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Perspective

The recent new findings of periodontal systemic connection from Taiwan's National Health Insurance Research Database

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The National Health Insurance (NHI) program in Taiwan is a single-payer insurance system by government. In 2014, almost whole Taiwanese population was enrolled in this compulsory and universal health insurance program.¹ The disease identification is based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. The NHI claims data was edited into National Health Insurance Research Database (NHIRD) maintained by the National Health Research Institutes for public research purposes. NHIRD contains the de-identified secondary data of claims for reimbursement for routine health care services and medical benefit claim data from NHI program. With the standard clinical diagnosed criteria by ICD-9, the Bureau of NHI routinely samples patient charts randomly to cross-check the quality of claims from all medical institutions. Therefore, the possible bias from miscoding or misclassification would be minimized. This registry-based databank could accurately reflect the health conditions of general population in Taiwan. This nationwide population-based database can provide sufficient sample size, generalizability, and statistical power for medical and public health research, such as disease prevalence, health

service utilization, and association between exposure and health outcomes.^{2,3,4}

Periodontitis is an inflammatory disease that is initiated by the accumulation of bacteria biofilm and its products, with subsequent gingival bleeding, periodontal pocket formation, alveolar bone resorption, and even tooth loss. It is well-known that the certain bacterial species and their virulence factors are directly related to the susceptibility and the progression of periodontitis. Indigenous periodontal pathogens can trigger a series of host inflammatory–immunologic reactions. Clinical evidences have indicated that periodontitis could cause chronic systemic inflammatory diseases, such as chronic obstructive pulmonary disease, chronic kidney disease, rheumatoid arthritis, cognitive impairment, obesity, and metabolic syndrome.⁵

In addition to pervious well-established periodontal-systemic connections, the authors have further evaluated the possible periodontal-systemic connections by using Taiwan's NHIRD. We first reported that the patients with chronic periodontitis had higher risk for developing Alzheimer's disease during 10-year follow up period by the matched-cohort study design.⁶ This study indicates that periodontal inflammations could be linked with neurodegenerative disorders.

From the literature reviews, periodontitis and psoriatic diseases share the common risk factors and co-morbidities. With a cohort design, we first found that the incidence rate

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of periodontitis was higher in patients with psoriatic arthritis.⁷ The psoriatic arthritis was positive relation to the severity of periodontitis. Taken together, periodontitis is demonstrated to be associated with immune-mediated skin disease.

Oral cavity is recognized as the upper part of digestive system. The microorganisms in dental biofilm and saliva may act as a potential reservoir during chewing and swallowing into digestive tract. Our previous cohort study showed that patients with inflammatory bowel disease increased the chance of having periodontitis comparing without inflammatory bowel disease group.³ Moreover, we reported that periodontitis is a potential risk factor for subsequent pyogenic liver abscess.⁸ Dental prophylaxis within 1 year was correlated with a decreased risk of pyogenic liver abscess in patients with and without periodontitis. Taken together, these findings display the connection of inflammation between oral cavity and digestive system.

Polycystic ovary syndrome is a complex endocrine disorder among women. Polycystic ovary syndrome is characterized by menstrual irregularity, obesity, infertility, excessive amounts of androgenic hormones, and polycystic ovaries. Polycystic ovary syndrome is believed with gingival inflammation associated with hormone imbalance. To the best of our knowledge, we first found that the risk of polycystic ovary syndrome in female patients with chronic periodontitis exposure was higher than comparison group.⁹ Thus, the periodontal inflammation and endocrine-related gynecological diseases can not be disregard.

The relationship between periodontitis and neuropsychiatric disorders has recently attracted researchers' attention. Bipolar disorder is a psychiatric mood disorder and relevant to low-grade chronic inflammation in the peripheral nervous system and the brain. Recently, we first reported a higher risk of bipolar disorder in patients with chronic periodontitis exposure than those who never received a diagnosis of chronic periodontitis from NHIRD by cohort design.¹⁰ Therefore, the findings imply the potentially causal link of periodontitis to neuropsychiatric disorders.

Based on the aforementioned innovative findings, chronic inflammation can be regarded as an identical point between periodontitis among Alzheimer's disease, psoriatic arthritis, inflammatory bowel disease, pyogenic liver abscess, polycystic ovary syndrome, and bipolar disorder. The biological mechanisms by which periodontitis causes specific systemic organ inflammation can be presumed to consist of two possibilities. The upregulation of pro-inflammatory mediators may be activated by oral bacterial biofilms and their products via circulatory system to target organs. The other possibility might explain that periodontal bacteria and bacterial molecules might directly invade the target organs through the blood stream. Via either of two pathways, infiltration of periodontal bacteria/virulent factors into target organ could result in immune-inflammatory reaction. However, the actual cause-relation or bi-direction speculation still need further investigation.

From 2016, Health and Welfare Data Center was established as the data repository site that centralizes the NHIRD by using ICD-10 NHI claims data and linkable health care

databases for academic researches. In addition, researchers should only access NHIRD on site at the Data Science Center for further strengthening the protection of health care database. With the continuous expansion in the volume and amounts of data, Health and Welfare Data Center can provide the reliable resources for big data analysis. This could represent a powerful research engine to support clinical decisions, health care policy-making, and the real-world evidence-based medicine in Taiwan.

Taken together, the periodontal-systemic connection has the innovative findings with the advantage of comprehensive high quality NHIRD. After establishment of such a link, a broad spectrum of periodontitis associated with systemic diseases may be preventable by daily dealings for oral hygiene and regular oral check-up. Dentists should pay more attention to periodontitis patients with systemic diseases.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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