

Risk Factors Leading To the Severe Exacerbation of COVID-19 Include Male, Elderly, Obesity and Diabetes

Bando H^{ab*}

^aTokushima University / Medical Research, Tokushima, Japan

^bIntegrative Medicine Japan (IMJ), Shikoku Island division, director, Tokushima, Japan

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***Corresponding author:** Bando H, Tokushima University, Medical Research, Nakashowa 1-61, Tokushima 770-0943 Japan; TEL: +81-90-3187-2485; E-mail: pianomed@bronze.ocn.ne.jp DOI: <https://doi.org/10.36266/IJED/120>

Abstract

The risk factors for coronavirus disease (COVID-19) were investigated. Latest cohort study for 28,095 cases was conducted in United States. It included obesity 61.9% and type 2 diabetes mellitus (T2D) 15.8%. They showed 4 influential factors, which are male, age of 65 < years, obesity and T2D. The risk level was counted for digit number of 0-4. As a result, hazard ratio (HR) risk for level 0-4 was 1.0, 3.1, 6.5, 16.2, 19.0 for hospitalization, and 1.0, 3.4, 15.2, 38.0, 55.8 for critical care, respectively. This suggested the important lifestyle continuation for the perspective of Hinohara-ism by Dr. Shigeaki Hinohara.

Keywords: Coronavirus Disease (COVID-19); Risk Factors; Type 2 Diabetes Mellitus (T2D); Hinohara-ism; Dapagliflozin in Respiratory Failure in Patients with COVID-19 (DARE-19)

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Commentary

Pandemic of coronavirus disease (COVID-19) has been social and medical problem worldwide [1]. The influence has been crucial to all countries and districts [2]. Latest data have been shown from John Hopkins University every day [3]. As to the actual ratio of exacerbating the severe situation on COVID-19, statistical investigation was reported [4].

Among patients of COVID-19 with various complication and background, some are recovered, and others are aggravated to the severely ill [5]. What may bring such difference for clinical course? Several influencing factors may include higher age, underlying diseases such as diabetes, obesity, hypertension, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), atherosclerotic cardiovascular disease (ASCVD) [6]. Further, smoking, sedentary life, inactivity and others exist [7]. Some reports are present for the risk of severe COVID-19, which were not sufficient due to overlapping risk factors [8]. Then, it may be a useful method to analyze several risks and severity of COVID-19 by using electronic medical record (EHR) database to large degree.

The severity of risk factors on COVID-19 were reported. The investigation was to conduct a cohort study using 28,095 cases of COVID-19 from database during January to November, 2020 [9]. The analyzed factors included age, sex, race, and complications of type 2 diabetes (T2D), oral hypoglycemic agent (OHA), body mass index (BMI). Furthermore, treatment

situation such as hospitalization and/or critical care as main outcomes of COVID-19 for 30 days. As a result, 4 risk factor scores were selected for male, age of 65 < years, obesity and T2D. Among the cases, obesity was 61.9%, and T2D was 15.8%. The study clarified how many risk factors were present for each case as 0,1,2,3 and 4. Regarding hospitalization risk, hazard ratio (HR) was 1.0, 3.1, 6.5, 16.2, 19.0, respectively. Furthermore, regarding critical care risk, HR was 1.0, 3.4, 15.2, 38.0, 55.8, respectively. Consequently, the risk of aggravation can be reduced by controlling obesity, diabetes and avoiding these risks. As current cases were patients with United States, successive study will be planned for patients with Asian people including Japanese. It will bring clarifying the relationship between risk factors and pathophysiological situation [9].

Current results suggested elevated risk for exacerbation of COVID-19 by advancing age, male, comorbidities of obesity and diabetes. Concerning these factors, several reports have been presented for the elevated risk for aggravation of COVID-19. Among some factors, age has been the strongest risk factor for severe COVID-19 [10]. According to the analyses of Center for Disease Control (CDC) of US, COVID-19 risk of age can increase with advancing age. When the standard level is set at 1.0 for 18-29 age group, 85-year group showed 13- and 630- fold elevation in hospitalization and mortality, respectively [11]. Detail statistics are found from the Ministry of Health and Labor, Welfare, Japan [12] in the following. For age group, exacerbating ratio showed remarkable result: age 30-39 (30s) sets the standard level as 1.0, 4.0 in 40s, 10 in 50s, 25

in 60s, 47 in 70s and more than 70 in 80s<, respectively. In contrast, younger generation showed as follows: 0.5, 0.2, 0.3 in the age of <9, 10-19, 20-29 years, respectively. These data were reported by research group of Prof. Nishiura, Kyoto University [4,13].

As to the difference of male and female, many reports are found for remarkable risk for male cases. For example, 82% of cases were men who was admitted to intensive care units (ICUs) [14]. Further, obesity was reported to increase the risk of COVID-19, ICU admission, and death by 1.46-, 2.13-, and 1.74-fold, respectively, suggesting that obesity may affect lung function and immune function [15]. Elevated waist-to-hip ratio can raise infection risk, and elevated BMI can raise the risk of COVID-19 hospitalization [16]. From previous reports, combined diabetes and metabolic syndrome have elevated infection risk remarkably [17,18]. Regarding more than 9.5% of HbA1c, young adults with COVID-19 were remarkably associated with mortality. Then, diabetes can elevate the risk to severe ill and death irrespective of the age [17]. Furthermore, to control the values of HbA1c and HDL could decrease the infection risk [16]. Thus, glucose and lipid metabolism can be related with hospitalization risk in obesity.

Some reports were observed for the beneficial effect of metformin and sodium-glucose cotransporter-2 inhibitor (SGLT2i). For the prognostic analysis of diabetic patients with COVID-19, metformin decreased the death incidence until 28 days after hospitalization [19]. Furthermore, metformin could reduce the mortality in the United States, France and China [20]. The association of SGLT2i and COVID-19 were investigated in the series of Dapagliflozin in Respiratory Failure in Patients with COVID-19 (DARE-19) study [21]. It has been a randomized, double-blind, placebo-controlled trial for hospitalized COVID-19 patients, which is focused at least one cardio metabolic risk factor. In the latest report of 2021, the result did not show statistic significant risk reduction in the factors of organ dysfunction and death ($p=0.17$), clinical improvement ($p=0.14$) for 1250 diabetic cases with COVID-19 divided by SGLT2i group and control group [22]. General application of SGLT2i to COVID-19 is suggested to decrease the cardiovascular risk. From pathophysiological point of view, SGLT2i has anti-inflammatory property, which may reduce the development of cytokine storms [23]. SGLT2i was reported to decrease diabetes-related cardiovascular disorder and its mortality risks for COVID-19 cases as well as its hypoglycemic efficacy [24].

In summary, this article described the topic of COVID-19, suggesting the importance of non-communicable disease (NCD) and lifestyle style-related disease. For COVID-19 prevention, daily successive control of our body and mind would be important, in which prominent Sir William Osler and Dr. Shigeaki Hinohara have enlightened the essence of the

perspectives, by Oslerism and Hinohara-ism [25]. This article will be hopefully useful for research development of COVID-19.

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