Medical Research Archives

ESMED
European Society of Medicine

OPEN ACCESS

Published: June 30, 2023

**Citation:** Momčilović B, 2023. Sex Dimorphism of Calcium and Magnesium Metabolism, Medical Research Archives, [online] 11(6). https://doi.org/10.18103/mra.v11i6.3939



DOI
https://doi.org/10.18103/mra.v11i6.3939

ISSN: 2375-1924

RESEARCH ARTICLE

# Sex Dimorphism of Calcium and Magnesium Metabolism

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**ABSTRACT**

Background. There is a need for assessing personalized nutritional status of the bio elements magnesium (Mg) and calcium (Ca).

Objective. We studied the Mg and Ca nutritional status by analyzing their concentrations frequency distribution in the long-term biological indicator tissue of hair.

Design. Hair Mg and Ca were analyzed in 1073 apparently healthy white adult Caucasians of both sexes [734 women (♀) and 339 men (♂)] with the ICP MS. The concentrate frequency distribution data were log transformed and the nutritional status assessed with the Median Derivatives Bioassay.

Results. The hair median values ($\mu g \cdot g^{-1}$) were Women (♀) Mg 254 and Men (♂) Mg 137.2 whereas W (♀) Ca median was 721.4 and M (♂) Ca 492.0, respectively. Adequate nutritional status range limits arranged themselves along the linear part of the sigmoid saturation curve. These linear adequate window range limits were for women magnesium W (♀) Mg 29.7–270.6 and for men M (♂) Mg 20.5–90.2. The adequate range limits for calcium were W (♀) Ca 487.7–4456.8 and M (♂) Ca 26.1–816.4. The bone seeking bio elements Ca, Mg, and Sr showed the same increasing affinity for women hair deposition, whereas the major cellular electrolytes of sodium and potassium were almost imperceptibly higher in men than women.

Conclusions. Women hair incorporates Mg and Ca at about 2.5 times higher rate than men hair. The hair Median Derivatives Bioassay is a convenient painless way to assess and monitor the personalized dietary nutritional status of Mg and Ca in women and men.

**Keywords:** Magnesium; Calcium, Hair, Sex, Nutritional Status, Personalized Dietary Requirements, Physiological bio element entanglement

## Introduction

Hair makes an attractive biological indicator tissue for assessing the bio element nutritional status because they tend to irreversibly incorporate in hair pile[1]. The term bio element is used here as a common denominator name for major elements or electrolytes, trace bio elements and ultra-trace bio elements[2]. However, the great hopes for massive using of noninvasively collected hair for bio element analysis in clinical practice and epidemiological studies[3,4] faded when the analysis of the hair replicate samples yielded an excessive dispersion of the supposedly identical hair replicates samples[5]. It was assumed that the observed variability is related to the inaccuracies of chemical analysis of hair samples until Dinh and Wong[6] showed that what was considered to be the replicate of the hair sample was in fact a non-homogenous random mixture of hair piles in their various stages of hair developmental cycle. In short, the treads of the hair sample collected from even the same head are not to be considered the identical replicates. Indeed, if we divide some hair sample in more subsamples, these subsamples can be not considered to be identical replicates of the entire sample set, Thus, the difference in the analytical results doesn't matter because the hair traits of the same sample are not to be considered the replicates.

Morović et al[7] in their summary article reported how a log transformed hair bio element frequency distribution data yields the dose response sigmoid saturation curve when subjected to the median derivatives bioassay. The aim of this article is to demonstrate how the linear segment of the hair bio element sigmoid saturation curve may be subtly graded to assess the personalized nutritional status of magnesium (Mg) and calcium (Ca). In addition, an attempt was made to compare the simultaneous behavior of the adequate concentrations of the physiologically entangled bio element pairs of sodium and potassium (Na·K) with that of magnesium and calcium pair (Mg·Ca) in women and men. Similarly, the sex dependent difference between the triplet of osteotrophic (bone seeking) bio elements of calcium, magnesium, and strontium (Ca·Mg·Sr) was compared between women and men.

## Subjects and Methods

This prospective, observational, cross- sectional, and exploratory epidemiological study was approved by the Ethical Committee of the Institute for Research and Development of the Sustainable Eco Systems (IRES), Zagreb, Croatia (8). Every subject gave his/her written consent to participate in the study and filled out a short questionnaire on his/her health status and medical history (data not shown)[9]. They all used only standard hair shampooing.

Hair magnesium and calcium were analyzed in a random sample of 1073 apparently healthy white Caucasian adults (339 men, 734 women. The median age of women and men was 47 and 50 years, respectively. Our population came mostly from the capital city of Zagreb, Croatia by the people who were interested in their bio element health status: All of them consumed home prepared mid-European diet; and none of them had claimed medical health problems.

Hair Mg and Ca were analyzed with the inductively coupled plasma mass spectrometry (ICP-MS, Elan 9000, Perkin Elmer, Canada) at the Center for Biotic Medicine (CBM), Moscow, Russia as presented in full detail previously[10]. CBM is the ISO Europe certified commercial laboratory that analyze bio elements in different biological matrices in health and disease. The CBM is distinguished member of the External Quality Assessment of the UK Surrey scientific group for the quality control of trace element analysis. Hair Mg and Ca analyses were performed following the International Atomic Energy Agency recommendations[11] and other validated analytical methods and procedures[12].

The detection limits for hair Mg and Ca were 4.3 ppm for Mg and 0.3 ppm for Ca. All chemicals were of *pro analysis* grade (Khimmed Sintez, Moscow, Russia).

To scrutinize the respective hair magnesium and calcium concentration frequency distribution, we used the Median Derivative Bioassay[10] of the log transformed data to fit the sigmoid logistic regression function[13] for men and women separately: $A2 + (A1 - A2)/[1+(x/x_0)^p]$

Where A1 is the initial value (lower horizontal asymptote), A2 is the final value (upper horizontal asymptote), $x_0$ is the center (point of inflection) is the median (M0) detected), p is power (the parameter that affects the slope of the area about the inflection point). The OriginPro 8.0 data analysis graphic software (OriginLab Corp., OriginPro Version 8.0., Northampton, MA) and IBM SPSS Statistics for Windows, version 20 (IBM Corp., Armonk, N.Y., USA) was used for this analysis.

The deposition of a Mg and Ca below the linear segment range of the sigmoid saturation curve indicates a low (deficient) hair uptake of Mg and Ca;. When their concentration is within the linear segment range it indicates safe and adequate hair Mg and Ca uptake, and when Mg

and Ca concentrations are above the linear segment range of the sigmoid power curve, that denotes excessive level of their hair uptake[13]. We consider that the linear segment range of the sigmoid saturation curve may be subdivided by the 30:60:10 ratio. The initial 30% represent the low adequate or subclinical deficiency, the next 60% of that adequate linear segment is the true adequate range, and the upper (top) 10% of the linear part is an over abundant or high adequate region.

**Results**

To correct for the skewedness of the collected data, we separately log transformed men and women hair magnesium and calcium concentration data. By this act, the collected data get expressed as a standard bell-shaped Gaussian frequency distribution. Hair magnesium data frequency distribution for both men and women are shown in Fig.1 Top, whereas the data for calcium frequency distribution are shown in Fig.1.Bottom). Hair calcium concentration was higher than that of magnesium in both men and women. However, both the median hair calcium and magnesium concentration were more than two times higher in women than men. When the Gaussian hair bio element data distribution was transformed to the sigmoid saturation curve, the sex difference in the tilt and range of magnesium and calcium adequate linear segment became evident.

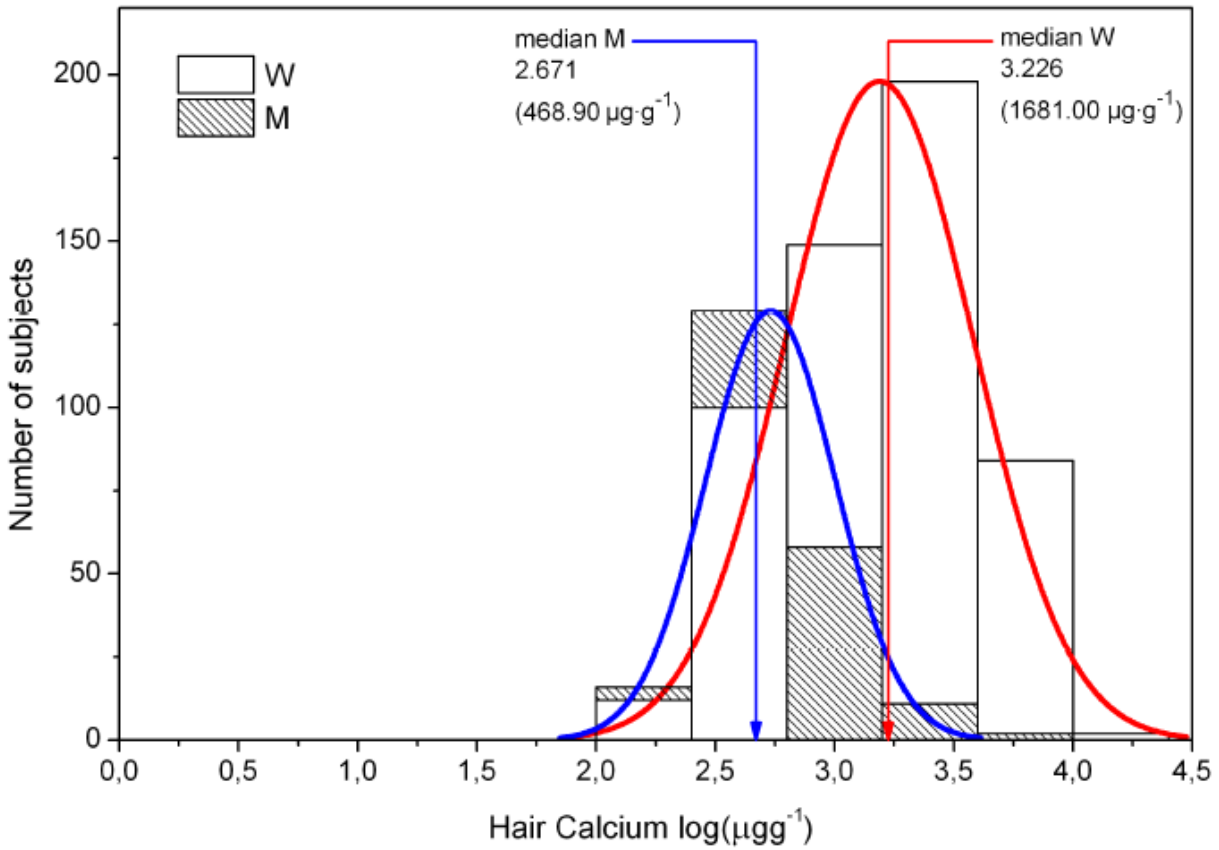


**Figure 1. Top** Hair Calcium frequency distribution

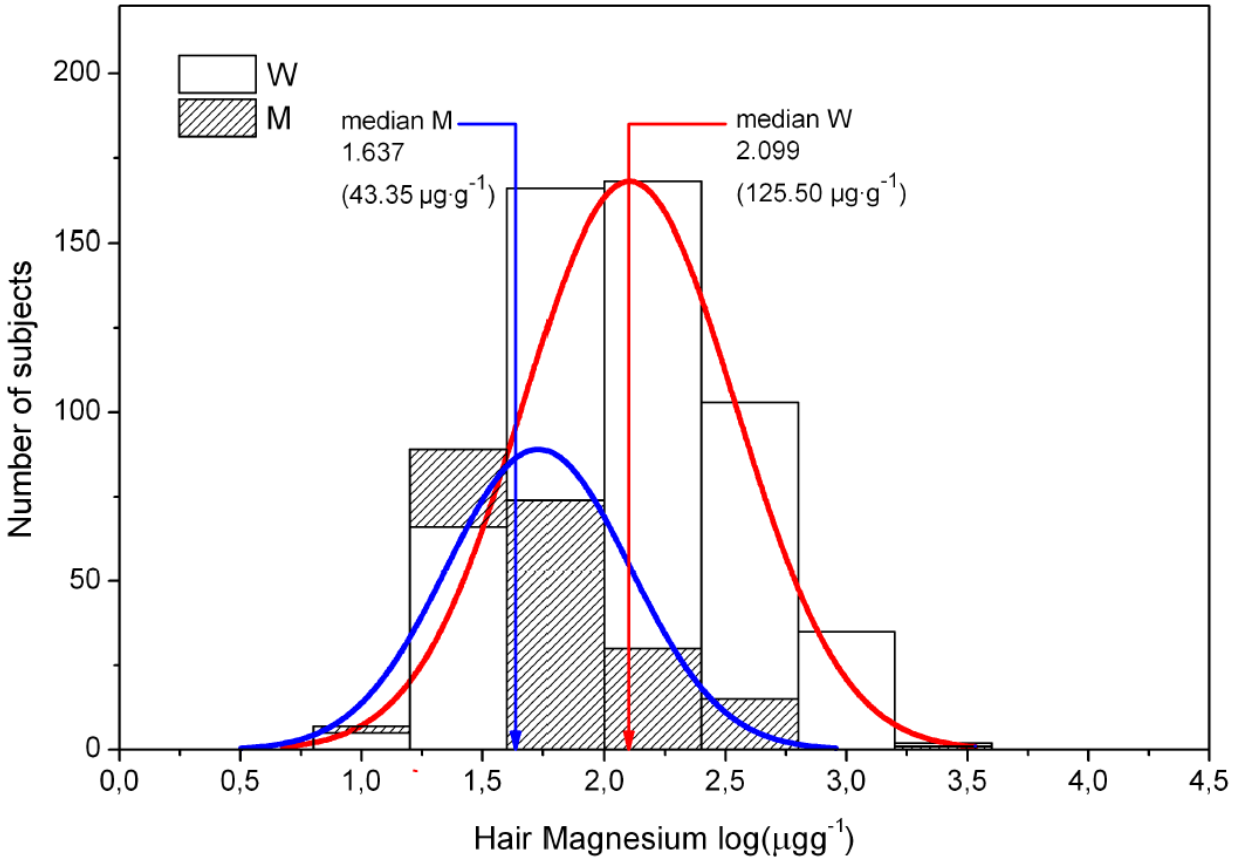


**Figure 1. Bottom** Hair Magnessium freque ncy distribution

The hair magnesium Median (M) concentration was (µg·g$^{-1}$) 47.1 for men and 137.2 for women (Fig.2.Top), whereas calcium median concentration was 1721.4 in women and 492.0 in men (Fig.2.Bottom). The adequate Mg nutritional status, based on the presented linear segment of the sigmoid saturation curve was 29.7 - 270.6. for women and 20.5 – 90.2 for men. At the same time, the adequate Ca nutritional status range was 487.7 - 4476.8 for women and 261.1 – 616.4 for men

The sigmoid saturation curves magnesium and calcium started to get linear at W ♀·d3 and M ♂·D3. Thereafter the difference between the tilts of the linear segment of slopes grow more rapidly in women than man all the way up until the end of the linear upward trend at W♀·u3 and M ♂·U3. The comparative women hair calcium and magnesium ranges and median concentrations were longer and higher than that in men. Also, the comparative median magnesium to calcium ratio (Mg/Ca) was 0.0997 for M ♂·and 0.0796 for W ♀, respectively, i.e. women Mg/Ca Median ratio was about 20%lower in women than men.

**Table 1.** Median Derivatives Bioassay*

| Median (MD µg·g$^{-1}$) Range P = 1.000 | |
|---|---|
| Downward Median Branch (D) | Upward Median Branch (U) |
| D1 P/2 – 0.500 | U1 P + P/2 = 1.500 |
| D2 P/4 = 0.250 | U2 P + P/4 = 1.750 |
| D3 P/8 = 0.125 | U3 P + P/8 = 1.875 |
| D4 P/16 = 0.064 | U4 P + P/16 - 1.969 |
| D5 P/32 = 0.032 | U5 P + P/32 = 2.001 |
| D6 P/64 = 0.016 | U6 P + P/64 = 2.017 |

* Cantor's set

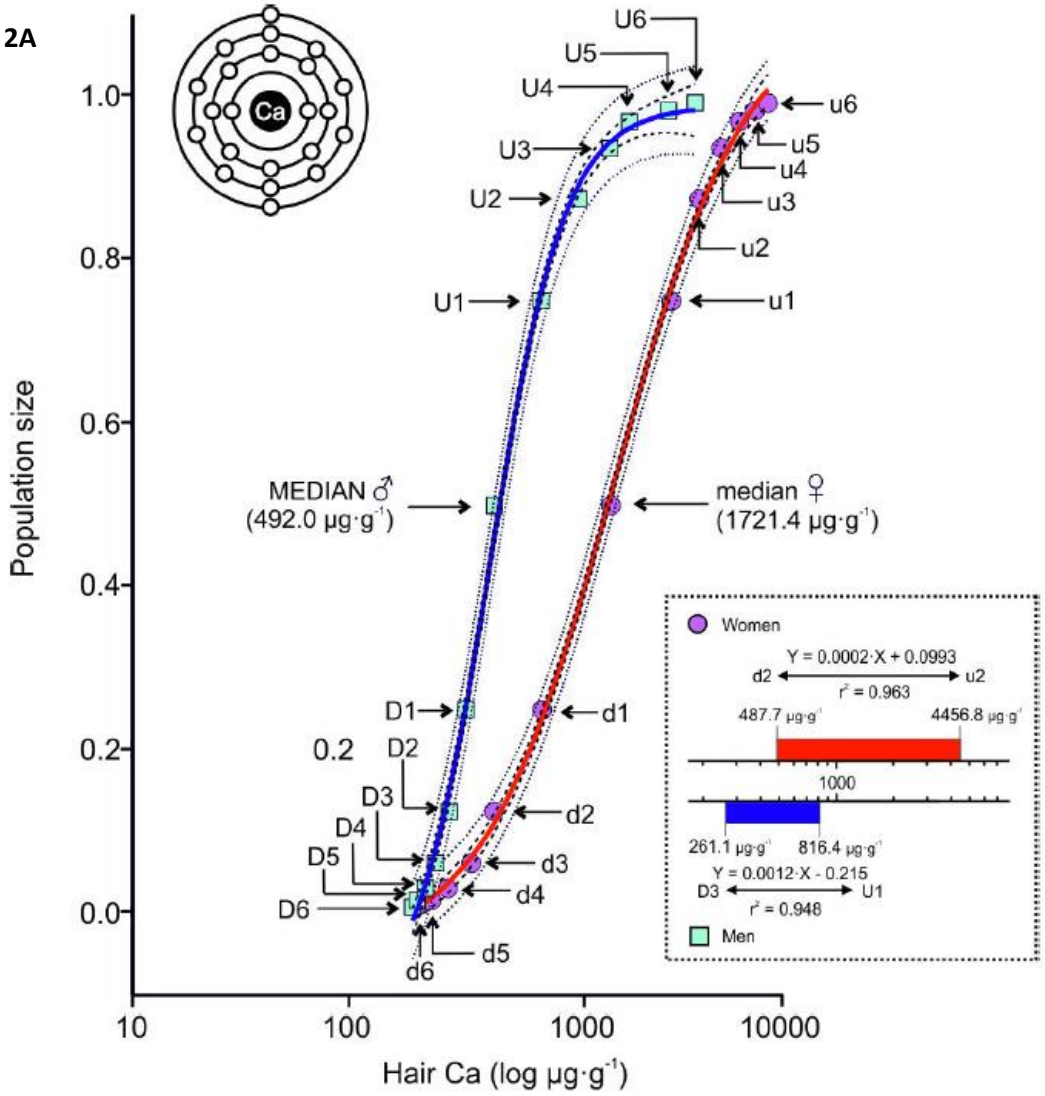


**Figure 2. Top** Hair Clsium sigmoid saturation curve

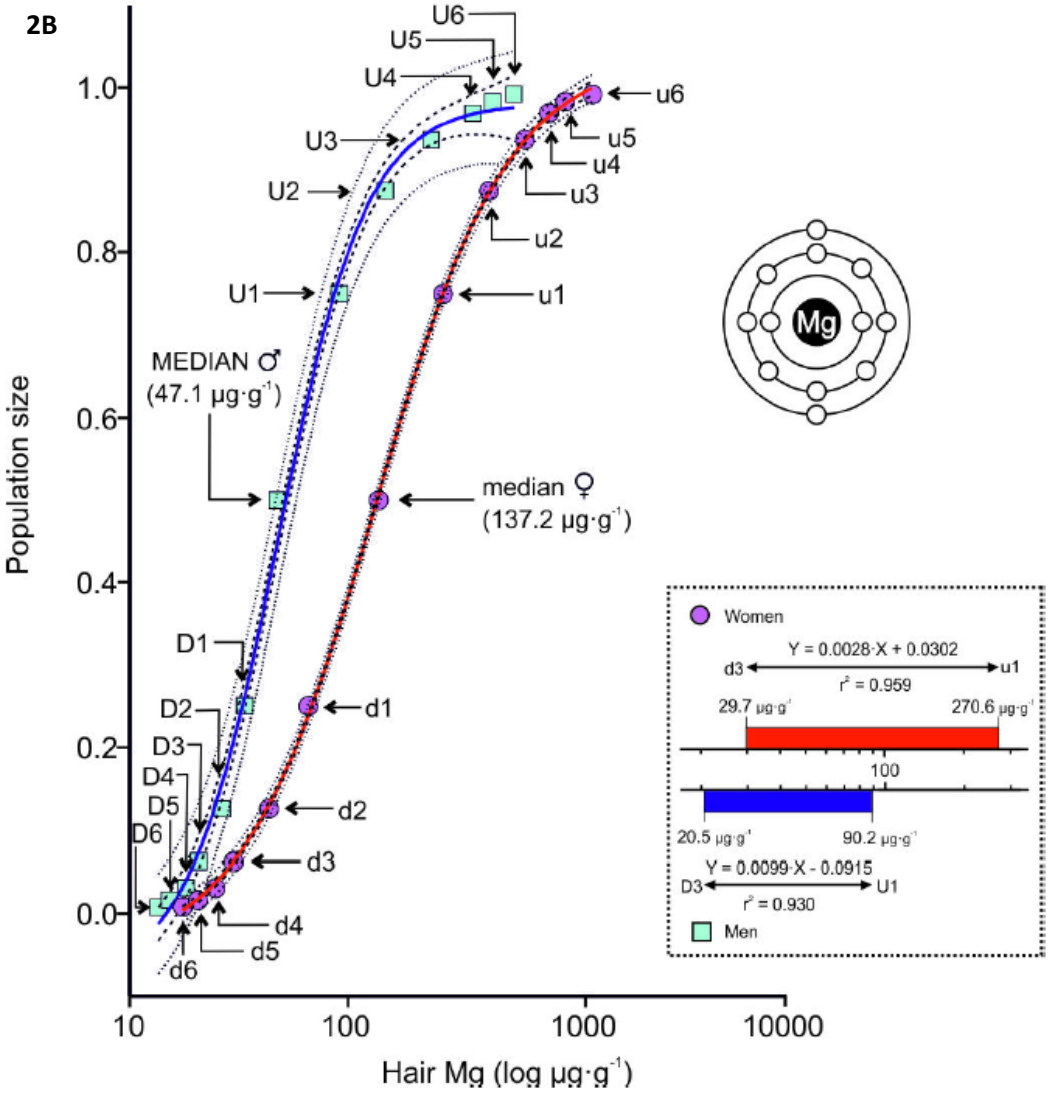


**Figure 2. Bottom** Haoir Magnesium sigmoid saturation curve

Evidently, magnesium and calcium hair deposition is regulated differently in men and women: These two major bio elements preferably accrue in the hair of women than men. However, the opposite pattern was observed for the physiologically entangled biological pair of K·Na in comparison with the Mg·Ca entangled pair[13a]. Indeed, men sodium and potassium entangled pair tend to be somewhat higher in men than women, presumably due to the higher muscle muss of men than women (Tabl.2, Fig3). But the same trend of preferably women hair bio element accumulation was observed for the osteotrophic (bone seeking) triplet of bio elements Ca, Mg, and Sr (Tbl 3)[13b].

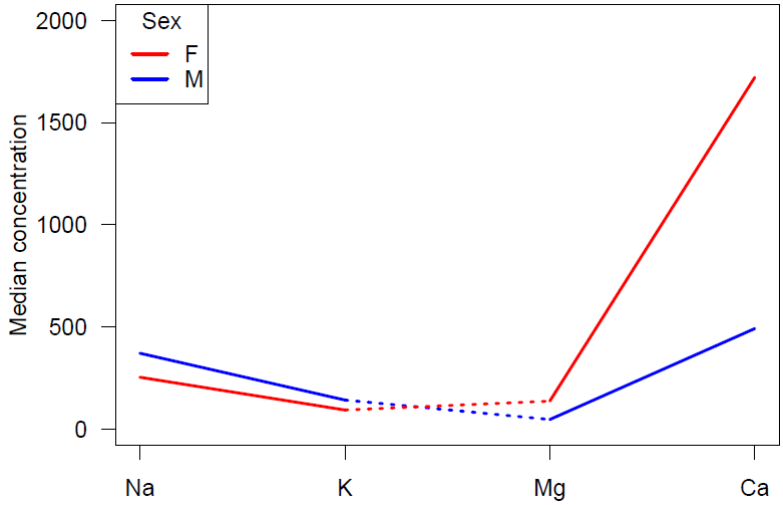


**Figure 3:** Women and men handles differently the entangled bio element pairs of Na·K) and Mg·Ca

**Table 2.** The median concentrations of biologically entangled pairs Na·K, and Mg·Ca bio elements in the hair of men and women (μg·g$^{-1}$)

| | Sodium (Na)[1] | | Potassium (K)[1] | | Magnesium (Mg) | | Calcium (Ca) | |
|---|---|---|---|---|---|---|---|---|
| | Women | Men | Women | Men | Women | Men | Women | Men |
| Lower limit | 55.6 | 84.0 | 8.9 | 25.9 | 29.7 | 20.5 | 483 | 291 |
| **Median** | **254.0** | **471.4** | **14.25** | **31.5** | **137.2** | **47.1** | **1721** | **492** |
| Upper limit | 1397 | 1450 | 467 | 1079 | 279.6 | 98.2 | 4426 | 816 |

[1]Momčilović B, 2021.

**Table 3.** Women has Increased hair median concentrations of the osteotrophic (bone seeking) bio elements calcium, magnesium and strontium (μg·g$^{-1}$)

| | Calcium (Ca) | | Magnesium (Mg) | | [1]Strontium (Sr) | |
|---|---|---|---|---|---|---|
| | Women | Men | Women | Men | Women | Men |
| Lower limit | 483 | 291 | 29.7 | 20.5 | 0.850 | 0.420 |
| **Median** | **1721** | **492.1** | **137.2** | **47.1** | **1.28** | **0.867** |
| Upper limit | 4426 | 816 | 279.6 | 98.2 | 7.26 | 3.120 |

[1]Prejac et al (13b).

## Discussion

Current Recommended Dietary Allowances (RDA) for magnesium are set at 300-350 mg per day[15] and those for calcium are set at 800 mg pe4r day[14]: pregnant and lactating women have higher Mg and Ca dietary requirements. However, current Recommended Dietary Allowances (RAD's) are aimed for the requirements of a group, whereas the Median Derivatives Bioassay allowed for planning and monitoring the individual, i.e., personalized, dietary requirements.

Hair growth is a unidirectional process and, indeed, about one cm of human hair is a one-month log of cumulative natural deposition of Mg and Ca in the human hair[1]. It should be noted that the Median Derivatives Bioassay sigmoid saturation curve steamed directly from within the observed real data set, and that the data were not forced to fit some presumed assessment model. In a way, the Median Derivatives Bioassay allows our metabolism to reveal it's bio element nutritional status history.

The observed difference in the homeostatic control of magnesium and calcium bio element metabolism between women and men is a fact of life; regardless of our appreciation, negation, or political corrections considerations. Evidently, the reproductive biological capacity of women is a fundamental sex difference that certainly has its metabolic price, as clearly revealed in this study. It

is well known that human diseases are not equally divided between women and men, but that the osteoporosis and stone forming diseases (calculosis) are more prevalent in women than men[17,18]. It should be noted that Both Mg and Ca belong to the second column of the Periodic Table, whereas sodium and potassium belong to the first column of the same Periodic Table[16]. No question that the entangled sodium and potassium (NA·K) bio element pair has the central role in cell physiology, the role which is both within both the realm of life and reproduction.

Thus far the scientists examined pretty extensively the problem of bio element interactions within the conceptual frame of varying one parameter at a time. However, the complex multi component system interaction, like calciphylaxis[19] , appears to go far beyond the experimental concept of varying one parameter at a time. Indeed, in calciphylaxis, or excessive tissue calcification, which is induced by combined high dietary levels of Ca and vitamin D together with high parenteral parathyroid hormone administration and low dietary Mg levels. Currently, the principal components analysis is available method of choice to approach the multicomponent interacting systems, what has its own limitations. It remains to be seen if the artificial intelligence hierarchical layer and node cross reaction network concept would offer for the cognition of the simultaneous multi component biological interactions[20]

## Conclusion

The homeostasis of the osteotrophic bio elements calcium, magnesium and strontium is regulated differently in women than men.

## Acknowledgement

The initial summary of this study was in part presented at the 2015 Experimental Biology meeting (FASEB J 2015;29:S1). The author would like to express his thanks to Prof., Diana Šimić for her help with statistical analysis.

## Disclaimer

The Author claims no conflict of interest.

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