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Prevalence and physician factors associated with Vitamin B12 prescriptions at King Khalid University Hospital

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ABSTRACT

Background: Recent studies suggested a high prevalence of Vitamin B12 prescriptions; most lack evidence of Vitamin B12 deficiency. This research aims to estimate the prevalence of Vitamin B12 prescription without laboratory evidence of deficiency at King Khalid University Hospital, assess the physician characteristics associated with such B12 prescribing, and compare between gender and sub-specialty. *Methods:* A retrospective cohort study perfumed at King Khalid University Hospital using health system administrative databases (E-sihi system). All patients who received at least one prescription of oral Vitamin B12 between January 1st, 2021 to August 31st, 2022 were included. *Results:* A total of 19920 oral Vitamin B12 were prescribed to 10980 patients by 947 physicians. Most physicians were male, 61%. 57% are specialists. 10417 (94.8%) patients received oral Vitamin B12 prescriptions without laboratory evidence of deficiency. Type of practice and physician gender was not significantly related to inappropriate prescriptions. Medicine and emergency department are most likely to prescribe inappropriately, whereas family medicine is more likely to prescribe appropriately. *Conclusion:* As much as 94.8% of vitamin B12 prescriptions were written despite a lack of laboratory evidence of a deficiency, suggesting that such widespread use is unnecessary. In addition, the highest prescription rates were related to medicine and the emergency departments, whereas the lowest rates were linked to family medicine. Therefore, we suggest campaigns be launched to draw physicians' attention to such practice and its consequences and encourage them to examine the available evidence about Vitamin B12.

Keywords: Vitamin B12; Oral; Inappropriate prescription; Vitamin B Complex

1. INTRODUCTION

Recent data has shown that inappropriate parenteral Vitamin B12 prescriptions are written at a high rate worldwide, with the vast majority of these prescriptions being written without laboratory proof of deficiency. As a result, the adverse effects increase, as well as the cost of health care (Silverstein et al., 2019). Vitamin B12 is an essential water-soluble vitamin that

plays a major role as a co-enzyme in DNA synthesis for neurological and hematological systems development and maturation (Kennedy, 2016; Green, 2017). The recommended daily intake varies by age, but it ranges between 0.4 mcg per day in neonate up to 2.4 mcg per day in adult male and female, with little increase during lactation and pregnancy. The primary source of vitamin B12, which has a higher bioavailability, is essentially from food of animal origin, especially eggs, meat, poultry, fish, and dairy products (Watanabe, 2007).

Multiple complications were linked to vitamin B12 deficiency, including megaloblastic anemia, thrombotic microangiopathy, Subacute combined degeneration of the spinal cord, dementia syndrome, and neuropsychiatric symptoms, especially in the elderly age group (Thomas, 1998; Lachner, 2012; Green & Datta, 2017; Tran & Tran, 2018). However, vitamin B12 deficiency not exclusively affects adult or elderly people but also causes major morbidity to the fetus antenatally during pregnancy, including anencephaly, neural tube defect, and neonatal development (Schorah et al., 1980; Kirke et al., 1993; Molloy et al., 2008). Vitamin B12 deficiency was between 12% in the Framingham study and 34.9% in another. However, these two studies focus on the elderly age group mainly, which may give an inaccurate estimation of the prevalence (Lindenbaum et al., 1994; Wong et al., 2015). Vitamin B12 deficiency is defined as a B12 serum level below 200 pg/ml (below 148 pmol/L) (Matchar et al., 1994; Antony, 2005). However, our body can store one to five mg of vitamin B12, therefore it takes time to deplete in the serum (Hunt, 2014; Langan & Goodbred, 2017). On contrary, a high level of vitamin B12 was associated with a higher risk of cancer among participants in a study conducted in United Kingdom (Arendt et al., 2019). Moreover, a retrospective review study found that inflammatory condition, hematologic malignancy, hematopoietic, myelodysplastic syndrome, liver disease, and liver cancer tend to be increased among patients with elevated level of vitamin B12 (Jammal et al., 2013).

Inappropriate prescription is one of the most common errors in health care facilities and seems to be a significant problem internationally, involving the use of medication where the adverse drug events (ADEs) are greater than the clinical benefit, especially when effective and safer alternatives are available (Farhat et al., 2021). Inappropriate prescription includes the overuse or underuse of clinically indicated medicines (i.e., prescribing omission) and the use of a drug that increases the risk of interaction between another drug or disease (Farhat et al., 2021). Inappropriate prescription has been associated with hospitalization, intensive care unit admission, preventable side effects, and death in older patients (Boeker et al., 2015; di Giorgio et al., 2016; Hudhra et al., 2016; Desnoyer et al., 2017; Farhat et al., 2021) with the increase in the older population in coming years. Prescription quality and safety are becoming a major public health problem (Farhat et al., 2016; WHO, 2017).

Based on a study done in Canada Ontarians, about inappropriate B12 prescription and physician factors are related to it. The result shows that in the year before being prescribed parenteral vitamin B12, 63.7% of the prescriptions were inappropriate. 25% of them do not have biochemical evidence of B12 deficiency and 38% did not have a documented B12 level. These inappropriate prescriptions annual costs are estimated 46 million CAD. Despite being only a vitamin, vitamin b12 can cause several adverse reactions. Anaphylactic reactions can even occur in patients with sensitivity Aside from that, allergic reactions such as itching, erythema, and wheals can occur. There has been a reported case of B12 toxicity induced by high doses of cyanocobalamin in a young Hispanic woman with severe pernicious anemia treated with frequent 1 mg daily of Vitamin B12.The patient received a 12 mg of Vitamin B12, she experienced multiple symptoms. Some are dermatological, like flushing or acne, and others are related to the cardiovascular and central nervous system. After stopping the drug, she improved two weeks later. Neither a sequelae nor a complication occurred (Morales-Gutierrez et al., 2020). Other common adverse effects include Shortness of breath, swelling, rapid weight gain, Hypokalemia, Fever, Itching or rash (Vasavada & Sanghavi, 2022).

Inappropriate Vitamin B12 prescription is a concern in globally, particularly in private practice. To our knowledge, there are no studies in our region that estimate the Vitamin B12 prescriptions and explain the physician factors that are related to their practices. This research aims to estimate the prevalence of oral Vitamin B12 prescription (without laboratory evidence of deficiency) at King Khalid University Hospital, assess and characterize the physician factors associated with B12 prescribing, and compare between gender, sub-specialty, and type of practice.

2. METHODS

This is a retrospective cohort study perfumed at King Khalid University Hospital (KKUH) using health system administrative databases (E-sihi system). All patients who received at least one prescription of oral Vitamin B12 from January 1st, 2021 to August 31st, 2022 were included. Inclusion criteria include KKUH patients who received oral Vitamin B12. Exclusion criteria include non-KKUH patients and intramuscular injection of Vitamin B12. The data collection form consisted of patient's age and gender. In addition, it included doctor's age, gender and specialties. The Route of administration of Vitamin B12 and Laboratory result of serum b12 level within one year of prescription were documented.

The study was approved by the Institutional Review Board of Health Sciences Colleges Research on Human Subjects, King Saud University College of Medicine (IRB Approval of Research Project No. E-22-7018). Informed consent was obtained from all participants. All collected data were treated with strict confidentiality.

Data were analyzed using SPSS statistical software (version 24.0). The mean and standard deviation were used to describe the continuous measured variables, frequency, and percentages for the categorically measured factors. The Univariate Non-parametric chi-squared test was employed to analyze the correlation between appropriateness and physician's characteristics univariately. The physician's characteristics contain physician gender, subspeciality, and type of practice. The multivariate logistics regression was used to examine the relationship between appropriateness and physician's characteristics in multivariate way. The odds ratio is used for explaining the appropriateness differences between categories based on physician gender, subspeciality, and type of practice. P-value and confidence interval were included in this research to present the significance of appropriateness differences between each physician category.

3. RESULTS

A total of 19920 oral Vitamin B12 were prescribed to 10980 patients by 947 physicians. The average patient's age is 54 years, with a 15.8 standard deviation. By categorizing patient's age, most of the patients who received oral Vitamin B12 are 41 – 60 Years (39.44%). Patients under 20 years are the least receiving vitamin B12 (1.93%) compared to other categories. Patients who received oral Vitamin B12 were dominated by females (57.97%) (Table 1).

Table 1 Patient characteristics

Item	**No**	**%**
Age:		
Mean (SD)	54.6 (15.8)	
Median (IQR)	57 (22)	
Range	0-103	
Age Categorized:		
0 - 20 Years	212	1.93
21 - 40 Years	2074	18.89
41 - 60 Years	4331	39.44
61 - 80 Years	3949	35.97
81+ Years	414	3.77
Sex:		
Female	6365	57.97
Male	4615	42.03

Regarding physician characteristics (Table 2), most physicians were male (61.35%). Based on the physician's type of practice, most of them (57.34%) are specialists. Physicians with medicine subspecialty were dominant (27.24%) in this study in prescribing oral Vitamin B12 compared to other subspecialties. (Figure 1) 10417(94.8%) patients received oral Vitamin B12 prescriptionwithout laboratory evidence of deficiency, 1448 patients whose Vitamin B12 level was more than 148 pmol/L, and the rest, 8969 patients, had no documented Vitamin B12 level within 12 months before prescription (figure 2).

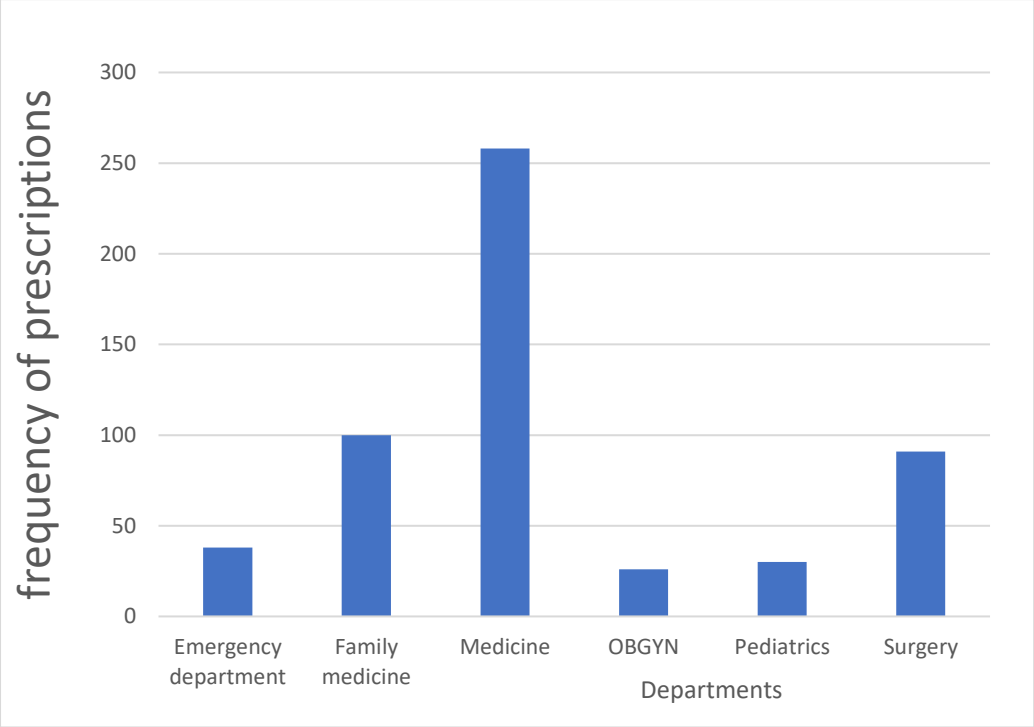

Figure 1 Frequency distribution of Vitamin B12 prescriptions by clinical departments

Table 2 Physician Characteristics

Item	No	%
Sex:		
Female	366	38.65
Male	581	61.35
Type of practice:		
Resident	404	42.66
Specialist	543	57.34
Subspeciality:		
Emergency department	38	4.01
Family medicine	100	10.56
Medicine	258	27.24
OBGYN	26	2.75
Pediatrics	30	3.17
Surgery	91	9.61

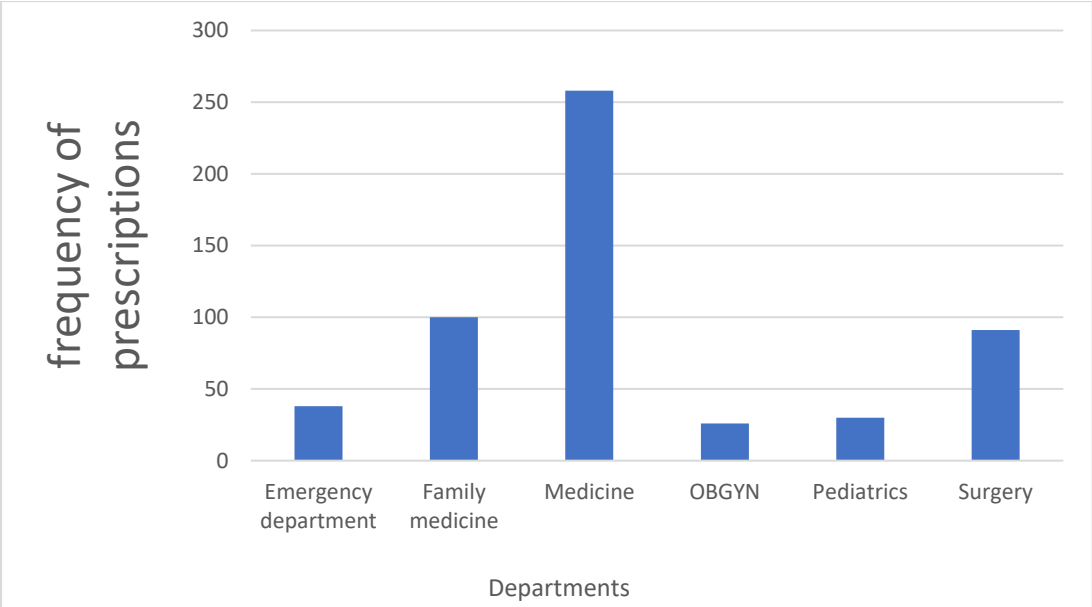

Figure 2 Frequency distribution of Vitamin B12 prescriptions by clinical departments

Physician gender was not found to be significantly related to the rate of prescription. Physician subspecialties that were more likely to prescribe Vitamin B12 were Medicine (OR, 1.417; 95% CI, 0.851–1.557) and emergency department (OR, 1.521; 95% CI, 1.001–2.311). Family medicine subspecialists were less likely to prescribe Vitamin B12 (OR, 0.683; 95% CI, 0.544–0.856). Type of practice was not significantly related to the rate of prescription (Table 3).

Table 3 Physician characteristics associated with Vitamin B12 prescription without laboratory evidence of deficiency

Independent Variable	Univariate		Multivariate	
	OR (95% CI)	P-Value	OR (95% CI)	P-Value
Physician's Gender (Female vs Male)	0.912 (0.769,1.081)	0.743	1.059 (0.886,1.265)	0.530
Subspeciality:				
Medicine	1.397 (1.029, 1.897)	0.032	1.417 (0.851, 1.557)	0.027
Family Medicine	0.679 (0.542, 0.852)	0.000	0.683 (0.544, 0.856)	0.001
Surgery	1.351 (0.872, 2.092)	0.178	1.390 (0.889, 2.172)	0.148
Emergency department	1.477 (0.982, 2.220)	0.061	1.521 (1.001, 2.311)	0.049
OBGYN	0.473 (0.199, 1.121)	0.089	0.471 (0.199, 1.117)	0.087
Pediatrics	1.003 (0.239, 4.201)	0.997	1.019 (0.243, 4.275)	0.979
Type of Practice (Specialist vs Resident)	0.883 (0.711, 1.097)	0.262	-	-

4. DISCUSSION

Majority of oral Vitamin B12 were prescribed without B12 level proceeded by 12 months, 43.65% of them had no B12 level in the past 3 years. This could be due to patients demand. Possible reasons why Vitamin B12 is over prescribed could be due to high prevalence of Type 2 Diabetes Mellitus (T2DM) in Saudi Arabia. Estimated prevalence was 18.2% in Eastern province, and 31.6% in Riyadh (Alotaibi et al., 2017). As recommended by American Diabetes Association and the European Association for the Study of

Diabetes, Metformin is used as a first line treatment for T2DM (35). A study conducted in Riyadh addressed that 9.4% of Metformin users were Vitamin B12 deficient (Alharbi et al., 2018).

Regarding physician factors, there are dissimilar findings compared to Canadian study (Silverstein et al., 2021). Our study shows no significant relationship between physician gender and the rate of prescription. In addition, we found that type of practice did not play a significant role in Vitamin B12 appropriateness. This may be due to low emphasis on Vitamin B12 during medical school or residency training period. In terms of subspecialties, medicine and emergency department were more likely to prescribe Vitamin B12 than other specialties.

Another study conducted in Canada showed that family physicians are less aware of the evidence supporting B12 supplementation than other specialties (Graham et al., 2007). However, our observations indicate that family physicians are more likely than other providers to accurately prescribe oral Vitamin B12. A higher standard of care is likely to be provided by these physicians since they are more likely to adhere to clinical guidelines.

The limitations of this study include that we could not address the patient's status in terms of income, diet, or comorbidities (malabsorption, Diabetes Mellitus, dementia, chronic Vitamin B12 deficiency). Further studies should assess the prevalence of intramuscular Vitamin B12 injections as it costs more money compared to oral forms.

5. CONCLUSION

In conclusion, the Vitamin B12 prescriptions without laboratory evidence of B12 deficiency were high, reaching 94.8%. This practice needs further review to avoid potentially inappropriate medications. In addition, Physicians working in medicine and emergency departments prescribed more Vitamin B12 than family physicians. Therefore, we recommend an in-depth study to determine why the prescription is high, and there are discipline differences. Such research may draw the attention of health professionals to unnecessary prescriptions and may lower the adverse effects and cost of Vitamin B12.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data materials availability

Data that support the findings of this research are embedded within the manuscript

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