ulcer Group 1	Patients without ulcer Group 2	P value
Age (years)	53.09 ± 11.018	53.43 ± 11.404	.141
Male/Female	119/73	98/94	.534
T2DM/T1DM	156/36	150/42	.100
BMI (kg/sq mt)	20.18 ± 4.10	20.20 ± 4.10	.011
Systolic BP (mmHG)	131.66 ± 18.55	131.97 ± 18.56	.009
Diastolic BP (mmHG)	85.20 ± 16.12	85.18 ± 16.20	.067
HbA1c(%)	9.68 ± 2.06	7.929 ± .8613	.108
Serum creatinine (mg/dL)	1.22 ± 0.54	1.09 ± .323	.241
LDL-C (mg/dL)	75.88 ± 18.55	75.81 ± 18.64	.663
HDL-C (mg/dL)	34.64 ± 3.479	34.64 ± 3.49	.685
Total cholesterol (mg/dL)	137.01 ± 14.12	137.02 ± 14.19	.663
Triglycerides (mg/dL)	96.04 ± 21.35	96.04 ± 21.46	.570
CAD	521.66 ± 172.48	521.4 ± 173.3	.847
Therapy			0.011
Insulin	56 (29.1%)	86 (44.7%)	
OHA	90 (46.8%)	26 (13.5%)	
Both	46 (23.9.5%)	80 (41.6%)	
Grade of ulcer (Texas)			0.000
1	78 (40.6%)		
2	84 (43.7%)	–	
3	30 (15.6%)		

Data are mean ± sd or n (%) unless otherwise indicated. T1DM: Type 1 diabetes mellitus, T2DM: type 2 diabetes mellitus, BMI: Body mass index, syastolic BP: syastolic blood pressure; diastolic BP: diastolic blood pressure; CAD: coronary artery disease; OHA: Oral Hypoglycaemic Agents; HDL-C: High-density lipoproteins; LDL-C: Low-density lipoprotein.

Table 2
Ulcer healing rate.

Demographic data	Impaired ulcer healing	Improved Ulcer Healing	Healed with intact skin	P value
Sex				
Female	6 (20%)	34 (38.63%)	33 (38.37%)	.261
Male	12 (80%)	54 (61.36%)	53 (60.91%)	
Lipid Profile				
TC (mg/dL)	18.18 ± 3.708	18.22 ± 3.920	18.05 ± 4.124	.720
TG (mg/dL)	163.89 ± 96.40	168.07 ± 101.63	154.43 ± 69.210	.315
HDL (mg/dL)	44.14 ± 7.551	43.74 ± 7.038	43.23 ± 7.816	.116
LDL (mg/dL)	106.56 ± 35.19	107.17 ± 38.62	105.29 ± 40.020	.741
VLDL (mg/dL)	43.67 ± 47.76	43.37 ± 47.22	39.41 ± 39.393	.280

Data are mean ± sd or n (%) unless otherwise indicated. TC: Total cholesterols; TG: Triglycerodes; HDL-C: High-density lipoproteins; LDL-C: Low-density lipoprotein; VLDL: very low density lipoprotein.

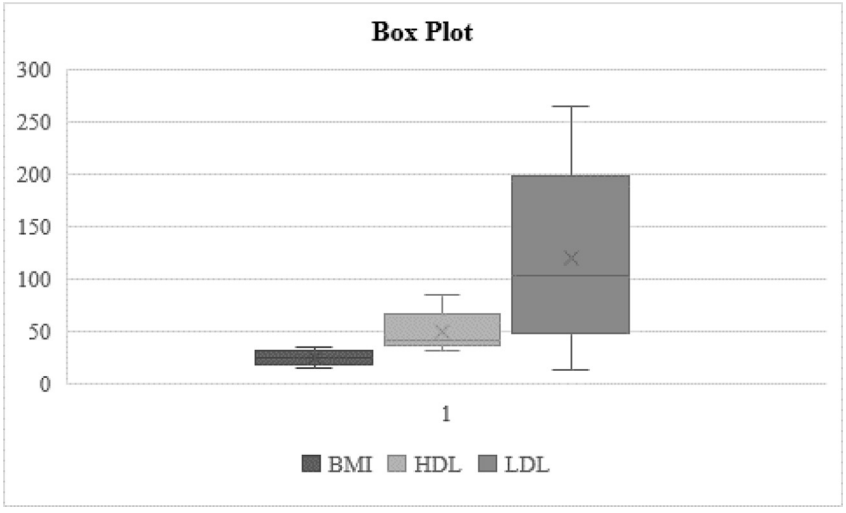

Fig. 1. Box plot of BMI, HDL and LDL in diabetic ulcer patients.

Table 3
Correlation of inflammatory with the healing of ulcer.

Data	Adiponectin		Cathepsin D		25(OH)-D		HSP-70		HSP-47	
	r	p	r	p	r	p	r	p	r	p
ABI	0.153	0.034	0.353	0.054	0.353	.134	.087	.234	0.153	0.254
TBI	−0.037	0.613	−0.137	0.163	−0.137	.179	.128	.079	−0.037	0.063
HSP-70 (pg/ml)	0.089	0.219	0.189	0.129	0.189	.000			0.089	0.029
HSP-47 (ng/ml)	−0.097	0.182	−0.297	0.821	−0.297	.000	-.495	.000		
Adiponectin (ng/ml)			−0.028	1	−0.028	.794	-.010	.894	−0.097	0.021
Cathepsin D (RFU/ml)	−0.028	.702			1	.023	.112	.123	−0.028	.032
25(OH)-D (ng/ml)	0.203	.005	0.213	.035			.035	.634	0.203	.015
HbA1c (%)	0.082	.260	0.812	.160	0.812	.035	.057	.435	0.082	.060
HDL-C (mg/dL)	−0.038	0.598	−0.308	0.398	−0.308	.047	-.005	.947	−0.038	0.398
LDL-C (mg/dL)	0.060	0.410	0.600	0.110	0.600	.044	.106	.144	0.060	0.010
Total Cholesterol (mg/dL)	−0.059	0.418	−0.509	0.118	−0.509	.747	-.036	.847	−0.059	0.018
Serum Albumin (SA) (gm%)	0.154	0.033	0.514	0.023	0.514	.032	-.386	.032	0.154	0.023
Serum Globulin (SG) (gm%)	0.173	0.016	0.713	0.036	0.713	.053	-.033	.653	0.173	0.036

Heat Shock Protein 70 (mg/ml) and Heat Shock Protein 47 (mg/ml); ABI: ankle-brachial index, TBI: toe-brachial index, HDL-C: High-density lipoproteins; LDL-C: Low-density lipoprotein; 25(OH)-D; 25 hydroxy vitamin D; HbA1c: glycated haemoglobin.

HbA1c, serum albumin (SA) and serum globulin (SG) with 25(OH)D.

4. Discussion

The results have provided an in-depth understanding of the cases, used to examine the ulcer healing rate among diabetic patients. The findings have shown significant association among adiponectin, Cat D, and ulcer healing rates. These findings have emphasized a crucial role of both proteins in rapid healing process of ulcer wounds among diabetic patients. However, the study is limited to found any significant association of other cases; such as HbA1c, Lipid Profile, S. creatinine, HSP70, HSP47 and 25-hydroxy vitamin D with ulcer healing rates. The findings of current study are supported by following studies.

Tuttolomondo, Maida & Pinto [13] assessed the implications of a possible cardiovascular marker in diabetic patients for diabetic foot syndrome. The study has evaluated that adiponectin and Cat-D are efficient and effective biomarkers, associated with foot ulcers pathogenesis by inflammatory and microvascular mechanisms. These biomarkers have significantly reduced pathogenic risks among diabetic patients and contributed a vital role in diabetic patients. Taha & Omar [14] investigated the association between high-sensitivity C-reactive protein and plasma Cat-D among diabetic foot ulcer patients. The findings have shown higher mean plasma levels of Cat-D among diabetic patients with foot ulcer syndrome. The study has positively reported a significant correlation between Cat-D and level of ulcer ($p = 0.001$). Thereby, the study has recommended that diabetic patients with foot ulcer syndrome should be associated with higher level of Cat-D and high-sensitivity C-reactive protein. Ahmad et al. [15] assessed the correlation between Cat-D, adiponectin, and high-sensitivity C-reactive protein among diabetic foot ulcer patients. The findings have shown a positive and significant correlation between ulcer grades, and Cat-d, adiponectin and BMI among diabetic patients.

Similarly, Tuttolomondo, Maida & Pinto [13] examined higher association between the pathogenic aspects and grades of ulcer. These pathogenic aspects include adiponectin and Cat-D that positively and directly contribute in the insulin resistance, blood lipid disorder, obesity, hypertension, prothrombotic state and diabetes. Furthermore, findings have indicated lower plasma levels of adiponectin and Cat-D that characterized the adipo-vascular axis among diabetic patients. Thereby, the study has recommended that the infections and peripheral arteriopathy should be treated by inflammatory features of diabetic foot syndrome. Shibata et al. [7] assessed the involvement of adiponectin in wound healing process using ERK signaling pathway. The study has examined a potent mediation of adiponectin in the healing process of diabetic patients. The study has recommended that management of diabetic wounds is positively observed through the upregulation of systemic and local adiponectin levels.

Shashanka & Palachandra [3] have assessed the importance of HbA1c as an effective biomarker in the wound healing prediction among diabetic patients. The study has revealed that there was no significant evidence regarding the HbA1c and grades of ulcer among diabetic patients. The findings of Shashanka & Palachandra [3] supported current findings that HbA1c and grades of ulcer are indirectly correlated with each other. Thereby, the study has recommended that increased HbA1c levels can be associated with slower wound healing and can be used as an independent biomarker for wound healing assessment in diabetic foot ulcer patients.

Dhamodharan et al. [16] investigated the association between HSP-70 and diabetic foot ulcer patients in their diagnosis procedure. The study has found an insignificant correlation between HSP70 and grades of ulcer among diabetic patients at the time of treatment. Similarly, the study has indicated association of HSP70 with renal complications among diabetic patients. Bellini et al. [17] have reviewed the efficacy of HSP70 in the vascular diabetic complications. The study has reported that HSP is used as a valuable biomarker in examining the therapeutic effectiveness among diabetic patients. In contrast, the study reveals that there is low-level of association between HSP and grades of ulcer and; thus, recommends to gain a comprehensive understanding of HSP relevance to diagnose diabetic patients.

5. Conclusion

The study has aimed to assess the role of HbA1c, Lipid, S. Creatinine, Adiponectin, Cat D, HSP70, HSP47, and 25-hydroxy vitamin D and to evaluate the rate of healing of ulcer among the diabetic patients. A retrospectively data has been incorporated to assess the role of these predictors. The findings have shown positive and significant correlation between Cat-D and Adiponectin with grades of ulcer among diabetic patients. However, the study has revealed insignificant correlation of HbA1c, Lipid Profile, S. creatinine, HSP70, HSP47 and 25-hydroxy vitamin D with ulcer healing rates. Several limitations have been identified, which restricted to fulfill the novelty of this study. Firstly, only two predictors were positively associated with grades of ulcer healing among diabetic patients. These include Cad-D and adiponectin,

while others were insignificantly associated with grades of ulcer healing, leaving a question mark for future studies. Although, previous studies have assessed positive association between HbA1c, S. creatinine, HSP47,70 and 25-hydroxy vitamin D with ulcer healing grades; this study failed to achieve significant evidence regarding these predictors. Thereby, it is essential for future studies to assess the role of these insignificant predictors in the diagnosis of wound infections among diabetic patients.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of interest

The author declares no competing interest.

Author's contribution

M.Z.: researched data, wrote the manuscript, and contributed to the discussion. J.A.: contributed to the discussion and reviewed/edited the manuscript.

Funding

This research is not funded by any resource.

Acknowledgement

The author is very thankful to all the associated personnel in any reference that contributed in/for the purpose of this research.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2018.12.004.

References

[1] Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. Jama 2005 Jan 12;293(2):217–28.
[2] Viswanathan V, Kumpatla S, Gnanasundaram S, Gopanakrishna G, Das B. Assessment of ulcer related outcomes in type 2 diabetic patients with foot ulceration in India. J Diabet Foot Complicat 2009;1(2):40–6.
[3] Shashanka R, Palachandra A. Hemoglobin A1c in diabetic foot patients: a predictor of healing rate. 2016.
[4] Semadi IN, Irawan H. Blood glucose and lipid profile in patients with diabetic foot ulcer that underwent hyperbaric oxygen therapy. Bali Med J 2017 Jan 1;6(2):405–8. https://doi.org/10.15562/bmj.v6i2.606.
[5] Gulcan E, Gulcan A, Erbilen E, Toker S. Statins may be useful in diabetic foot ulceration treatment and prevention. Med Hypotheses 2007 Jan 1;69(6):1313–5.
[6] Lee KM, Kim WH, Lee JH, Choi MS. Risk factors of treatment failure in diabetic foot ulcer patients. Arch Plast Surg 2013 Mar;40(2):123. https://doi.org/10.5999/aps.2013.40.2.123.
[7] Shibata S, Tada Y, Asano Y, Hau CS, Kato T, Saeki H, Yamauchi T, Kubota N, Kadowaki T, Sato S. Adiponectin regulates cutaneous wound healing by promoting keratinocyte proliferation and migration via the ERK signaling pathway. J Immunol 2012 Aug 17:1101739. https://doi.org/10.4049/jimmunol.1101739.
[8] Oh DK, Ciaraldi T, Henry RR. Adiponectin in health and disease. Diabetes Obes Metab 2007 May;9(3):282–9.
[9] Sugden JA, Davies JI, Witham MD, Morris AD, Struthers AD. Vitamin D improves endothelial function in patients with Type 2 diabetes mellitus and low vitamin D levels. Diabet Med 2008 Mar;25(3):320–5.
[10] Yabunaka N, Ohtsuka Y, Watanabe I, Noro H, Fujisawa H, Agishi Y. Elevated levels of heat-shock protein 70 (HSP70) in the mononuclear cells of patients with non-insulin-dependent diabetes mellitus. Diabetes Res Clin Pract 1995 Nov 1;30(2):143–7.
[11] Zubair M, Ahmad J. Plasma Heat Shock Proteins (HSPs) 70 and 47 levels in diabetic foot and its possible correlation with clinical variables in a North Indian Tertiary care hospital. Diabetes Metab Syndrome: Clin Res Rev 2015 Oct 1;9(4):237–43.
[12] Sedgwick P. Retrospective cohort studies: advantages and disadvantages. BMJ 2014 Jan 24;348:g1072.
[13] Tuttolomondo A, Maida C, Pinto A. Diabetic foot syndrome as a possible cardiovascular marker in diabetic patients. J Diabetes Res 2015;2015.
[14] Taha A, Omar GA. Correlation of cathepsin D and hsCRP plasma levels with diabetic foot ulcer in Egyptian subjects: control study. Imper J Interdiscipl Res 2016 May 2;2(5).
[15] Ahmad J, Zubair M, Malik A, Siddiqui MA, Wangnoo SK. Cathepsin-D, adiponectin, TNF-α, IL-6 and hsCRP plasma levels in subjects with diabetic foot and possible correlation with clinical variables: a multicentric study. Foot 2012 Sep 1;22(3):194–9.
[16] Dhamodharan U, Ezhilarasi K, Ponjayanthi B, Sireesh D, Ramkumar KM, Viswanathan V. Association of A1538G and C2437T single nucleotide polymorphisms in heat shock protein-70 genes with diabetic nephropathy among South Indian population. Biosci Rep 2017 Feb 28. BSR20160605.
[17] Bellini S, Barutta F, Mastrocola R, Imperatore L, Bruno G, Gruden G. Heat shock proteins in vascular diabetic complications: review and future perspective. Int J Mol Sci 2017 Dec 14;18(12):2709.