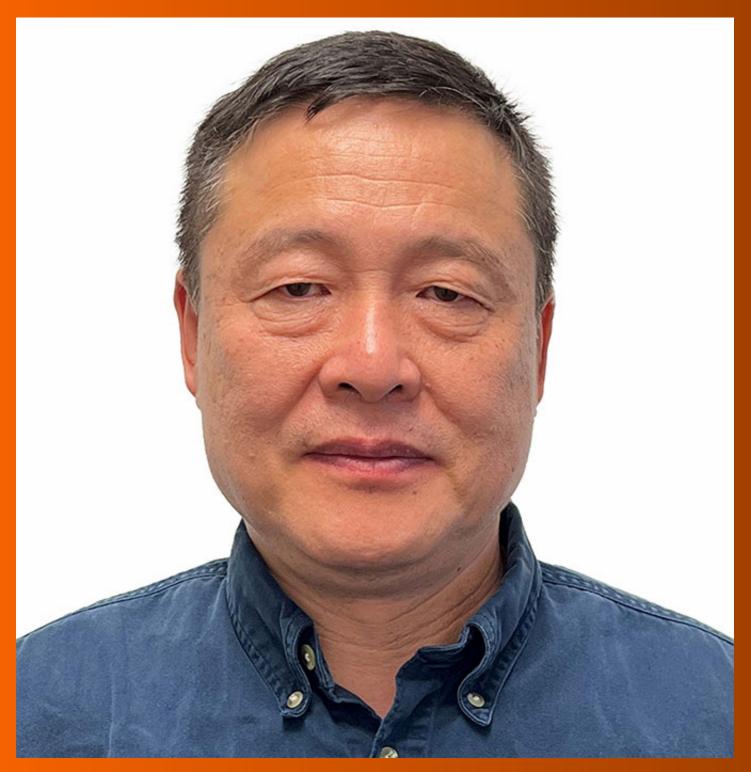
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ABOUT COVER

Editorial Board Member of World Journal of Diabetes, Guo-Xun Chen, PhD, Associate Professor, Director, Department of Nutrition, The University of Tennessee, Knoxville, TN 37909, United States. gchen6@utk.edu

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The primary aim of World Journal of Diabetes (WJD, World J Diabetes) is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

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LETTER TO THE EDITOR

Ca²⁺/cAMP ratio: An inflammatory index for diabetes, hypertension, and COVID-19

Leandro Bergantin

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Leandro Bergantin, Department of Pharmacology, Universidade Federal de São Paulo, São Paulo 04039-032, Brazil

Corresponding author: Leandro Bergantin, PhD, Professor, Department of Pharmacology, Universidade Federal de São Paulo, Rua Pedro de Toledo, 669 Vila Clementino, São Paulo 04039-032, Brazil. leanbio39@yahoo.com.br

Abstract

Ca²⁺/cAMP ratio could serve as an inflammatory index for diseases like hypertension, diabetes, and coronavirus disease 2019.

Key Words: Ca2+/cAMP ratio; COVID-19; Inflammatory index; Diabetes

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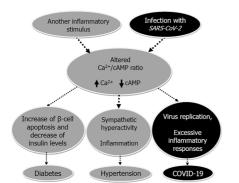
TO THE EDITOR

There is a clear relationship between Ca2+ signaling, e.g., increased Ca2+ signals, and inflammatory responses[1,2]. Considering the cumulative data from the scientific literature, including data of high evidence such as meta-analysis and systematic reviews, we can now link Ca2+ dyshomeostasis as an upstream factor for hypertension, diabetes, and other inflammatory processes[1,2]. In fact, severe inflammatory outcomes are described to be linked to a critical coronavirus disease 2019 (COVID-19) result[1,3]. Intriguingly, some reports have also observed an increased severity of COVID-19 in patients with diabetes [1,3]. To assess this issue, a meta-analysis [3] was performed by conducting a literature review of Scopus, PubMed, Science Direct, and



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Bergantin L. Ca²⁺/cAMP ratio as an inflammatory index



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Figure 1 Altered Ca2*/cAMP ratio resulting from an inflammatory stimulus and infection with SARS-CoV-2. Altered Ca2*/cAMP ratio stimulates uncontrolled inflammation, leading to virus replication, increase of β-cell apoptosis and decrease of insulin levels, and sympathetic hyperactivity. Up/down arrows: Increase/decrease; COVID-19: Coronavirus disease 2019.

> Web of Science. Observational studies, case-reports, and case-series reports that analyzed diabetes in COVID-19 patients were included in this meta-analysis[3]. The authors concluded that diabetes is a risk factor and plays a role in the disease severity and in the mortality of individuals with COVID-19. In fact, a bidirectional relationship between COVID-19 and diabetes has been established^[4]. Recent data have shown that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can produce a direct damage to the pancreas that could worsen hyperglycemia, and even cause the onset of diabetes in previously non-diabetic subjects[4]. Like diabetes, hypertension has also been recognized as a prevalent cardiovascular comorbidity in patients with COVID-19[5]. It is well established that hypertension increases the severity of SARS-CoV-2-infected patients^[5]. In addition, obesity is a well-known risk factor for metabolic syndrome (MetS), hypertension, and diabetes. Recent reports revealed that it is also a vital risk factor for COVID-19, as demonstrated by a recent phenome-wide analysis of COVID-19[6].

> Moreover, a link between infection with viruses and Ca^{2+} dyshomeostasis is well-discussed, *e.g.*, altering host cellular processes in the benefit of the viruses[7-10]. Thus, Ca²⁺ dyshomeostasis induced by viruses may trigger an alteration of the host cellular system that benefits virus survival and could serve as a link for an increased severity of COVID-19 in patients with diabetes[1,3].

> An interesting longitudinal study also evaluated the relationship between serum Ca²⁺ levels and the incidence of MetS, diabetes, and hypertension[11]. This study[11] was performed through crosssectional and longitudinal analyses (period 2010-2016). Logistic regression was used for cross-sectional analysis of the association between serum Ca2+ levels or albumin-corrected calcium (ACCA) and the prevalence of MetS, diabetes, or hypertension. Receiver operating characteristic curve analysis was applied for calculating an optimal cut-off value of serum Ca^{2+} levels and ACCA[1]. Cox proportional regression analysis for the development of MetS, diabetes, and hypertension according to different cutoff values of serum Ca²⁺ levels and ACCA was performed. At baseline, there were 27364 participants in this study [11]. The authors [11] concluded that higher serum Ca^{2+} levels were associated with an increased risk of MetS, diabetes, and hypertension. A hypothesis which could link hypertension and higher serum Ca^{2+} levels postulates that the influx of Ca^{2+} into the smooth muscle of the arteries could lead to muscle contracture, then increasing vascular resistance and, therefore, could result in the development of hypertension[11]. Our previous reports[1,2,12-15] also discussed this issue. In fact, we postulated that dysregulation of Ca²⁺ signaling is linked to a sympathetic hyperactivity, then leading to hypertension[1,12,16]. In addition, a hypothesis which could link diabetes and higher serum Ca²⁺ levels postulates that serum Ca^{2+} is associated with insulin resistance in adipocytes and skeletal muscle[17,18]. Our previous reports are in accordance with this hypothesis[1,12,15]. In fact, whereas a physiological increase in the cytoplasmic concentration of Ca2+ is a significant trigger for releasing insulin, an abnormal elevation of Ca^{2+} could stimulate β -cell apoptosis, then decreasing insulin levels, contributing to diabetes[1,15].

> Furthermore, reports of our group undoubtedly established that a rise of the concentration of cAMP can stimulate a Ca2+ release from the endoplasmic reticulum, entitled as Ca2+/cAMP signaling interaction [1,2,12-15]. In fact, a rise of the concentration of Ca^{2+} can markedly cause a decrease of the concentration of cAMP because of the negative feedback (Ca²⁺/cAMP signaling interaction). Thus, a disruption of this interaction can be linked with disorders, e.g., hypertension, diabetes, and COVID-19[1, 2,15]. Although the interaction between these disorders may be linked with continued increases of the concentration of Ca2+, whether these increases could disturb Ca2+/cAMP signaling interaction needs more studies, e.g., in animal models and clinical trials. Indeed, previous studies corroborate this concept. For instance, in patients with diabetes, plasma concentrations of cAMP were significantly lower than those of normal subjects^[19]. In addition, cAMP contents of platelets were measured and observed to be lower in hypertensive than in normotensive subjects[20]. Figure 1 summarizes previous discussion.

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In conclusion, Ca2+/cAMP ratio could serve as an inflammatory index for diseases like hypertension, diabetes, and COVID-19[21,22].

FOOTNOTES

Author contributions: Bergantin LB is the sole author.

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REFERENCES

- Bergantin LB. Diabetes and inflammatory diseases: An overview from the perspective of Ca(2+)/3'-5'-cyclic adenosine 1 monophosphate signaling. World J Diabetes 2021; 12: 767-779 [PMID: 34168726 DOI: 10.4239/wjd.v12.i6.767]
- 2 Bergantin LB. A Timeline of Ca(2+)/cAMP Signalling: From Basic Research to Potential Therapeutics for Dementia. Curr Alzheimer Res 2022; 19: 179-187 [PMID: 35430979 DOI: 10.2174/1567205019666220415125447]
- Abdi A, Jalilian M, Sarbarzeh PA, Vlaisavljevic Z. Diabetes and COVID-19: A systematic review on the current evidences. 3 Diabetes Res Clin Pract 2020; 166: 108347 [PMID: 32711003 DOI: 10.1016/j.diabres.2020.108347]
- Lima-Martínez MM, Carrera Boada C, Madera-Silva MD, Marín W, Contreras M. COVID-19 and diabetes: A 4 bidirectional relationship. Clin Investig Arterioscler 2021; 33: 151-157 [PMID: 33303218 DOI: 10.1016/j.arteri.2020.10.001
- 5 Peng M, He J, Xue Y, Yang X, Liu S, Gong Z. Role of Hypertension on the Severity of COVID-19: A Review. J Cardiovasc Pharmacol 2021; 78: e648-e655 [PMID: 34321401 DOI: 10.1097/FJC.000000000001116]
- Baranova A, Cao H, Teng S, Zhang F. A phenome-wide investigation of risk factors for severe COVID-19. J Med Virol 6 2023; 95: e28264 [PMID: 36316288 DOI: 10.1002/jmv.28264]
- Olivier M. Modulation of host cell intracellular Ca2+. Parasitol Today 1996; 12: 145-150 [PMID: 15275223 DOI: 7 10.1016/0169-4758(96)10006-5
- Nugent KM, Shanley JD. Verapamil inhibits influenza A virus replication. Arch Virol 1984; 81: 163-170 [PMID: 6743023] DOI: 10.1007/BF01309305]
- Dionicio CL, Peña F, Constantino-Jonapa LA, Vazquez C, Yocupicio-Monroy M, Rosales R, Zambrano JL, Ruiz MC, Del Angel RM, Ludert JE. Dengue virus induced changes in Ca(2+) homeostasis in human hepatic cells that favor the viral replicative cycle. Virus Res 2018; 245: 17-28 [PMID: 29269104 DOI: 10.1016/j.virusres.2017.11.029]
- 10 Scherbik SV, Brinton MA. Virus-induced Ca2+ influx extends survival of west nile virus-infected cells. J Virol 2010; 84: 8721-8731 [PMID: 20538858 DOI: 10.1128/JVI.00144-10]
- 11 Chou CW, Fang WH, Chen YY, Wang CC, Kao TW, Wu CJ, Chen WL. Association between Serum Calcium and Risk of Cardiometabolic Disease among Community-dwelling Adults in Taiwan. Sci Rep 2020; 10: 3192 [PMID: 32081877 DOI: 10.1038/s41598-020-60209-w]
- 12 Bergantin LB. Hypertension, Diabetes and Neurodegenerative Diseases: Is there a Clinical Link through the Ca2+/cAMP Signalling Interaction? Curr Hypertens Rev 2019; 15: 32-39 [PMID: 30117399 DOI: 10.2174/1573402114666180817113242]
- Caricati-Neto A, García AG, Bergantin LB. Pharmacological implications of the Ca(2+)/cAMP signaling interaction: from 13 risk for antihypertensive therapy to potential beneficial for neurological and psychiatric disorders. Pharmacol Res Perspect 2015; 3: e00181 [PMID: 26516591 DOI: 10.1002/prp2.181]
- Bergantin LB. The Interactions among Hypertension, Cancer, and COVID-19: Perspective with Regard to Ca(2+)/cAMP 14 Signalling. Curr Cancer Drug Targets 2022; 22: 351-360 [PMID: 35168520 DOI: 10.2174/1568009622666220215143805]
- 15 Bergantin LB. Debating the "bidirectional link" between diabetes and depression through the Ca(2+)/cAMP signalling: Off-label effects of Ca(2+) channel blockers. Pharmacol Res 2019; 141: 298-302 [PMID: 30639385 DOI: 10.1016/j.phrs.2019.01.008]
- 16 Miranda-Ferreira R, de Pascual R, de Diego AM, Caricati-Neto A, Gandía L, Jurkiewicz A, García AG. Single-vesicle catecholamine release has greater quantal content and faster kinetics in chromaffin cells from hypertensive, as compared with normotensive, rats. J Pharmacol Exp Ther 2008; 324: 685-693 [PMID: 17962518 DOI: 10.1124/jpet.107.128819]
- 17 Rooney MR, Pankow JS, Sibley SD, Selvin E, Reis JP, Michos ED, Lutsey PL. Serum calcium and incident type 2



diabetes: the Atherosclerosis Risk in Communities (ARIC) study. Am J Clin Nutr 2016; 104: 1023-1029 [PMID: 27510541 DOI: 10.3945/ajcn.115.130021]

- 18 Begum N, Leitner W, Reusch JE, Sussman KE, Draznin B. GLUT-4 phosphorylation and its intrinsic activity. Mechanism of Ca(2+)-induced inhibition of insulin-stimulated glucose transport. J Biol Chem 1993; 268: 3352-3356 [PMID: 8381427]
- Goldberg ML, Bohannon NV, Brooks RM, Tsalikian E, Lorenzi M, Forsham PH. Plasma cyclic nucleotide levels in 19 juvenile-onset diabetes. Diabetes 1977; 26: 936-943 [PMID: 198321 DOI: 10.2337/diab.26.10.936]
- Mazeaud MM, Le Quan Sang KH, Devynck MA. Platelet cyclic AMP in essential hypertension. J Hypertens 1989; 7: 501-20 506 [PMID: 2550542 DOI: 10.1097/00004872-198906000-00010]
- Bergantin LB. COVID-19 and Obesity: Reevaluating the Relationship Through Ca(2+)/cAMP Signalling. Curr Drug Res 21 Rev 2022; 14: 157-159 [PMID: 36281829 DOI: 10.2174/1573399818666220429100819]
- 22 Bergantin LB. Mental Disorders and Poor COVID-19 Prognosis: Reevaluating the Relationship through Ca(2+)/cAMP Signalling. Curr Top Med Chem 2022; 22: 1215-1218 [PMID: 35524666 DOI: 10.2174/1568026622666220504163811]





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