

# Diabetics and Sexual Disorders: Why both Men and Women with Diabetes Suffer from Impotence and Lack of Sexual Desire.

Ibrahim Abdelrahim Ibrahim Humaida

Associate Professor of Mental Health, Faculty of Arts /Department of Psychology, Omdurman Islamic University-Sudan.

**Corresponding Author:** Ibrahim Abdelrahim Ibrahim Humaida, Associate Professor of Mental Health, Faculty of Arts /Department of Psychology, Omdurman Islamic University-Sudan.

**Received Date:** November 09, 2022; **Accepted Date:** November 17, 2022; **Published Date:** November 23, 2022.

**Citation:** Ibrahim Abdelrahim Ibrahim Humaida, (2022) Diabetics and Sexual Disorders: Why both Men and Women with Diabetes Suffer from Impotence and Lack of Sexual Desire. *Clinical Genetic Research*, 1(2); **Doi:** 10.31579/2834-8532/006

**Copyright:** © 2022 Ibrahim Abdelrahim Ibrahim Humaida, This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

## Abstract

The main objective of this study was to investigate the prevalence of sexual disorders in diabetics, owing to diabetes constitutes a growing public health problem, leading to a variety of dysfunctions such as cardiovascular, psychological, and sexual dysfunctions, that is why Diabetes is a well-known cause of sexual disorders, with prevalence rates approaching 50% in both type 1 and type 2 diabetes, but the determinants of sex dysfunction in diabetic men as a result of the principal cardiovascular risk factors, such as hypertension, and also overweight obesity, in addition to metabolic syndrome, smoking, and sedentary lifestyles. Moreover, sexual disorders considered as important predictors of the development of major complaints in diabetic patients, on the other hand, the debate as to whether diabetes link with sexual dysfunction or not, is an issue of controversy, moreover, diabetic women suffer from the same neurovascular complications that contribute to the pathogenesis of SD in men, however, results of sexual functioning of diabetic women are less conclusive. Conclusion: extending beyond the specific effects on sexual dysfunction in men and women with diabetes, the adoption of these measures promotes a healthier life and increased well-being, which in turn, may help to reduce the burden of sexual dysfunction.

**Keywords:** diabetics; sexual dysfunction; impotence; desire

## 1. Introduction

The causes of erectile dysfunction in men with diabetes are complex and involve impairments in nerve, blood vessel, and muscle function [1].

To get an erection, men need healthy blood vessels, nerves, male hormones, and a desire to be sexually stimulated. Diabetes can damage the blood vessels and nerves that control erection. Therefore, and more likely, diabetics might have normal amounts of male hormones, have the desire to have sex, but still may not be able to achieve a firm erection [2].

Diabetes has been associated with sexual dysfunction both in men and in women. Diabetes is an established risk factor for sexual dysfunction in men; a threefold increased risk of erectile dysfunction (ED) found in diabetic compared with non-diabetic men. Among women, the evidence regarding association between diabetes and sexual dysfunction is less conclusive, although most studies have reported a higher prevalence of female sexual dysfunction (FSD) in diabetic women as compared with non-diabetic women [3].

Diabetic men showed more probability of having an impotency than men without diabetes; moreover, the age-adjusted risk of sexual impotence found in diabetic men compared with those without diabetes. In addition, it is estimated that the worldwide prevalence of impotence will rise to 322 million cases by the year 2025. Several cross-sectional and longitudinal studies showed an association between ED and most of the cardiovascular risk factors, such as diabetes, smoking, hypertension, metabolic syndrome, as well as depression, lower urinary tract symptoms, and poor health state. Moreover, ED is the marker of significantly increased risk of CVD, CHD, stroke, and all-cause mortality [4].

## The Scope and Statement of the Problem

Epidemiological studies suggest that both type 1 and type 2 diabetes are associated with an increased risk of ED, which is reported to occur in ≥50% of men with diabetes worldwide. In the Massachusetts Male Aging Study, diabetic men showed a threefold probability of having ED when compared to men without diabetes; moreover, the age-adjusted risk of ED

doubled in diabetic men when compared to those without diabetes [5]. Most of the studies that described the prevalence of ED in diabetes did not distinguish between type 1 and type 2 diabetics.

Two studies reported a similar likelihood of having ED among both type 1 and type 2 diabetic men, whereas another report showed a higher risk of developing ED in men with type 1 diabetes. The occurrence of ED is 10–15 years earlier in men with diabetes; moreover, ED is more severe and less responsive to oral drugs in diabetes, leading to reduced quality of life [6].

### Aim

To explore the effects of diabetes on sexuality, evaluate the impact of diabetes on sexual function, and assess the conventional and novel treatment approaches based on recent studies.

## 2. Literature Review

Advanced age and longer duration of diabetes have been associated with an increased risk of ED in diabetic patients [7]. Whether hyperglycemia is a risk factor for the development of ED in diabetic men is still not clear [8]. Some observational studies have shown an association between poor glycemic control, expressed by elevated levels of glycated hemoglobin (HbA<sub>1c</sub>), and ED, whereas other studies did not report any association [9]. The different methodological approaches used in the different studies may explain, at least in part, these divergent results [10]. Moreover, diabetes is commonly associated with hypertension, hyperlipidemia, overweight and obesity, metabolic syndrome, smoking, sedentary lifestyles, and autonomic neuropathy, which are recognized as risk factors for ED. Both microvascular and macrovascular diabetic complications also increase the risk of ED in diabetic men [11]. The use of several medications frequently assumed by diabetic patients, such as use of antihypertensive drugs ( $\beta$ -blockers, thiazide diuretics, and spironolactone), psychotropic drugs (antidepressants), and certain fibrates, have all been associated with an additive deleterious effect on diabetic ED [12]. A moderate consumption of alcohol (not more than 5% of the total daily caloric intake, or  $\leq 7$  alcoholic drinks per week) may exert a protective effect on ED in both the general population and in diabetic men [13].

### The Underlying Causes of Impotence in Diabetics

The pathogenesis of impotence in diabetes is due to many factors, as it depends on both psychological and organic factors, as well as psychological and relationship issues, which often coexist [14]. Heart disease, neuropathy, visceral adiposity, insulin resistance, and disturbed gonads represent the proposed mechanisms of erectile disorder in diabetic patients [15].

Erectile dysfunction ED, which is an inability to get or maintain an erection strong enough for sex, is common in men who are suffering from diabetes, especially those with type 2. It can also stem from damage to nerves and blood vessels caused by poor long-term blood sugar control [16]. As mentioned, several cardiovascular risk factors associated with diabetes contribute to the genesis of penile arterial insufficiency: all of them converge on endothelial dysfunction, which represents the common denominator leading to vascular ED [17].

The chronic insult of hyperglycemia on the endothelium results in endothelial dysfunction, which is suggested as the link between ED and CVD [18]. A diagnosis of ED regarded as a sentinel event that should prompt the investigation of coronary artery disease (CAD) in asymptomatic diabetic men. Endothelial dysfunction in diabetes is manifested as the decreased bioavailability of nitric oxide (NO), resulting in insufficient relaxation of the vascular smooth muscle [18]. The potential mechanisms involved in endothelial dysfunction include the accumulation of advanced glycation end products; increased levels of oxygen free radicals that reduce the bioavailability of NO; impaired endothelial and neuronal NO synthesis, expression, and activity; and an imbalance between the vasoconstrictive and vasorelaxation intracellular

pathways favoring increased vasoconstriction [19].

Microvascular disease determines ischemic damage in the distal circulation and autonomic and peripheral neuropathy [20]. Both somatic and autonomic neuropathies may contribute to diabetes-induced erection due to the impairment of sensory impulses from the penis to the reflexogenic erectile center and reduced or absent parasympathetic activity necessary for relaxation of the smooth muscle of the penis [21, 22].

Insulin resistance and visceral adiposity, which are both distinctive clinical traits of type 2 diabetes, are associated with inflammatory state that results in the decreased availability and activity of hormone, leading to ED in overweight and obese diabetic men [23–25].

Subnormal testosterone concentrations found in 25% of men with type 2 diabetes in association with inappropriately low luteinizing hormone (LH) and follicle-stimulating hormone (FSH) concentrations [26]. Testosterone regulates nearly every component of erectile function, from pelvic ganglions to smooth muscle, and to the endothelial cells of the gonads [27]. It also modulates the timing of the erectile process, which occurs as a function of sexual desire, coordinating penile erection with sex [28]. It is still unclear what level of testosterone needed for good erectile function; however, evidence derived from clinical and molecular studies supports the use of testosterone replacement in patients with erectile disorder, although the benefit–risk ratio is uncertain in advanced age [29–31].

### The Prevalence of Sexual Disorders in diabetic women

Sexual disorders reported in women with diabetes include the reduction or loss of sexual interest or desire, arousal or lubrication difficulties, and loss of the ability to reach orgasm [32, 33].

FSD has been associated with both type 1 and type 2 diabetes. A recent meta-analysis that included 26 studies, 3,168 diabetic women, and 2,823 controls showed that FSD is more frequent, and is associated with a lower Female Sexual Function Index (FSFI) score in diabetic women than in controls [34]. In particular, the risk for FSD was 2.27 (95% confidence interval [CI]: 1.23–4.16) and 2.49 (95% CI: 1.55–3.99) in type 1 and type 2 diabetic women, respectively [35]. Having a high sugar levels for a long period of time can cause sexual problems, women with diabetes are more at risk of having sex impairment. Diabetes can damage blood vessels and nerves that supply sex organs. This can restrict the amount of blood flowing to sexual organs, so the patient can lose sensation to sexual stimuli. This means she has a difficulty getting aroused, vaginal dryness, and painful sex as well. Furthermore, damage occurs throughout the body can affect the ability to experience sexual stimulation, arousal, and the release of vaginal lubricant [36]. Interestingly, an increased risk of having sexual intercourse found in premenopausal women with diabetes, owing to urinary tract infections, which can overall impact sexual performance [37]. Moreover, at meta-regression, among the independent variables, only BMI was significantly associated with the FSFI effect size ( $P=0.005$ ), suggesting that the higher frequency of FSD and lower FSFI score found in diabetic women may be related to body weight [38]. Several studies have already shown an increased prevalence of FSD in women affected by obesity and metabolic syndrome. Studies that have focused on type 1 diabetic women have provided a valid opportunity to investigate the role of diabetes on sexual function, independent of other associated defects [39]. In type 1 diabetic women, FSD appears to be correlated mainly to psychological factors, such as depression, anxiety, and marital status. Results from a large prospective study of 625 women with type 1 diabetes showed that depression was the major predictor of sexual dysfunction [40]. Studies examining FSD in individuals with type 2 diabetes are less conclusive and limited by small study sizes; the determinants of sexual function in type 2 diabetes include age, duration of diabetes, menopause, vascular complications, and psychological complaints. In one large study that evaluated 613 diabetic women and 524 controls, found that the longer duration of diabetes, older age, higher BMI, the presence of CVD, and the presence of diabetic complications

was significantly associated with worse sexual function. In a study by Esposito et al, found that metabolic syndrome an independent predictor of FSD in 595 type 2 diabetic women, although only depression and marital status were the strongest independent factors associated with FSD [41].

Diabetes-induced vascular and nerve dysfunctions may impair the sexual response by producing structural and functional changes in the female genitalia. Studies in animals showed that diabetes affect arousal and orgasmic sexual responses by inducing impaired relaxation responses of the vaginal tissue to almost all transmitter systems, decreasing nerve-stimulated clitoral and vaginal blood flow, producing diffuse fibrosis of the clitoris and vaginal tissues, and reducing the muscular layer and epithelial thickness in the vagina [42]. Vascular abnormalities, including atherosclerotic damage and diabetes-induced endothelial dysfunction, may be responsible for reducing the engorgement of the clitoris and for reducing lubrication of the vagina, leading to decreased arousal and dyspareunia during sexual intercourse. Diabetic neuropathy may further contribute to the pathogenesis of sexual dysfunctions by altering both the normal transduction of sexual stimuli and the triggered sexual response [43].

It has been hypothesized that FSD may be the consequence of an imbalance in the hormonal levels of diabetic women, as indicated by epidemiological studies showing a correlation between alterations in the levels of androgens, estrogens, as well as sex hormone-binding globulin and sexual problems in diabetic women. Moreover, several endocrine impairments that may be associated with diabetes, such as thyroid disorders, hypothalamic-pituitary dysfunctions, and polycystic ovarian syndrome, may further contribute to sexual dysfunctions in these women [44].

In conclusion, psychological concerns may play a significant role in the development of FSD in both type 1 and type 2 diabetes. This is in line with the complex nature of female sexuality, which is largely dependent on psychological and cultural factors, even more so than male sexuality [45].

### 3. Methodology

In this analytical study, the researcher adopted mixed approaches in data collection that concern spreading of sexual problems among the diabetics. Quantitative data collection instruments including obtaining data from available sources, such as electronic health records, systematic reviews, clinical data, and clinical case reports. Qualitative data, which is a method that a researcher can record the behaviors of his/her research respondents directly in real life settings (naturalistic observation) at their own physical environments. Besides, narratives.

### 4. Results

1- Male and female sexual dysfunctions are a significant complication of diabetes.

2- Men were more likely to express a lack of interest in sex if they had diabetes.

3- Men also were more likely to suffer erectile dysfunction if they had diabetes.

4- Women as well as men with diabetes reported a higher rate of orgasm difficulty, including climaxing too quickly or not at all, which was reported by both men and women.

### 5. Discussion

Deterioration in sexual functioning is one of the major and serious complications of diabetes. This common metabolic disorder not only affects sexuality through cardiovascular and nerve damage but also has psychological aspects. In men, the primary complications are erectile dysfunction, ejaculatory dysfunction, and loss of libido. Women similarly experience sexual problems, including decreased libido and decrease in arousal and lubrication resulting in painful intercourse, and loss of orgasm.

### 6. Conclusion

Diabetes mellitus (DM) is a systemic disease that is considered to play a principal role in the etiology of sexual dysfunction. The impact of neurogenic, psychogenic and vascular factors, usually combined in the pathogenesis of related complications were demonstrated in a large number of studies. Numerous medical researchers have shown that, prevalence of sexual dysfunction in men because of the degenerative effects of diabetes on vascular and neurologic structures ranges from 35 to 75%. It also documented that the etiology of ED may be neurologic in up to 82% of diabetic men. However, sexual dysfunction in diabetic women at neurological factors has not been investigated in details, because female sexual dysfunction is still unexplained as male sexual dysfunction. Although cranial neuropathy and cardiovascular autonomic neuropathy may be implicated in sexual performance in both males and females.

### 7. Recommendations and Suggestions

1- Diabetics should get enlightened with potential risks of their disease on sexual functioning.

2- A counseling is highly needed for patients with diabetes.

3- Experimental researches should be conducted regarding the effect of diabetes on impotence.

### References

1. Tamás V, Kempler P. Sexual dysfunction in diabetes. *Handb Clin Neurol.* (2014); 126: 223-232.
2. International Diabetes Federation. *Diabetes Atlas.* Fifth ed. Brussels, Belgium: International Diabetes Federation; (2015).
3. Campos C. Chronic hyperglycemia and glucose toxicity: pathology and clinical sequelae. *Postgrad Med.* (2012); 124 (6): 90-97.
4. Rahman S, Rahman T, Ismail AA, Rashid AR. Diabetes-associated macrovasculopathy: pathophysiology and pathogenesis. *Diabetes Obese Metab.* (2007); 9 (6): 767-780.
5. Fox CS, Coady S, Sorlie PD, et al. Increasing cardiovascular disease burden due to diabetes mellitus: the Framingham Heart Study. *Circulation.* (2007); 115 (12): 1544-1550.
6. Preis SR, Pencina MJ, Hwang SJ, et al. Trends in cardiovascular disease risk factors in individuals with and without diabetes mellitus in the Framingham Heart Study. *Circulation.* (2009); 120 (3): 212-220.
7. Lu CC, Jiann BP, Sun CC, Lam HC, Chu CH, Lee JK. Association of glycemic control with risk of erectile dysfunction in men with type 2 diabetes. *J Sex Med.* (2009); 6(6): 1719-1728.
8. Enzlin P, Rosen R, Wiegel M, et al. DCCT/EDIC Research Group. Sexual dysfunction in women with type 1 diabetes: long-term findings from the DCCT/EDIC study cohort. *Diabetes Care.* (2009); 32 (5): 780-785.
9. Maseroli E, et al. Cardiometabolic risk and female sexuality: focus on clitoral vascular resistance. *J Sex Med.* (2016) Nov; 13 (11): 1651-1661.
10. Phillips A, Phillips S. Recognising female sexual dysfunction as an essential aspect of effective diabetes care. *Appl Nurs Res.* (2015) Aug; 28 (3): 235-238.
11. Olarinoye J, Olarinoye A. Determinants of sexual function among women with type 2 diabetes in a Nigerian population. *J Sex Med.* (2008); 5 (4): 878-886.
12. Giugliano F, Maiorino M, Bellastella G, Gicchino M, Giugliano D, Esposito K. Determinants of erectile dysfunction in type 2 diabetes. *Int J Impot Res.* (2010); 22 (3): 204-209.
13. Johannes CB, et al. Incidence of erectile dysfunction in men 40 to 69 years old: longitudinal results from the Massachusetts Male Aging Study. *J Urol.* 2017; 163: 460-463.
14. Hackett G, et al. Coronary heart disease, diabetes, and sexuality in men. *J Sex Med.* 2016 Jun; 13 (6): 887-904.
15. Esposito K, Maiorino MI, Bellastella G, Giugliano F, Romano M, Giugliano D. Determinants of female sexual dysfunction in type 2

- diabetes. *Int J Impot Res.* (2010); 22 (3): 179-184.
16. Seftel AD, Sun P, Swindle R. The prevalence of hypertension, hyperlipidemia, diabetes mellitus and depression in men with erectile dysfunction. *J Urol.* (2004); 171 (6 Pt 1): 2341-2345.
17. Kizilay F, et al. Diabetes and sexuality. *Sex Med Rev.* 2017 Jan; 5 (1): 45-51.
18. Lewis RW, Fugl-Meyer KS, Corona G, et al. Definitions/epidemiology/risk factors for sexual dysfunction. *J Sex Med.* (2010); 7 (4 Pt 2): 1598-1607.
19. Miner M, Esposito K, Guay A, Montorsi P, Goldstein I. Cardio metabolic risk and female sexual health: the Princeton III summary. *J Sex Med.* (2012); 9 (3): 641-651. quiz 652.
20. Esposito K, Ciotola M, Maiorino MI, et al. Hyperlipidemia and sexual function in premenopausal women. *J Sex Med.* 2009; 6 (6): 1696-1703.
21. Esposito K, Ciotola M, Marfella R, Di Tommaso D, Cobellis L, Giugliano D. Sexual dysfunction in women with the metabolic syndrome. *Diabetes Care.* (2005); 28 (3): 756.
22. Isidori AM, Buvat J, Corona G, et al. A critical analysis of the role of testosterone in erectile function: from pathophysiology to treatment – a systematic review. *Eur Urol.* 2017; 65 (1): 99-112.
23. Bellastella G, Maiorino MI, Olita L, De Bellis A, Giugliano D, Esposito K. Anti-pituitary antibodies and hypogonadotropic hypogonadism in type 2 diabetes: in search of a role. *Diabetes Care.* 2013; 36 (8): e116-e117.
24. Meeking DR, Fosbury JA, Cummings MH. Sexual dysfunction and sexual health concerns in women with diabetes. *Practical Diabetes.* 2016; 30 (8): 327-331.
25. Ponholzer A, Temml C, Mock K, Marszalek M, Obermayr R, Madersbacher S. Prevalence and risk factors for erectile dysfunction in 2869 men using a validated questionnaire. *Eur Urol.* (2005); 47 (1): 80-85. discussion 85-86.
26. Go AS, Mozaffarian D, Roger VL, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee Heart disease and stroke statistics – 2013 update: a report from the American Heart Association. *Circulation.* 2013; 127 (1): e6-e245.
27. Giuliano FA, Leriche A, Jaudinot EO, de Gendre AS. Prevalence of erectile dysfunction among 7689 patients with diabetes or hypertension, or both. *Urology.* (2004); 64 (6): 1196-1201.
28. Maria Ida Maiorino, Giuseppe Bellastella, and Katherine Esposito Diabetes and sexual dysfunction: current perspectives *Diabetes Metab Syndr Obes.* 2014; 7: 95–105. Published online 2014 Mar 6. doi: 10.2147/DMSO.S36455
29. Demir O, Akgul K, Akar Z, et al. Association between severity of lower urinary tract symptoms, erectile dysfunction and metabolic syndrome. *Aging Male.* (2009); 12 (1): 29-34.
30. Turek SJ, Hastings SM, Sun JK, King GL, Keenan HA. Sexual dysfunction as a marker of cardiovascular disease in males with 50 or more years of type 1 diabetes. *Diabetes Care.* (2013); 36 (10): 3222-3226.
31. Dong JY, Zhang YH, Qin LQ. Erectile dysfunction and risk of cardiovascular disease: meta-analysis of prospective cohort studies. *J Am Coll Cardiol.* (2011); 58 (13): 1378-1385.
32. Araujo AB, Travison TG, Ganz P, et al. Erectile dysfunction and mortality. *J Sex Med.* (2009); 6 (9): 2445-2454.
33. Thorve VS, Kshirsagar AD, Vyawahare NS, Joshi VS, Ingale KG, Mohite RJ. Diabetes-induced erectile dysfunction: epidemiology, pathophysiology and management. *J Diabetes Complications.* (2011); 25 (2): 129-136.
34. Corona G, Giorda CB, Cucinotta D, Guida P, Nada E, Gruppodi studio SUBITO-DE The SUBITO-DE study: sexual dysfunction in newly diagnosed type 2 diabetes male patients. *J Endocrinol Invest.* (2013); 36 (10): 864-868.
35. Chew SKh, Taouk Y, Xie J, et al. Relationship between diabetic retinopathy, diabetic macular oedema and erectile dysfunction in type 2 diabetics. *Clin Experiment Ophthalmol.* 2014; 41 (7): 683-689.
36. Al-Hunayan A, Al-Mutar M, Kehinde EO, Thalib L, Al-Ghorory M. The prevalence and predictors of erectile dysfunction in men with newly diagnosed with type 2 diabetes mellitus. *BJU Int.* 2007; 99 (1): 130-134.
37. Rosen RC, Wing RR, Schneider S, et al. Erectile dysfunction in type 2 diabetic men: relationship to exercise fitness and cardiovascular risk factors in the Look AHEAD trial. *J Sex Med.* (2009); 6 (5): 1414-1422.
38. Corona G, Giorda CB, Cucinotta D, Guida P, Nada E, Gruppodi studio SUBITO-DE The SUBITO-DE study: sexual dysfunction in newly diagnosed type 2 diabetes male patients. *J Endocrinol Invest.* 2015; 36 (10): 864-868.
39. Chew SKh, Taouk Y, Xie J, et al. Relationship between diabetic retinopathy, diabetic macular oedema and erectile dysfunction in type 2 diabetics. *Clinical Experiment Ophthalmology.* (2013); 41 (7): 683-689.
40. Heruti RJ, Uri I, Arbel Y, Swartzon M, Galor S, Justo D. Erectile dysfunction severity might be associated with poor cardiovascular prognosis in diabetic men. *J Sex Med.* (2007); 4 (2): 465-471.
41. Chew KK, Bremner A, Jamrozik K, Earle C, Stuckey B. Male erectile dysfunction and cardiovascular disease: is there an intimate nexus? *J Sex Med.* (2008); 5 (4): 928-934.
42. Foresta C, Caretta N, Corona G, et al. Clinical and metabolic evaluation of subjects with erectile dysfunction: a review with a proposal flowchart. *Int J Androl.* (2009); 32 (3): 198-211.
43. Hackett G, et al. Coronary heart disease, diabetes, and sexuality in men. *J Sex Med.* 2016 Jun; 13 (6): 887-904.
44. Bal MD, Yılmaz SD, Celik SG, Dinçag N, Beji NK, Yalçın O. Does the diabetes of type 2 affect the sexual functions of women? *J Sex Marital Ther.* (2015); 41 (1): 107-13.
45. Thorve VS Diabetes-induced erectile dysfunction: epidemiology, pathophysiology and management. *J Diabetes Complications* (2011) 25: 129-136.



**Ready to submit your research? Choose ClinicSearch and benefit from:**

- fast, convenient online submission
- rigorous peer review by experienced research in your field
- rapid publication on acceptance
- authors retain copyrights
- unique DOI for all articles
- immediate, unrestricted online access

**At ClinicSearch, research is always in progress.**

Learn more <http://clinicsearchonline.org/journals/clinical-genetic-research->



© The Author(s) 2022. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.