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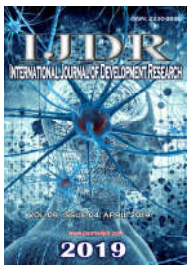

REVIEW ARTICLE OPEN ACCESS

ANALYSIS OF VITAMIN A SERUM PROFILE IN PATIENTS ATTENDED AT A TERTIARY HEALTHCARE TEACHING HOSPITAL LABORATORY

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ABSTRACT

Aim: Characterize the Vitamin A serum profile, by means of lab exams done in Brazilian patients, from 2012 to 2016, in a Tertiary Teaching-Hospital laboratory, correlating it with gender, age range, and health care systems types - Public or Private, correlating it with gender, age range and types of health care systems. **Material and Method:** Retrospective, descriptive work using 234 Vitamin A serum dosage reports performed in routine consultations. Data collected: gender, age, whether by Public or Private health care system. **Results:** Female patients done 181 (77%) Vitamin A exams and male 53 (33%).Private health care system done 222 (95%) exams, and Public system: 12 (5%) (p = 0.4762).Male patients' age, in the Public system, varied from 56 to 69 years (M = 62.5 years; SD ± 5.86) and in Private, it varied from 2 to 81 years (M = 43.4 years; SD ± 18.39) (p = 0.0312).Female patients' age in Public system varied from 19 to 60 years (M = 40.87 years; SD ± 12.99) and for the Private, it varied from 7 to 84 years (M = 44.23 years; SD ± 15.11) (p = 0.6388).The age ranges with the highest requests were adult (44.9%) and young adult (42.3%) (p = 0.9341). **Conclusion:** There has been a higher prevalence in the request of Vitamin A exams for female patients in the Private system. Levels of Vitamin A Deficiency were found in both genders, in adult and young adult age ranges, exclusively in the Private system.

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INTRODUCTION

One in every three people in the world is affected by vitamin and micronutrient deficiencies, especially Vitamin A, Vitamin D, iron or iodine. Clinical manifestation of these deficiencies such as mother's or child's death, decreased immune response, blindness, mental retardation and anemia, affect more than half a billion of the world population. The Nourishment and Nutrition National Policy, approved in 1999 by the Health Ministry in accordance with the National Policy of Basic Attention of our country, has as the fundamental axis the promotion of the human right fulfillment of nourishment, nutritional and nourishment safety and the nutrition of the whole our population, besides the prevention and control of nutritional disorders and of diseases associated with nourishment and nutrition (BHM 2013, 2017; Schmitz, 2007). The individuals, mainly the elderly, as well as children, pregnant women and nursing mothers, are particularly prone to protein-energy, vitamin and mineral malnutrition. The main causes of malnutrition in the elderly are diminished food intake, altered nutrients needs, bad absorption, bacterial flora abnormal presence, interaction with drugs, alcoholism, increased catabolism, diminished nutrients reserve and lower vitamin conversion into their active form (BSP, 2012; Knapik *et al*., 2017; Wolf *et al*., 2017). Vitamin A is a micronutrient essential for the maintenance of the normal physiological functions of the organism. In its broad spectrum of performance, only partially known, stand out the functions connected to the visual cycle, to the integrity of biological membranes, to epithelial maintenance and differentiation, as well as the glycoprotein formation, to mucus production and the resistance against infections, mediated by the modulating action of the immune response. In general terms, one can claim that Vitamin A increases humoral immunity, the concentration of the active antibodies, the number of splenic cells formers of antibodies and local immunity, besides stimulating phagocytosis and the activity of the polymorphonuclear neutrophils and macrophages (Blaner *et al*., 2016; Bouamama *et al*., 2017; Saeed *et al*., 2017). Vitamin A deficiency is responsible for a series of health problems. The chronic Vitamin A deficiency is still one of the most resistant nutritional problems in developing countries, despite the fact that symptoms are not difficult to identify, that the etiology is well known, the treatment is available, and in most of the situations, there are available and affordable sources of

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Vitamin A, either from carotenoids or retinol (Wirth *et al*., 2017). Hypovitaminosis A may lead to blindness, such lack affects millions of children in the world. Even in the mild deficiency cases, it can affect the immune system, what lowers the resistance to diarrhea and measles (Schmitz, 2007). Thus, the present study aims to characterize the Vitamin A serum profile, based on appraisals of laboratory exams carried out in patients from 2012 to 2016, in the laboratory of clinical analysis of a Teaching-Hospital correlating it with gender, age range, types of health care systems - Private System or the Public System, in order to know the local serum reality of this micronutrient.

MATERIALS AND METHODS

Retrospective, descriptive, whose data were obtained by revision of Vitamin A serum dosage exam reports carried out in patients, both male and female, from the age of 2, requested in routine consultations, in the clinical analysis laboratory in a tertiary Teaching-Hospital, from 2012 to 2016. The tertiary Teaching-Hospital data bank system, for being electronic via, allowed direct filtering of criteria to be analyzed, excluding automatically, serum dosages of pregnant women, hospitalized patients, patients suffering from chronic diseases, transplanted patients, institutionalized or making use of vitamin supplementation. The following data were collected: gender, age at the laboratory collecting time, exams carried out by the Public or Private Health Care System. In order to get a better demographic characterization age range was classified according to recommended growing phases: infancy (2-10 years), adolescence (11-17 years), young adult (18-40 years), adult (41-65 years) and elderly (> 65 years) (WHO, 2013). In the tertiary Teaching-Hospital clinical analyses laboratory, Vitamin A is identified by the HPLC method (High Performance Liquid Chromatography), with the following Reference Values: Insufficiency < 0,2 mg/L; Sufficiency 0,2 - 0,7 mg/L; Increase > 0,7 mg/L According to the Regulatory Norms for Research involving human beings, Resolution Number 466/12 of the Health Ministry the present study was approved by the Ethics Committee of the Medical School (Report #2.131.310/2017), and for being a laboratory registry-scan study the informed consent was not applied.

Statistical Analysis: The results were previously submitted to descriptive statistics to determine normality. The Mann-Whitney test was used for independent samples with non-normal distribution and the Student T test was used for samples with normal distribution. When applicable, Chi-square (χ^2) or Fisher exact tests were used for comparison between variables. Significance level was established in 5%. The results were expressed in percentages (%), mean (M) and standard deviation (SD). The statistical tests were performed using the GraphPad InStat program, 3.0 version, GraphPad Software Inc, San Diego - California, USA, www.graphpad.com.

RESULTS

In a five-year period (2012 to 2016) 264 exams were requested for assessment of Vitamin A serum levels, being 234 collected and carried out in a tertiary Teaching-Hospital laboratory. The remaining 30 exams were not collected, being therefore, excluded from the analysis. From the 234 exams, 181 (77%) were done in female patients and 53 (23%) in male patients and, in relation to both health care systems, 222 exams (95%) were carried out by Private and 12 (5%) by Public systems. The difference between the number of patients from both genders and the type of health care systems was not significant (Fisher Exact Test; p=0.476). Figure 1 shows the distribution of Vitamin A reference serum levels (Deficiency, Sufficiency, Increase), obtained after analyses of the exams carried out by 234 patients, according to age range. The age ranges with the highest serum dosage number were adult (44.9%) and young adult (42.3%), and also, only in these were found serum levels of Vitamin A Deficiency, totaling 5.5%. Despite these differences, there has not been statistical significance (χ^2=3.00; p=0.934). (Figure 1).

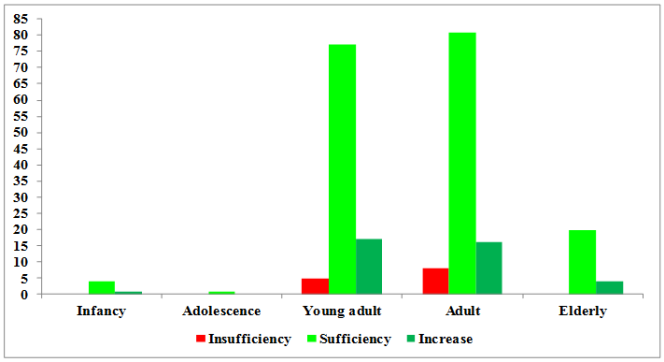

Figure 1. Distribution of the number of Vitamin A dosages, according to serum level by patients' age range

Thus, the number (N) distribution of male and female patients, from Public and Private system, in relation to age range, is demonstrated, respectively, on Tables 1 and 2. There has been a higher prevalence in male patients from Private system (92.5%) in all age ranges, in relation to patients from Public system, but this difference has not been significant (χ^2=5.45; p=0.246), probably because the low Case Study in Public system. The young adult and adult age range were the most prevalent in the Private system, in about 77% of cases, indicating, therefore, a higher number of dosages requested for these phases, followed by the elderly one in 15.25% (Table 1).

Table 1. Distribution, in percentage, of the number of male patients from Public and Private Health Care System, according to age range

Age Range/ Health Care System	Male Public N=4 (7.5%)		Male Private N=49 (92.5%)		Total N=53	
	N	%	N	%	N	%
Infancy	0	0.0	3	6.5	3	6.5
Adolescence	0	0.0	1	1.5	1	1.5
Young adult	0	0.0	19	36.0	19	36.0
Adult	2	3.75	20	37.0	22	40.75
Elderly	2	3.75	6	11.5	8	15.25

N- Number of patients

Table 2. Distribution, in percentage, of the number of female patients from Public and Private Health Care System, according to age range

Age Range/ Health Care System	Female Public N=8 (4.5%)		Female Private N=173 (95.5%)		Total N=181	
	N	%	N	%	N	%
Infancy	0	0.0	2	1.25	2	1.25
Adolescence	0	0.0	0	0.0	0	0.0
Young adult	3	1.75	77	42.5	80	44.25
Adult	5	2.75	78	43.0	83	45.75
Elderly	0	0	16	8.75	16	8.75

N- number of patients

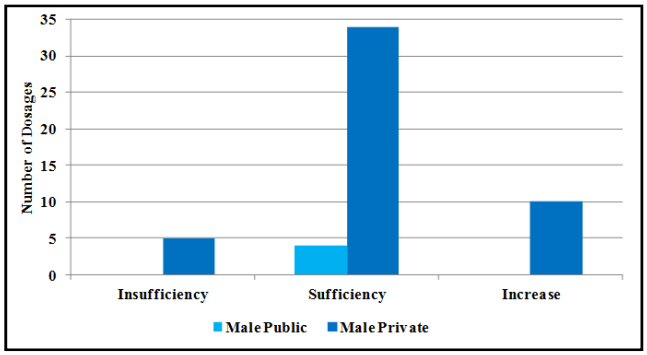

Figure 2. Distribution of the number of Vitamin A dosages, according to serum level, between male patients from Public and Private Health Care Systems

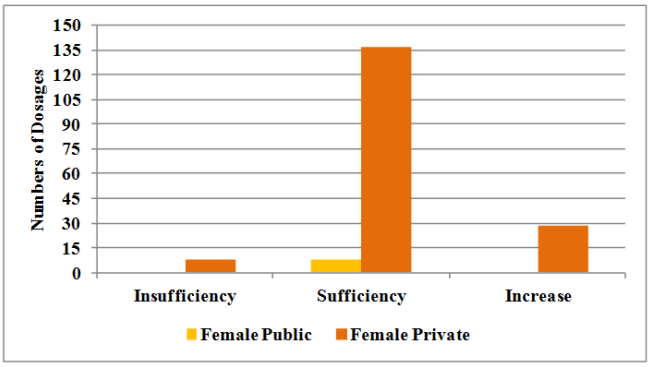

Figure 3. Distribution of the number of Vitamin A dosage numbers, according to serum level of female patients from Public and Private Health Care Systems

The following results were carried out in order to achieve a better comparative analysis of gender by health care systems, age range and serum levels. Age for male patients from Public system varied from 56 to 69 years (M=62.5 years; SD± 5.86; CI95%=53.45-71.54), and for the Private system it varied from 2 to 81 years (M=43.4 years; SD±18.39; CI95%=38.16-48.73), being this difference statistically significant (p=0.003). The Private System showed higher prevalence in female patients (95.5%), in all age ranges, when compared to Public system, being this difference significant (χ^2=21.372; p=0.0003). As in male patients, young adult and adult age ranges were the most prevalent in the Private system, in 90% of cases, demonstrating, consequently, a higher number of dosages requested for these ranges, followed by the elderly's, but only in about 9% (Table 2). Age for female patients from Public system varied from 19 to 60 years (M=40.87 years; SD±12.99; CI95%=30.0-51.74) and for the ones from the Private system, it varied from 7 to 84 years (M=44.23 years; SD±15.11; CI95%=41.98-46.86), not showing statistically significant difference between variables (p=0.638).

Figures 2 and 3 show, respectively, the distribution of the dosage numbers, by serum levels, in male and female patients in the Public and Private health care systems. Among the 53 male patients 49 (92.5%) have Private system and 4 (7.5%) are assisted by Public system (Table 1). Concerning serum levels, 38 (71.75%) presented Sufficiency levels, being 34 (64.25%) from Private system and 4 (7.5%) from Public system. Patients from Public system did not present Deficiency of Vitamin A, whereas 5 (9.0%) from the Private system did. Ten (19.25%) patients from Private system are with vitamin Increase. Despite the higher prevalence of Sufficiency serum levels in the Private system, the difference between vitamin levels and health care systems has not been statistically significant (χ^2=1.70; p=0.425) (Figure 2). The serum levels values for male patients from Public system varied from 0.55 to 0.65 mg/L (M=0.60 mg/mL; SD±0.043, CI95%=0.53-0.67) and for those from the Private system, varied from 0.08 to 1.41 mg/L (M=0.56 mg/mL; SD±0.22; CI95%=0.50-0.62), not being this difference statically significant (p=0.479). In relation to age range, in the Public system there has not been any request for exams in the infancy, adolescence or young adult range, as shown in Table 1. The only four exams (7.5%) were 2 (3.75%) in the adult range and also 2 (3.75%) in the elderly, showing Sufficiency serum levels in both (Figure 2). In the Private system, the distribution of exam numbers by serum levels in relation to age range, in order of prevalence, was: Sufficiency- 15 (28.5%) young adult range exams, 12 (23%) adult; 4 (7.5%) elderly, 2 (3.75%) infancy and 1 (1.5%) adolescence range; Increase- 4 (7.5%) adult range exams, 3 (6.5%) young adult, 2 (3.75%) elderly and 1 (1.5%) infancy range; Deficiency- 4 (7,5%) adult range exams and 1 (1.5%) young adult range (Figure 2).

From the 181 female patients, 173 (95.5%) have a Private system and 8 (4.5%) are assisted by Public system (Table 2). Regarding serum levels, 145 (79.75%) presented Sufficiency levels, being 137 (72.25%) from Private system and 8 (4.5%) from Public system. Patients from Public system did not present Vitamin A Deficiency, whereas eight (4.5%) from the Private system did. Twenty eight (15.75%) patients from Private system have vitamin Increase. Despite higher prevalence of Sufficiency serum levels in the Private system, the difference between vitamin levels and health care systems has not been statistically significant (χ^2=2.07; p=0.353) (Figure 3). The serum levels values for female patients from Public system varied from 0.30 to 0.70 mg/L (M=0.46 mg/L, SD±0.12; IC95%=0.35-0.55) and for those from the Private system, they varied from 0.20 to 0.97 mg/L (M=0.53mg/L; SD±0.16; IC95%=0.50-0.55), not being this difference statistically significant (p=0.223). Concerning age range, in the Public system there has not been any requests for exams in infancy, adolescence and elderly ranges. The only eight exams (4.5%) were 5 (2.7%) adult and 3 (1.75%) young adult, presenting Sufficiency serum levels in both (Figure 3). In the Private system except for adolescence there has not had any request for Vitamin A dosage, the distribution of the number of exams by serum levels, by prevalence order, was as follows: Sufficiency- 62 (34%) exams in the adult range;, 59 (32.5%) young adult, 14 (8%) elderly and 2 (1.25%) infancy; Increase- 14 (8%) exams in young adult, 12 (6.5%) adult and 2 (1.25%) elderly; Deficiency- 4 (2.25%) young adult and 4 (2.25%) adult (Figure 3).

DISCUSSION

Vitamin A is an important nutrient for the immune system integrity, visual accuracy, growth and development. Due to the fact that it is not synthetized by the organism, people from all age ranges can be affected by its deficiency (Chea & Milstein, 2018). Based on the analysis of two hundred and thirty four reports of laboratory exams, the present study presents the Vitamin A serum profile of both male and female patients, who had them done in the laboratory of the Institution by the Private and the Public Care Health Systems, in routine consultations, in a five-year period (2012-2016). In the literature, there are several studies about hypovitaminosis A (Mayo-Wilson *et al.*, 2011; Song *et al.*, 2017; Malik *et al.*,

2018), but in our country, besides outdated references, there is still little information about this condition, being most part of the studies presenting general nutritional facts, in population groups from certain regions or institutions such as day care, nursery schools, old age homes, etc, and also, from some age groups (Carvalho *et al*., 2015; Felizola *et al*., 2015; Pedraza *et al*., 2016; Sangali *et al*., 2016; Deminice *et al*., 2018**).** For the profile analysis of serum levels in a certain population in routine outpatient care consultations, as done in the present study, there are no recent data in the literature for comparisons. Among the medical reports analyzed, the highest prevalence obtained, of exam requirements to assess the serum levels of Vitamin A, was for female gender (77%) and carried out by the Private system (95%). Gender prevalence maybe explained by a greater concern of women about going to routine and preventive consultations in relation to men, since about 40% of them do not seek for attendance in basic attention to health. This fact may be due to man´s social role in society, in which masculinity is subordinated to values or attributes such as strength, aggressiveness and competitiveness which were socially built, contributing to characterize the male characteristic of morbimortality (Oliveira *et al*., 2015).

Regarding age range, in the Public system there has not been any exam request for male gender in infancy, adolescence and young adult. In the Private system, only about 7% of the exams were for infancy and adolescence. For female gender, likewise, in the Public system has there been no request for infancy, adolescence and elderly ranges. In the Private system, only 1% of the exams were in the infancy phase and there has not been any request in the adolescence range for female gender. With respect to the serum levels for both genders, the prevalence varied from 72% to 80% for Sufficiency levels, with higher prevalence in the Private system. Serum levels for Increase varied from 16% to 19%, exclusively in the Private system. The explanation for these increased numbers is that the Vitamin A stays stocked in the tissues for long periods, by adequate or steady intake, of food sources of the vitamin or by the rapid conversion, in Vitamin A, of the ingested carotenoids most recently, causing thus, the detection of serum levels above the reference values (Blaner *et al*., 2016). Deficiency serum levels varied, between genders, from 4% to 9%, exclusively in the Private system, probably due to the higher number of exam requests in this type of health care system. Patients from Public system did not present Deficiency of Vitamin A, certainly because of the few exam requests by this health care system, in the study period. Vitamin A low chronic intake of diets is the main underlying cause of Deficiency, especially in periods nutritiously demanding of life, as in the early childhood and old age, besides pregnancy (Chea & Milstein, 2018). In Brazil, deficiency of Vitamin A, is still a nutritional problem in many locations in the North, Northeast and Southeast regions. Despite the lack of information, there are reports that from 16% to 55% of children presented Insufficiency or Deficiency Vitamin A dosage, characterizing endemic lack (BHM 2013). In the present study, the prevalence has been found, in approximately, 6% of deficiency serum levels, in patients in routine consultation. A high rate when compared to reported data in such needy localities in the three Brazilian regions analyzed (BHM 2013). Preschool is the most affected group and the one under the highest risk for hypovitaminosis A, due to their fast growth and development, demanding a higher contribution of vitamin and other nutrients. The justification for this deficiency in this pediatric age range is associated with inadequate dieting, such as short time of breastfeeding or breastfeeding deficient in Vitamin A, produced by mothers who have hypovitaminosis A; use of whole cow´s milk; early introduction of industrialized food rich in lipids, sugar and salt and complementary feeding deficient in fruits and vegetables rich in beta-carotene and foods of animal origin. Moreover, children are more susceptible to diarrhea pictures and respiratory diseases, depleting even more their stock of Vitamin A. The disease leads to anorexia and malabsorption, decreasing ingestion and use of the nutrients (Konstantyner *et al*., 2014). Elderly individuals have a higher risk of presenting a deficient nutritional state of several micronutrients due to socioeconomic, psychosocial and dental factors, prolonged use medication and higher prevalence of chronic diseases which may cause loss of appetite or even anorexia (Chen *et al*., 2017). It demonstrates the importance of investigating the micronutrients deficiency in age ranges in both extremes of life in infancy and in the elderly, in order to supply subsidies for the most adequate and effective therapeutic approach, what has not been verified in the present study. Both age ranges, including adolescence were the ones that did not receive any request to investigate Vitamin A or, when they did, they were non-representative.

Several times, when the clinical signals and symptoms became more evident, the vitamin deficiency had already been installed. Therefore, health professionals must be aware of this condition and include Vitamin A dosage in the routine of health basic attention, as recommended. Such a fact has not been evidenced in the present study, because in six years, there has only been, in average, requests of only 47 exams/year, and even then, evidencing Deficiency serum levels. Besides, there must be planning and organization of preventive strategies and of nutrition education through encouragement, both to patients, in routine consultation, and to population in general, of the intake of foods rich in carotene, and, also, those which contain pre-formed Vitamin A in order to maintain adequate levels of this micronutrients.

Conclusion

The serum profile analysis of Vitamin A in patients, in routine consultations, allows the conclusion that has been higher prevalence of requests for exams for the female gender and by the Private health care system. Deficiency levels have been found in both genders, in adult and young adult age ranges, exclusively in the Private system, but were more prevalent in female gender. The prevalence of Vitamin serum levels of Deficiency and Insufficiency in individuals, in routine consultations, allows drawing attention in order to reevaluate the need of requesting Vitamin A dosages, in these groups, as control and prevention measures in order to avoid the consequences resulting from inadequate concentrations of Vitamin A.

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