**Identification of the Risk Factors for Metformin-Related Vitamin B12 Deficiency**

**Introduction:**

Persons with diabetes often utilize different forms of medications with various effects due to associated symptoms. In particular, patients often use metformin in order to treat hyperglycemia due to its limited side effects (Kim et al. 1). Metformin functions by reducing the production of hepatic glucose and enhancing the use of peripheral glucose (Owhin et al. 2). ((Foretz et al., 2019)). The prevalence of DM worldwide has been found to increase over years and it is predicted to keep raising unless preventive measures taken (Saeedi et al., 2019; Sharma et al., 2016; Webber, 2021). According to American Diabetes Association (ADA), the global estimated prevalence of diabetes will increase significantly within 2000-2030 to reach 366 million (Wild, Roglic, Green, Sicree, 2004). Another report of the Centers for Disease Control and Prevention (CDC) of the US population states that the prevalence of diabetes for 2018 is 34,2 million people which represents 10,5% of the US population. Among this population, 7.3 million were undiagnosed (US Department of Health and Human Services, 2018). The International Diabetes Federation, IDF, report shows almost doubling the Saudi Arabia population with diagnosed diabetes from 2021 to 2045, 4.274.1 million people to reach 7.537.3 million by 2045.(*Saudi Arabia Diabetes Report 2000 — 2045*, n.d.) These reports also indicate that the treatment in question enhances insulin sensitivity and decreases the possibility of cardiac mortality in patients (Yakubu et al. 60). The benefits offered via metformin among diabetic patients contribute to positive health outcomes. Patients with diabetes often utilize different forms of medications, in particular metformin, in order to treat hyperglycemia due to its limited side effects. However, despite the widespread use of the respective treatment, studies have linked metformin to vitamin B12 deficiency (Damião *et al*., 2016; Chapman *et al*., 2016; Khan *et al*., 2020). The incidence of vitamin B12 deficiency in type 2 diabetes individuals using metformin was 17.5%. This risk may grow with extended metformin treatment and is impacted by the onset and duration of diabetes ((Almatrafi et al., 2022). Metformin alters actions required for the uptake of vitamin B12, leading to adverse outcomes such as compromised immunity, anemia, neuropathy, and cognitive incapacities (Kim *et al*., 2019; Tarry-Adkins *et al*., 2019; Ijäs et al., 2014, Sato *et al.*, 2013). (Vanita R Aroda). Accordingly, metformin causes the malabsorption of vitamin B12, leading to a sufficient risk of deficiency among patients with diabetes (Kim *et al*., 2019; Yakubu *et al*., 2019; Didangelos *et al*., 2021). A study found a significant frequency of Vitamin B12 deficiency in patients with T2DM on metformin, emphasizing the importance of frequent screening for blood Vitamin B12 in patients with T2DM taking metformin (Khan et al., 2021). In addition, studies show that long-term use of metformin results in extensive vitamin B12 deficiency, causing subsequent health problems for patients with diabetes (Tarry-Adkins *et al*., 2019; Yousef *at al.*, 2021). (Aroda, V)( (Hasan et al., 2019)). A study conducted in a tertiary care hospital in Pakistan, vitamin B12 deficiency was shown to have a substantial effect on metformin-treated patients. As a result, it is recommended to notice B12 insufficiency as a possible adverse effect of long-term metformin treatment. A periodic B12 test in such individuals, followed by vitamin B12 administration, is an effective and safe method of preventing the development or worsening of peripheral nerve damage and other clinical symptoms ((Baig et al., 2022)). A study support monitoring individuals with additional risk factors for vitamin B12 insufficiency, such as concurrent medicine usage with other vitamin B12 lowering drugs or clinical signs of deficiency, such as peripheral neuropathy ((Longo et al., 2019)). Based on clinical trials, vitamin B12 malabsorption due to metformin intake can be managed efficiently via supplementation. (Yang, W.) (Didangelos, T.). Studies have shown that supplementation with vitamin B12 in patients using metformin reverses symptoms stemming from deficiency (Tarry-Adkins et al., 2019). ((Owhin et al., 2019)). Despite this, researches examining the risk factors that relate to Vitamin B12 deficiency, and the use of metformin are inconclusive due to limited findings. Based on a study conducted on 2019, only 25% of the population in the study had their vitamin B12 level measured in the last five years. (Longo, S. L.). The regular measurement of vitamin B12 concentrations during long term metformin treatment should be strongly considered.( Jolien de Jager) (Kancherla et al., 2017)