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REFERRAL TRENDS OF VITAMIN B_{12} TESTING TO A COMMUNITY MEDICAL PRACTICE LABORATORY IN JORDAN

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ABSTRACT

A Vitamin B_{12} deficiency is a prevalent health problem worldwide. Screening populations for this deficiency is neither feasible nor recommended. Available strategies advocate testing when signs and symptoms are suggestive of vitamin B_{12} deficiency. The aim of this investigation was to determine the referral trend of Vitamin B_{12} by health service providers to a community medical practice laboratory in Jordan. From January to December of 2014 a total of 208 patients were referred to the Diagnostic Medical Laboratory for vitamin B_{12} testing and all were included in this study. The percentage of patients referred to the same laboratory for Vitamin B_{12} testing constituted 2.45 % of the total number of patients received. The majority of the referred patients were female (63%) and the highest proportion of patients in both genders was stratified in the 21-40 years age group (46%), whereas the lowest referral was in patients below 20 years of age (3.7%). Internists, general practitioners and Gynecologist (in a descending order) accounted for 79.4 % of all referrals. Memory impairment and numbness were the most clinical manifestations which perhaps resulted in most of the referrals. Only 26 % of the referred subjects were with normal vitamin B_{12} level whereas 36 % and 38 % were identified as on the borderline or with frank vitamin B_{12} deficiency, respectively. It is concluded that health service providers in the private medical practice of Jordan are rationale in requesting Vitamin B_{12} test for their patients.

INTRODUCTION

Vitamin B_{12} (cobalamin) is necessary for hematopoiesis and normal neuronal function. Vitamin B_{12} is bound to protein in food and is available for absorption after it has been cleaved from protein by the hydrochloric acid produced by the gastric mucosa (O'Leary and Samman, 2010). Vitamin B_{12} enters the circulation about 3–4 hours after intake and remains in blood bound to transcobalamins (Carmel, 2003). Measurement of vitamin B_{12} in serum is the most common assay used to evaluate vitamin B_{12} levels. Lack of vitamin B_{12} may be caused by insufficient intake of this micronutrient or by its mal-absorption. However, insufficient intake of vitamin B_{12} is seen in people with poor nutrition, elderly as well as vegetarians (Allen, 2009). Deficiency due to low intake of vitamin B_{12} is not considered as common in industrialized parts of the world (Hunt *et al*, 2014), but has been referred to as a major factor for the prevalence of B_{12} deficiency in third world communities (Pawlak *et al*, 2013).

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Studies conducted in the kingdom of Jordan have demonstrated that the prevalence of this condition varies between 16 to 50% (Barghouti *et al*., 2009; Abu-Samak *et al*., 2008; El- Qudah *et al*, 2013). In a more comprehensive survey conducted in the country which included 5640 subject, it was found that almost 1/3 of the Jordanian population have vitamin B_{12} deficiency with no gender difference (El-khateeb *et al*, 2014). Literature regarding various aspects of vitamin B_{12} deficiency among Jordanians is available including the relationship between this deficiency and body mass, presence of *H. pylori* as well as other diseases (El-Qudah *et al*, 2013; Al-Fararjeh *et al*, 2011; Ayesh *et al*, 2013).

The British Columbia Medical Association (Anon 1, 2013) recommend that patients with symptoms or signs of vitamin B_{12} deficiency anaemia (macrocytic anaemia or macrocytosis) and patients with suspected neuropsychiatric abnormalities should be tested for vitamin B_{12} deficiency. Other conditions where testing is also recommended include the followings: the elderly; long-term vegans, people on drugs that interfere with vitamin absorption and patients with inflammatory bowel

disease (Hunt *et al*, 2014). A part from the vitamin B_{12} testing report published by the Australian government- department of health (Anon 2, 2014) and the early work of Hølleland *et al* (1999), literature is scant, if at all available which reports on the pattern of vitamin B_{12} test utilization by health care providers. International guidelines related to testing vitamin B_{12} vary widely in their recommendations. Some recommend vitamin B_{12} testing as a screening tool in commonly encountered illnesses; others suggest the restriction of testing to patients who have already undergone pre-test investigations, such as full blood examinations (Anon 3, 2012). Medical and health care services in Jordan are provided by two independent sectors. The public sector which is funded by the government and the private sector. Little is known about the strategies followed for vitamin B_{12} testing as a diagnostic tool in both of the public and private medical practice. This communication reports on the experience of a private medical laboratory in relation to the referral pattern of vitamin B_{12} by community practice health care providers.

MATERIALS AND METHODS

All patients referred to the Medical Diagnostic Laboratory to have their blood tested for vitamin B_{12} from the first of January/ 2014 to the end of December of the same year were included in this investigation. Blood samples were drawn by trained technicians, placed in a plain tube, centrifuged and serum collected. Patients were asked why "according to their judgment" they were referred to the laboratory for vitamin B_{12} testing and answers were recorded. A written consent was obtained from each patient that his or her results will appear in a scientific publication with their names being anonymous. Vitamin B_{12} testing was carried out in Sultan Medical Laboratory in Amman- Jordan within less than 24 hours of collection. Method of determination relied on Chemiluminescent emission which is then measured by a photomultiplier using COBAS 600 (Roche Diagnostics- USA). Vitamin B_{12} deficiency was defined at a concentration below <200 pg/ml, whereas 350 pg/ml was taken as a value which indicated a borderline deficiency (Khateeb *et al*, 2014). Statistical analysis was carried out to determine the significance of difference in vitamin B_{12} readings between various age groups of patients in relation to their genders using SPSS package. Calculations used were mean, standard deviation and student *t* test. A p value < 0.05 was considered of statistical significance.

RESULTS

This investigation was carried out in the Diagnostic Medical Laboratory located in the central commercial area of the city of Zarqa- Jordan. This laboratory receives approximately 8500 patients per annum. Throughout the year 2014, a total of 208 patients were referred to this laboratory for vitamin B_{12} test and 23 similar tests were performed in the same laboratory upon patient's requests. Only results of referred subjects are included in this investigation. Table 1 demonstrates that 63% of the referred patients were female and the highest proportion of patients in both genders was stratified in the 21- 40 years age group (46%), whereas the lowest referral was in patients below 20 years of age (3.7%).

Table 1. Number and percentages of referred patients for vitamin B_{12} testing according to gender and age group

Gender	Age Group in Years (%)				Total
	<20	21- 40	41-60	> 60	
Female	5	62	47	16	131
Male	3	34	23	18	77
Total	8	96	70	34	208

It was of interest to establish the pattern of B_{12} referral according to the specialty of the attending physician and this is illustrated in Table 2. It is clearly evident from this table that internists and general practitioners were the most to request this test, whereas pediatricians were the least in their requests. It is worth mentioning that the number of tests ordered along with vitamin B_{12} varied between specialties. In most cases internists requested more than 3 laboratory tests including complete blood count while for other specialties the number of tests was a lot lower. In many occasions B_{12} testing was ordered alone or in conjunction with complete blood count.

Table 2. Number and percentages of patients tested in 2014 for vitamin B12 according to the specialty of referring physician

Referring Physician	Number of referred patients	Percent
Internist	65	31.2
General practitioner	51	24.5
Gynecology and obstetrics	42	20.2
Neurosurgeons	17	8.2
Chest specialists	13	6.3
Cardiologists	9	4.3
E N T specialists	7	3.4
Pediatricians	4	1.9

The majority of patients complained of memory impairment followed by numbness in the limbs. The intake of drugs (metformin) was given as the highest reason for referral in the age group of > 60 years. Kidney disease was never quoted as a complaint but cardiac and gastrointestinal problems were mentioned as a cause of referral by 6 and 13 patients, respectively. Table 3 contains all of the answers given by the referred patients and here it should be noted that many patients gave one or more answers.

Table 3. Questioner results of patients to why vitamin test was requested for them

Reason for referral	Number of patients
Memory impairment	115
Numbness	64
Pregnancy	28
Use of metformin	22
Anemia	17
Gastrointestinal problems	13
Cardiac problems	6
Kidney disease	0

The cutoff value used in this study to establish frank vitamin B_{12} deficiency was a reading below 200 pg/ ml whereas; levels less than 350 pg/ ml were taken as borderline deficiency. It is clear from table 4 that only 26 of the referred patients were with normal vitamin B12 whereas, patients with frank B_{12} deficiency mounted to 38 % with females being almost double

the males placed in this category. Patients on the borderline constituted 36% of the patients included in the investigation.

Table 4. Vitamin B12 levels in patients included in this investigation

Gender	Vitamin B 12 concentration pg/ ml						
	< 200 N (%)	Mean± SD	200- 350 N (%)	Mean± SD	> 350 N (%)	Mean± SD	Total
Female	51(25)	124± 39	42(20)	270± 38	38(18)	468± 116	131(63)
Male	27 (13)	137± 36	33(16)	274± 41	17(8)	493± 125	77(37)
Total	78 (38)	128± 38	75(36)	\ 272± 40	55(26)	476± 102	208(100)

DISCUSSION

Guidelines to establish the rationale behind conducting vitamin B_{12} testing services were addressed by few international associations. The British Columbia Medical Association and Ministry of Health- Canada (Anon, 2012), concluded that routine screening for vitamin B_{12} deficiency is not recommended. The Australian study on strategies for vitamin B12 testing indicated that 71 % of the tests are requested by general practitioners and 14 % by internal medicine consultants followed by general surgeons (specialist – subspecialties). In Jordan, guide lines for requesting Vitamin B_{12} test are not available and studies to highlight the referral pattern of the test to medical laboratories is lacking. This communication is an attempt to address this subject as observed in a community practice medical laboratory. The Diagnostic Medical Laboratory in which the investigation was carried out receives 8500 patients per annum, in 2014 only 2.45% of patients were referred for Vitamin B_{12} testing. This percentage demonstrates that this test constitutes a tiny proportion of the overall work load carried out in the laboratory.

This finding is in contrast to the 5000 test carried out annually in an Italian hospital of 600 beds laboratory (Ferraro, *et al* 2013). These authors indicated that vitamin B12 testing in their laboratory constitutes an economic burden on the hospital budget. It is known that primary care accounts for approximately 50% of laboratory activity. Surveys suggest that tests including Vitamin B_{12} testing are often requested inappropriately and unnecessarily. Although, data to compare the annually referred number of Vitamin B_{12} tests to our laboratory with other local laboratories or those from other countries is not available, results presented herein suggest that the requests received were reasonable in number. Data shown in Table 1 demonstrate that 63% of the referred patients were female and the highest proportion (46%) of patients in both genders was stratified in the 21- 40 years age group, while the lowest referral (3.7%) was in patients below 20 years of age. Female prevalence of patients in this investigation is consistent with those included in other published work from Jordan (Barghouti *et al*, 2009; Qutob *et al*,2011), but in clinical sense it does not mean a lot as it might be by pure incident that the number of referred females was higher than males.

This argument is substantiated by the fact that this presentation is not concerned with the prevalence of vitamin B_{12} deficiency in a population. The same interpretation applies to patients stratified in various age groups. It was interesting to note that the majority of patients were referred by internal medicine consultants, general practitioners, and then followed by gynecologists (31.2%, 24.5% and 20. 2%, respectively). It is evident that referral pattern of vitamin B_{12} for testing by health care providers is in relative agreement with the report published from Australia (Anon, 2014). The low number of referral by other medical specialties can be attributed to several factors among which the following are important: first, the number of practicing physicians of these specialties in the city where this work was conducted is low and second, patients may have not complained of symptoms that warrant vitamin B_{12} testing. Clinical manifestations from which patients complained is illustrated in Table 3. It is well known that vitamin B_{12} deficiency is associated with a wide range of clinical manifestations including memory impairment and numbness; these two were the most prevalent among the patients included in this investigation. Al-Fararjeh *et al* (2011) found statistically significant relationship between the mean value of vitamin B_{12} levels and psychological as well as biological activity of patients with reduced vitamin B_{12}. The same authors found that memory loss was the most prevalent manifestation; in agreement with what is reported herein. In regard to pregnancy, 13.5 % of the subjects studied indicated that the reason of referral was pregnancy. This is justified as it is documented that pregnancy causes a lowering of serum vitamin B_{12} (Baker, *et al* 2002; Cherry, *et al* 2002). In normal pregnancy total serum vitamin B_{12} levels fall by 30% by the third trimester.

It was of uppermost importance during the course of this investigation to establish if health service providers are rationale in their referral of patients for vitamin B_{12} testing and the answer to this query is clearly given in Table 4. This table demonstrates that only 26 % of referred subjects were with normal vitamin B_{12} readings whereas 36 % and 38 % were identified on the borderline or with frank vitamin B_{12} deficiency, respectively. In a population based study, El-Khateeb *et al* (2014) found that 32.2 % of Jordanians have vitamin B_{12} deficiency with no gender difference. They also found that 13.4 % of the subjects studied had vitamin B_{12} in the borderline of deficiency while 56 % of the population included was with normal level of vitamin B_{12}. The difference between the values obtained here and those of El- Khateeb *et al* (2014) are most probably due to the fact that our subjects were definitely high risk individuals who were referred to the laboratory as part of medical advice seeking process or perhaps treatment from specific complaints, while the other authors have assessed vitamin B_{12} in a national sample of subjects with no criteria for selection.

Conclusion

In conclusion it must be emphasized that although no strategies are available in Jordan to guide health care providers to how

and when to order vitamin B_{12} testing, such a test is ordered by physicians in a very rational manner.

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