

## STUDY OF EFFECT OF DURATION AND SEVERITY OF SMOKING ON SERUM MAGNESIUM LEVELS IN YOUNG SMOKERS

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### ABSTRACT

#### BACKGROUND

The commonest method of smoking today is through cigarettes. Global surveys show a fourfold increase in prevalence of smoking habit between ages 15-29 years in last decade. Magnesium is involved in more than 300 essential metabolic reactions. Smoking causes magnesium deficiency due to decreased supply and reduced absorption caused by disturbances in the digestive system functions.

#### METHODS

150 young smokers, between the age group of 18 to 40 years were included in the study and classified into groups A, B & C based on the years of smoking habit (less than 5 years, 6-10 years and more than 10 years respectively), with a minimum of smoking 2 cigarettes per day for a minimum period of 1 year. Based on the number of cigarettes smoked per day the subjects were classified into mild, moderate and heavy (2-5 cigarettes/day, 6-10 cigarettes/day, more than 10 cigarettes/day, respectively). Serum magnesium levels were measured in all the study subjects and compared based on the age of the subjects, duration of smoking and number of cigarettes smoked/day. Smoking index was calculated by multiplying the Number of cigarettes smoked per day x duration (years).

#### RESULTS

The two-way ANOVA indicated that severity of smoking ( $p < 0.001$ ) and duration of smoking ( $p < 0.001$ ) were significant predictors of serum magnesium levels. As interaction was not statistically significant ( $p = 0.058$ ), Tukey's procedure was used to conduct pairwise comparisons. There was a statistically significant difference in magnesium levels between all three different levels of severity and duration of smoking ( $p < 0.0001$ ). There was a very high negative correlation between serum magnesium and smoking index ( $r = -0.85$ ) and moderate correlation with age ( $r = -0.685$ ).

#### CONCLUSIONS

Severity of smoking and duration of smoking were significant predictors of low serum magnesium levels. There is a statistically significant difference in magnesium levels between all three different levels of severity and duration of smoking. There is a high negative correlation between serum magnesium levels and smoking index. Low serum magnesium levels may be considered as the earliest risk marker of cardiovascular and other non-communicable diseases in young smokers.

#### KEYWORDS

Effect of Smoking, Serum Magnesium, Young Smokers.

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#### BACKGROUND

The documented history of smoking in India is first mentioned in Atharvaveda (2000 B.C.) where the substance smoked was cannabis. The commonest method of smoking

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today is through cigarettes.<sup>1</sup> Global and Nationwide surveys such as "The Special Fertility and Mortality Survey (1998)", "The Sample Registration System Baseline Survey (2004)" and "the Global Adult Tobacco Survey (2010)" show that during the period between 1998 to 2015, there is a two fold increase of cigarette smoking in men, with a increased prevalence at ages 15-69 years and a fourfold increase in prevalence between ages 15-29 years.<sup>2</sup>

Magnesium is the fourth most abundant essential mineral in the human body after sodium, potassium, and calcium<sup>3</sup>, and is a cofactor for more than 300 enzymes that regulate a variety of biochemical processes, such as, Protein synthesis, DNA/RNA synthesis and glycolysis oxidative phosphorylation.<sup>3,4</sup> Magnesium acts as a cofactor for many

intracellular processes. It is involved in more than 300 essential metabolic reactions, some of which are involved in energy production, synthesis of essential molecules, structural roles, ion transport across cell membranes, cell migration, and cell signaling.<sup>5</sup> The immune system of the body is associated with Serum levels of magnesium; *in vitro* experiments have showed that intracellular free magnesium ions are an important second messenger in the immune activation of T lymphocytes<sup>6</sup> and B lymphocytes,<sup>7</sup> and magnesium channels and transport proteins play an important role in normal immune function.<sup>6,8,9</sup> Severe and even life-threatening metabolic abnormalities such as coronary heart disease, kidney failure, liver disease, lung infection, and disorders of endocrine system may occur due to mineral disturbances.<sup>10</sup> Smoking causes magnesium deficiency due to decreased supply (lesser appetite) and reduced absorption caused by disturbances in the digestive system functions.<sup>11</sup> It has been experienced that serum CRP is increased in smokers as compared to non-smokers.<sup>11</sup> Studies have shown that magnesium intake was associated inversely with levels of CRP, IL-6, and other inflammatory markers<sup>12,13</sup> and that supplementation of magnesium citrate can downregulate genes associated to metabolic and inflammatory pathways.<sup>14</sup>

With this background, the current study aims to study the effect of duration and severity of smoking on serum magnesium levels in young smokers

## METHODS

A total of 150 young smokers, between the age group of 18 to 40 years, were included as study subjects. The subjects were classified into groups A, B & C based on the years of smoking habit, with Group A- less than 5 years (n=50), Group B- 6 to 10 years of smoking (n=50), Group C- more than 10 years of smoking (n=50). Smoker status was defined by subjects who identified themselves as smokers with minimum of smoking 2 cigarettes per day for a minimum period of 1 year. Also based on the Number of cigarettes smoked per day the subjects were classified into Mild (2- 5 cigarettes/day), moderate (6- 10 cigarettes/day) and heavy (more than 10 cigarettes/day). Individuals with known history of bone mineral disorders, hypothyroidism, chronic constipation on laxatives, hypertension, renal disorders, diabetes, GI disorders, alcoholism, were excluded from the study. Serum magnesium levels were measured in all the study subjects and compared based on the age of the subjects, duration of smoking and Number of cigarettes smoked/day. Smoking index was calculated by multiplying the Number of cigarettes smoked per day x duration (years). Based on inclusion and exclusion criteria, the subjects were included in the present study after obtaining an informed consent. Smoking history was elucidated, clinical examination was done and recorded in a protocol format. A proforma was used to record relevant information and patient's data. The data for the study was collected from the patients visiting for general health check-up, between the period of June 2017 to January 2018, at Trichy Medical Center, Trichy.

Quantitative analysis of Serum magnesium levels was done in fully automated Cobas Integra 400 analyser, which used the colorimetric method with Chlorophosphonazo III.

## Statistical Analysis

To better study the effect of severity of smoking and duration of smoking on serum magnesium level, we performed Two-way ANOVA. The analysis was performed with SAS (version 9.4; SAS institute, Cary, NC, USA).  $P < 0.05$  was considered statistically significant. The relationship between the variables was tested by Pearson's correlation coefficient and spearman correlation coefficient and a p value of less than 0.05 was considered statistically significant.

## RESULTS

A total of 150 subjects participated in the study.

The subjects were classified into groups A, B & C based on the duration of smoking, with a minimum of 1 year of cigarette smoking as a habit.

**Group A-** 1 to 5 years of smoking (n=50)

**Group B-** 6 to 10 years of smoking (n=50).

**Group C-** more than 10 years of smoking (n=50).

All our study subjects were males.

All the subjects included in the study were between the age of 18 to 40 years (Chart 1).

31.3% (n= 47) belonged to age group 18 to 25,

30.6% (n=46) belonged to age group 26 to 35 and

38% were between 36 to 40 age group.

- **Group A** had the highest number of smokers between age of 18 to 25 years, n=38 out of 50 subjects (76%) with a mean age of  $24.58 \pm 4.19$ .
- **Group B** had the highest number of smokers in 25 to 35 years age group, n = 25 out of 50 Group B subjects (50%) with a mean age of  $31.86 \pm 4.07$
- **Group C** had highest number of smokers in 35 to 40 age group, n= 37 out of 50 Group C subjects (74%) with a mean age of  $36.7 \pm 2.31$ .

In this study, based on Number of cigarettes smoked per day the study subjects were classified into

- Mild smokers - 2 to 5 cigarettes/day,
- Moderate smokers - 6 to 10 cigarettes/day and
- Heavy smokers - more than 10 cigarettes/day
  - 32% (n = 49) were mild smokers
  - 41% (n=61) were moderate smokers and
  - 27% (n = 40) were heavy smokers (Chart 2).

Means and standard deviation for each combination of the groups of the independent variable is given.

The two-way ANOVA indicated that severity of smoking ( $p < 0.001$ ) and duration of smoking ( $p < 0.001$ ) was a significant predictor of serum magnesium levels. As interaction was not statistically significant ( $p = 0.058$ ) Tukey's procedure was used to conduct pairwise comparisons.

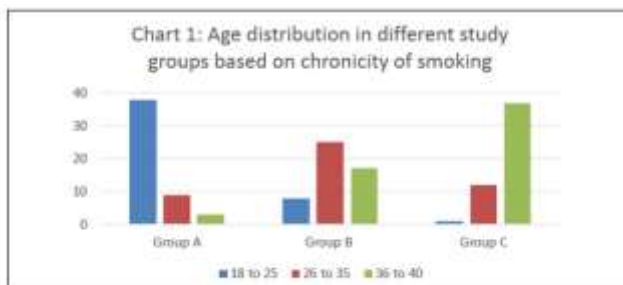


Chart 1. Age Distribution of Smokers in the Different Groups

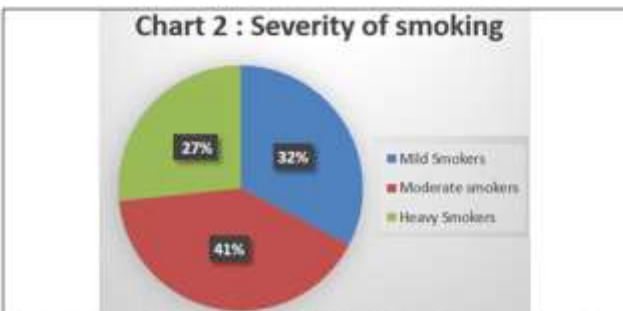
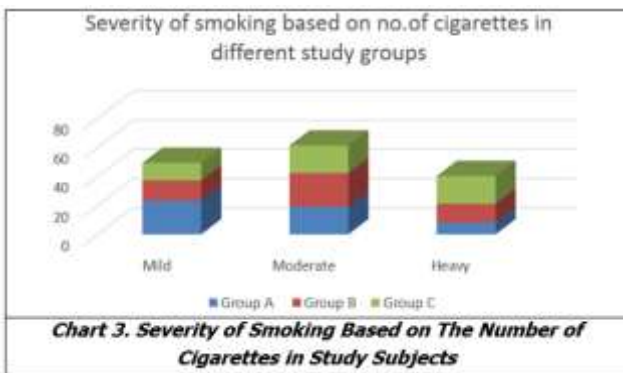


Chart 2. Severity of Smoking in Study Subjects Based on The Number of Cigarettes Smoked Per Day



Groups	Group A		Group B		Group C	
Parameters	Range	Mean±SD	Range	Mean±SD	Range	Mean±SD
Age in years	18-39	24.58±4.19	21-39	31.86±4.07	30-40	36.7±2.31
Duration of smoking (years)	1-5	2.88±0.86	6-10	7.6±1.01	11-22	17.12±2.61
Number of cigarettes/day	2-20	7.2±3.5	2-30	9.64±5.03	2-30	11.58±6.09
Smoking Index	3-100	23.04±14.8	12-250	75.6±41.8	24-510	207±114.8
S. Magnesium levels (mg/dl)	1.7-2.4	1.97±0.15	1.6-2.3	1.79±0.12	1.5-2.2	1.7±0.09

**Table 1. Combined Data in Different Groups- Based on Duration of Smoking, Number of Cigarettes Smoked/Day, Smoking Index & S. Magnesium Levels**

(\* Normal reference range for serum magnesium- 1.7mg/dl to 2.4 mg/dl)<sup>15</sup>

Serum Magnesium Levels (mg/dl) Mean±SD	Group A	Group B	Group C
Mild smokers	2.12±0.13	1.98±0.13	1.85±0.07
Moderate smokers	1.86±0.06	1.76±0.08	1.73±0.05
Heavy smokers	1.84±0.08	1.65±0.05	1.60±0.04

**Table 2. Serum Magnesium Levels in Different Groups Based on Severity of Smoking**

Groups	Group A	Group B	Group C
Age in years (Mean±SD)	21.3±1.75	26.7±3.6	32.27±1.33
Duration of smoking in years (Mean±SD)	2.4±0.82	6.76±0.82	12.72±1.28
Number of cigarettes/day (Mean±SD)	3.4±0.94	3.07±0.87	3.36±.94
Smoking Index (Mean±SD)	8.6±4.4	21.23±7.51	42.18±10.7
S. Magnesium levels in mg/dl (Mean±SD)	2.12±0.13	1.98±0.13	1.85±0.07

**Table 3. Combined Data Based on Number of Cigarettes Smoked- Mild Smokers (2-5 Cigarettes/Day)**

Groups	Group A	Group B	Group C
Age in years (Mean±SD)	24±2.7	32.17±2.63	37.9±1.74
Duration of smoking in years (Mean±SD)	3±0.7	7.8±0.99	18.2±2.1
Number of cigarettes/day (Mean±SD)	7.89±1.17	7.83±1.32	8.15±1.21
Smoking Index (Mean±SD)	23.47±6.8	60.82±11.1	149.2±29.5
S. Magnesium levels in mg/dl (Mean±SD)	1.86±0.06	1.76±0.08	1.73±0.05

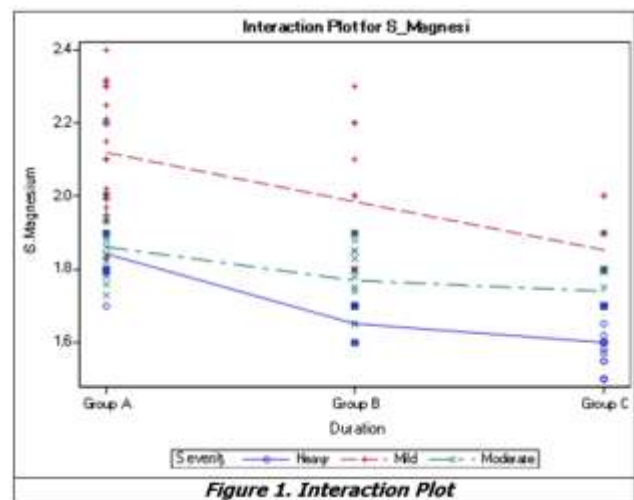
**Table 4. Combined Data Based on Number of Cigarettes Smoked- Moderate Smokers (6-10 cigarettes/Day)**

Groups	Group A	Group B	Group C
Age in years (Mean±SD)	33.7±3.22	36.14±1.83	38.05±1.06
Duration of smoking in years (Mean±SD)	3.77±0.66	7.9±0.8	18.5±1.6
Number of cigarettes/day (Mean±SD)	15.3±2	18.7±4.14	19.35±4.2
Smoking Index (Mean±SD)	57.3±12.4	150.5±45.14	352.55±69.24
S. magnesium levels in mg/dl (Mean±SD)	1.84±0.08	1.65±0.05	1.6±0.04

**Table 5. Combined Data Based on Number of Cigarettes Smoked- Heavy Smokers ( More than 10 Cigarettes/Day)**

Source	F	p Value
Duration	42.139	.000
Severity	74.583	.000
Duration * Severity	2.335	.058

**Table 6. Tests Between Subject Effects of Duration and Severity of Smoking**



Duration (I)	Duration (J)	Mean Difference (I)-(J)	p Value	95% Confidence Interval	
				Lower Bound	Upper Bound
Group A	Group B	.1804	.000	.1284	.2324
	Group C	.2628	.000	.2108	.3148
Group B	Group A	-.1804	.000	-.2324	-.1284
	Group C	.0824	.001	.0304	.1344

**Table 7. Multiple Comparison for Duration of Smoking**

Severity (I)	Severity (J)	Mean Difference (I)-(J)	p Value	95% Confidence Interval	
				Lower Bound	Upper Bound
Heavy	Mild	-.3508	.000	-.4060	-.2956
	Moderate	-.1205	.000	-.1723	-.0687
Mild	Heavy	.3508	.000	.2956	.4060
	Moderate	.2303	.000	.1795	.2811

**Table 8. Multiple Comparison for Severity of Smoking**

Variable	N	Mean±S D
Serum Magnesium level	150	1.82±0.194
Age	150	31.06±6.831
Variable	N	Median (IQR, Min, Max)
Smoking index	150	55.5(119,2,510)

**Table 9. Descriptive Statistics- Serum Magnesium & Smoking Index**

Variables	Serum Magnesium level (r)	p Value
Smoking Index	-0.85008	<.0001
Age	-0.68506	<.0001

**Table 6. Correlation Coefficients-  
Serum Magnesium Level, Smoking Index and Age**

From the results given about, we can see that there is a statistically significant difference magnesium levels between all three different levels of severity and duration of smoking ( $p < .0001$ ).

Apart from that correlation is also studied between Serum magnesium level and smoking index as well as age. Pearson correlation coefficient is reported for age and Serum magnesium level and Spearman rank correlation coefficient is reported for smoking index and serum magnesium level as smoking index is not normally distributed.

It shows there is very high negative correlation between serum magnesium and smoking index ( $r=-0.85$ ) and moderate correlation with age ( $r=-0.685$ )

## DISCUSSION

Even though there were no criteria set to differentiate the study subjects gender wise, still all subjects who confessed to smoking were only males. This might be due to the social stigma associated with women smoking in a conservative demography of the study.

All the subjects included in the study were between the age of 18 to 40 years. The groups A, B & C were classified only based on the duration of smoking and not depending on the age of the subjects with in the inclusion criteria set.

The mean age of the subjects was observed to be  $31.06 \pm 5.93$  (Table 1). It was observed that the mean age of the subjects with low duration of smoking (Group A <5 years) was the lowest with a mean of  $24.58 \pm 4.19$  years (Table 1). The mean age observed in Group B was  $31.86 \pm 4.07$  years & the mean age of smokers with high duration of smoking (Group C- more than 10 years) was the highest  $36.7 \pm 2.31$  years (Table 1). Serum magnesium levels showed moderate negative correlation with increased age ( $r = -0.85$ ). The mean duration of smoking in Group A was  $2.88 \pm 0.86$  years. Previous studies conducted about the smoking habits in adolescents by Nyi Nyi Naing et al. has also found to have similar results to the current study in this regard. The mean duration of smoking in Group C was the highest at  $17.12 \pm 2.61$  years. Previous studies on rat brain have demonstrated the interaction of nicotine with the cells regulating the output of a brain region involved in habit formation.<sup>16</sup> With increase in mean age across groups, the mean duration of smoking has also increased which is in accordance with this study.

In the current study, Severity of smoking ( $p < 0.001$ ) and duration of smoking ( $p < 0.001$ ) was a significant predictor of low serum magnesium levels. In the current study we observed that there is a statistically significant difference in magnesium levels between all three different levels of severity and duration of smoking ( $p < .0001$ ). Previous studies have shown that smoking cigarette causes decreased supply of magnesium due to decreased appetite and decreased absorption due to digestive system disturbances.<sup>11</sup> Our study results are in accordance to that

with a high negative correlation between serum magnesium and smoking index ( $r=-0.85$ ).

In prospective studies, serum magnesium levels have been inversely associated with the incidence of hypertension<sup>17</sup> and coronary heart disease (CHD).<sup>16</sup> It has been observed that people with hypertension and obesity has impaired vascular endothelial function; it occurs due to increase in plasma levels of CRP and hypomagnesaemia in cellular processes.<sup>18</sup> In previous studies, it was observed that severity of smoking is an important factor affecting the level of serum magnesium, which has an inverse relationship with hypertension and coronary heart diseases.<sup>17</sup> It has been observed that people with hypertension and obesity has impaired vascular endothelial function; it occurs due to increase in plasma levels of CRP and hypomagnesaemia in cellular processes.<sup>18</sup>

It is also seen in some studies, that smokers have increased glucose levels, decreased high density lipoproteins (HDL) cholesterol, and much more very low-density lipoproteins (VLDL) cholesterol. Since these variables are not direct measures of magnesium levels in smokers even then they clearly show that smoking decreases cellular magnesium concentration.<sup>19</sup>

Our study suggests with severity and duration, serum magnesium levels are decreasing. The United Nations' 2030 goals to decrease premature death from non-communicable disease.<sup>20</sup> The correlation between low serum magnesium levels and smoking and incidence of non-communicable diseases in smokers are to be considered together. A substantial reduction of smoking should be the target action and the assessment of Serum magnesium in young smokers with more than 10 years of smoking habit shall be considered

## Limitations

The status of smoking as inclusion criteria was only based on the subjects on their own identification and the number of cigarettes smoked is also a self-report of the subjects. We have not documented the food habits of the subjects included in the study as dietary intake may have a considerable amount of difference in serum magnesium levels. Also, the type of water consumed is not documented, where composition of water may cause disturbances in mineral levels.<sup>21</sup> Only internal comparison was done between the smokers, and non-smoking controls were not included in the study. A comprehensive study including these factors shall be considered as the future scope. Further the incidence of non-communicable disorders such as hypertension and CHD in smokers with low serum magnesium levels shall be studied.

## CONCLUSIONS

Severity of smoking and duration of smoking were significant predictors of low serum magnesium levels. There is a statistically significant difference in magnesium levels between all three different levels of severity and duration of smoking. There is a high negative correlation between serum magnesium levels and smoking index. Low serum

magnesium levels may be considered as the earliest risk marker of cardiovascular and other non-communicable diseases in young smokers.

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