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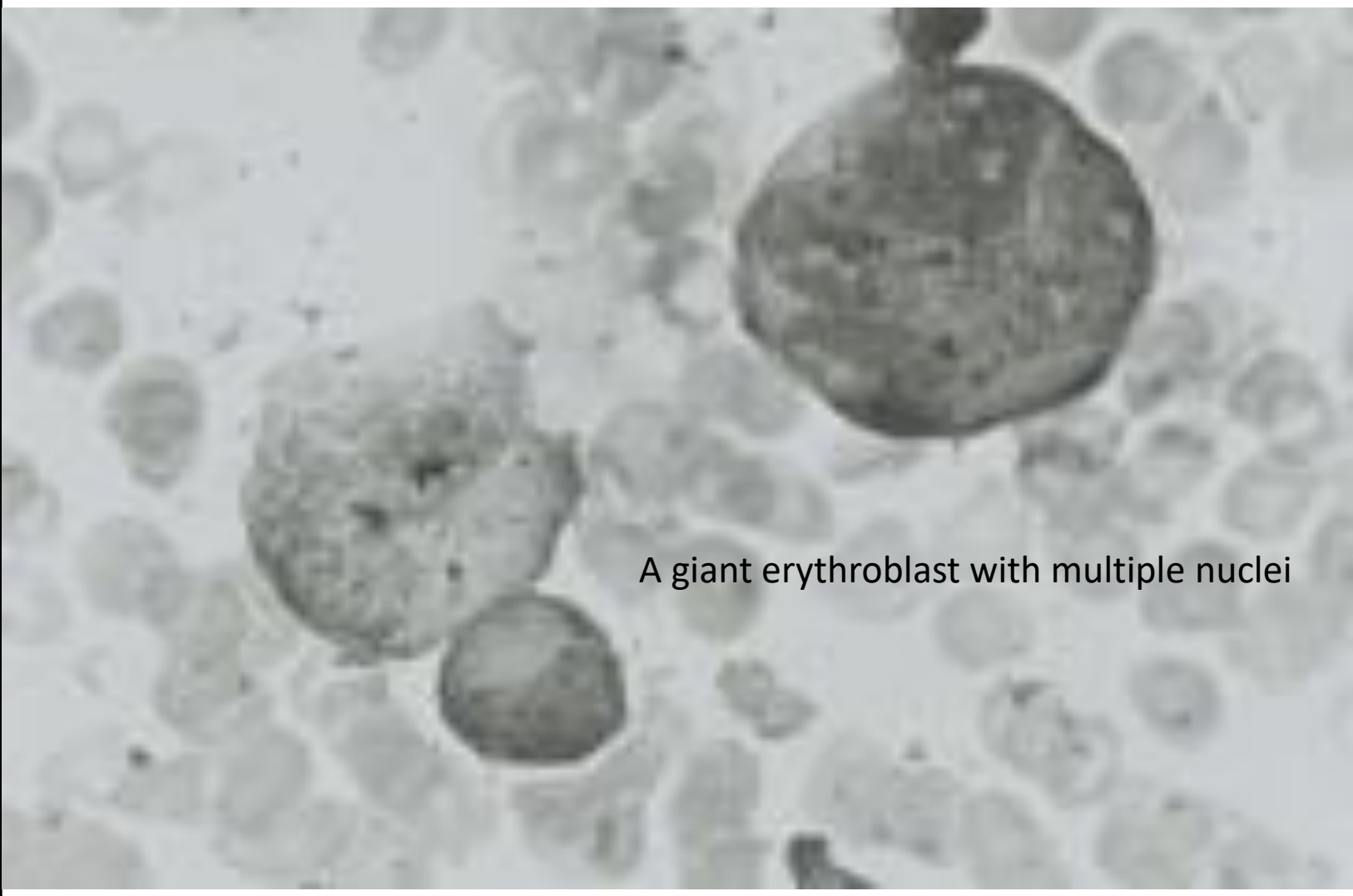

A giant erythroblast with multiple nuclei


- **Evaluation of the relationship between serum 25-hydroxyvitamin D levels and extended period of leg cramps in pregnant women**
- **Impact of menopause on quality of life: A cross sectional study in menopausal females in the north of Jordan**
- **Relationship of Total Antioxidant Capacity and Endothelin-1 levels in prehypertensive individuals among population attaining a sedentary lifestyle in central India**


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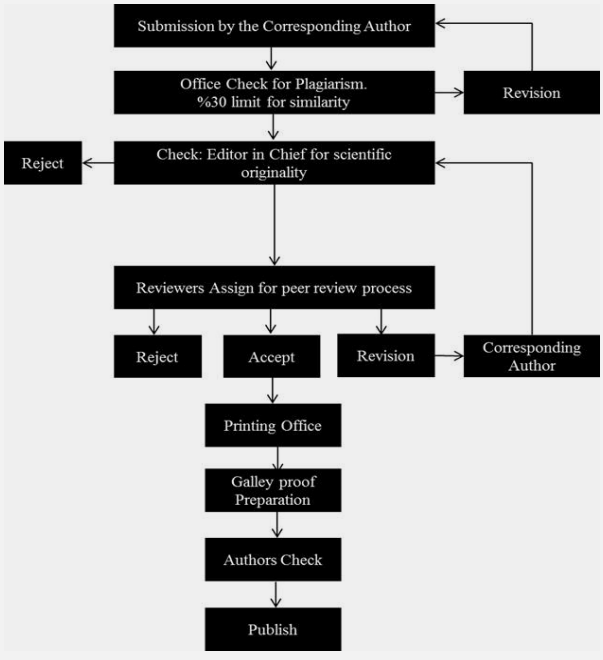

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# Evaluation of the relationship between serum 25-hydroxyvitamin D levels and extended period of leg cramps in pregnant women

**Pervin Karli[1]***

## Abstract

**Objective:** At least one-third of pregnant women suffer from leg cramps. While the cause of these leg cramps is not fully understood, it starts during the third trimester, likely due to pregnancy-related physiological changes. The relation of serum 25-hydroxyvitamin D [25(OH)D] levels and leg cramps has been evaluate in this research.

**Methods:** The study included 95 pregnant patients who visited our gynecology and obstetrics outpatient clinic in January 2017 during weeks 24–39 of their pregnancies. Demographic characteristics, vitamin supplement use, and other factors that might have affected the 25(OH)D levels of the participating pregnant women were recorded.

**Results:** A statistically significant difference ($p<0.0001$) was found in the serum 25(OH)D levels between the patients who did and did not use supplemental 25(OH)D. A statistically significant difference was found in the groups of pregnant women regarding 25(OH)D levels and weight 69.60 ± 2.43 ng/dl among the patients who did not use supplemental 25(OH)D compared to 77.69 ± 2.20 ng/dl for those who did; $p < 0.0162$). There was no significant difference between the 25(OH)D serum levels and the number of cramps. A significant difference was found between the intensity and duration of the cramps and the number and duration of the cramps ($p < 0.029$ and $p < 0.0001$, respectively).

**Conclusion:** The use of supplemental 25(OH)D did not have a statistically significant effect on the occurrence of pregnancy-related leg cramps. The 25(OH)D levels were higher in the that supplemental 25(OH)D used group. A significant difference was found between the pregnant women's weight and the occurrence of leg cramps ($p < 0.0162$). Vitamin D supplements may be used to prevent long period leg cramps for pregnant woman's.

**Keywords:** leg cramps, vitamin D, pregnancy

## Introduction

Muscle cramps are painful involuntary muscle convulsions that are strongly felt. Leg cramps are one of the most common side effects of pregnancy, especially in the third trimester (1, 2, 3). These cramps typically occur at night, usually not more than twice a week, and cease within a few minutes (2, 4). The cramps primarily strike only one side of the body (1, 3). The leg cramps do not originate within the muscle itself but are triggered by a spontaneous convulsion of the muscle's motor nerves (5). There is no standard treatment for leg cramps, but several studies have been conducted on this issue (6), as this side effect is experienced in 30–45% of pregnancies (4).

Leg cramps tend to disrupt sleep quality, and pregnant women with poor sleep quality have been found to have extended labor and increased rates of labor-related operations (7).

It has also been observed that pregnant women have lower serum magnesium levels than nonpregnant women (8), indicating that pregnancy cramps may be related to low magnesium levels. Although the cause of muscle cramps is not fully understood, neuromuscular changes, weight gain, joint looseness, decreased blood flow to the lower extremities, and increased pressure on the leg muscles during the last trimester of pregnancy are all potential contributing factors (3, 9).

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## Material and Methods

This study included 95 women who presented to our outpatient gynecology and obstetrics clinic in January 2017 during weeks 24–39 of their pregnancies. The women were surveyed on their experience with leg cramps. Positive responders were asked to specify the duration, frequency, and intensity of their cramps as well as the total number of cramps, whether they occurred during the day or night, and whether they occurred when the subject was moving or resting. Additional patient characteristics were recorded, including: age, weight, height, occupation, use of supplemental 25-hydroxyvitamin D [25(OH)D], use of multi-vitamins, use of anti-anemic treatments, whether the patient was veiled (to evaluate sun exposure), and whether the patient had additional illnesses. Serum 25(OH)D levels were tested in the morning with an empty stomach. The patient's morning hunger. For measurement, the ELISA (Enzyme-linked immunosorbent assay) was used and the results were recorded in ng/dl. Subjects who received oral magnesium to treat pregnancy cramps, those who had not yet reached the 24th week of pregnancy, or those who were beyond the 39th week of pregnancy were not included in the study. Oral and written consent was obtained from each woman who participated in the study. GraphPad Prism version 6.00 (GraphPad Software, La Jolla, California) was used to conduct the statistical analyses. The data was analyzed using definitive statistics, including the one-way analysis of variance test and the t-test. The results were evaluated using 95% reliability; p values < 0.05 were deemed significant.

## Results

This study evaluated 95 pregnant women who visited to our outpatient gynecology and obstetrics clinic. Among them, 73 were housewives, 6 were teachers, 5 were healthcare staff, 1 was a tradeswoman, and 8 had other occupations. There was no statistically significant difference between the pregnancy weeks and the heights of the women included in the study.

When the women were divided into groups according to whether they had experienced leg cramps, there was no statistically significant difference between the 25(OH)D levels of the groups; the mean 25(OH)D level in the group without leg cramps was higher than in the group with leg cramps (9.92 ± 1.42 ng/dl - 9,43 ± 0,94 ng /dl). The mean weight of the group without leg cramps was 69.60 ± 2.43 kg, while the mean weight of the group with leg cramps was 77.69 ± 2.20 (Table1). The pregnancy induced cramp was statistically significantly higher among the women with higher weights ($p < 0.0162$). The demographic features of the participating women are shown in Table 3. A statistically significant difference was found between the number of cramps and the duration of the cramps ($p < 0.0001$). No significant difference was found between the number of cramps and 25(OH)D levels. There was no significant difference between the women who were veiled and those who were not, but the 25(OH)D levels were higher in the non-veiled group (veiled, n = 62, 8.50 ± 0.64; non-veiled, n = 33, 11.56 ± 1.8).

A statistically significant difference was found between daily multivitamin usage and vitamin D levels (multivitamin users, n = 73, 10.34 ± 0.98; non-users, n = 22, 6.97 ± 0.75; p = 0.0297*).

A statistically significant difference was found between the women who took daily supplemental 25(OH)D (n = 24, 15.14 ± 2.53) and those who did not (n = 71, 7.67 ± 0.45) (p = 0.0001*).

There was a statistically significant negative correlation between 25(OH)D levels and the intensity of the leg cramps. As the vitamin D levels decreased, the leg cramp intensity increased (p = 0.029).

When comparing the times that cramps occurred, there was no significant difference between when the subject was moving or resting. Additional parameters are provided in the tables (Table 1-12).

**Table 1.** Comparison of patient characteristics and the occurrence of leg cramps.

| | No cramps (n = 25) | Cramps (n = 70) | p |
|---|---|---|---|
| **Vitamin D levels** | 9.92 ± 1.42 | 9.43 ± 0.94 | 0.9916 |
| **Height (cm)** | 160.5 ± 1.04 | 160.4 ± 1.34 | 0.4951 |
| **Weight (kg)** | 69.60 ± 2.43 | 77.69 ± 2.20 | 0.0162* |
| **Week of pregnancy** | 29.79 ± 1.11 | 30.65 ± 0.76 | 0.154 |

* p values < 0.05 are statistically significant

**Table 2.** The correlation between Vitamin D insufficiency and the occurrence of leg cramps in pregnant women.

| | No cramps | | Cramps | | $\chi^2$ | p |
|---|---|---|---|---|---|---|
| | n | % | n | % | | |
| **Not using 25(OH)D** | 17 | 69.9 | 48 | 73.8 | 0.0808 | 0.776235 |
| **Using 25(OH)D** | 7 | 29.1 | 17 | 26.2 | | |
| **Using multi-vitamins** | 19 | 82.6 | 57 | 83.8 | 0.0026 | 0.959068 |
| **Not using multi-vitamins(25(OH)D levels)** | 4 | 17.4 | 11 | 16.2 | | |
| **Veiled** | 18 | 72 | 44 | 62.8 | 0.6792 | 0.40985 |
| **Not veiled** | 7 | 28 | 26 | 37.2 | | |

**Table 3.** Definitive analyses of some demographic parameters

| | |
|---|---|
| **25-OH Vitamin D** | 9,56 ± 0,78 |
| **Age (years)** | 28,39 ± 0,52 |
| **Height (cm)** | 160,4 ± 1,02 |
| **Weight (kg)** | 75,56 ± 1,78 |
| **Week of pregnancy** | 29,61 ± 0,65 |

**Table 4.** The relation between the number of cramps and Vit D levels

| No cramps (n=25) | No. of cramps less than 3 (n=52) | No. of cramps 3-5 (n=11) | Number of cramps 5-10 (n=4) | No. of cramps more than 5 (n=2) |
|---|---|---|---|---|
| 9,92 ± 1,42 | 8,90 ± 0,65 | 8,1 ± 5,1 | 8,15 ± 1,77 | 6,8 ± 4 |

A statistical meaning could not be found among the groups ($p<0.05$).

**Table 5.** The relation between the intensity of cramp and Vit D levels

| Low (n=50) | Mid (n=22) | Intensive (n=9) | Very intensive (n=3) | P value |
|---|---|---|---|---|
| **8,76 ± 0,65** | 7,40 ± 2,84 | 6,29 ± 1,10 | 5,41 ± 2,32 | 0,029* |

A statistical meaning was found among the groups ($p<0.05$).

**Table 6.** The relation between the number of cramps and the duration of cramps

| No. of cramps | Duration of cramps | P value |
|---|---|---|
| **2 ± 0,08** | 1,40 ± 0,08 | < 0,0001* |

A statistical meaning was found between the number of cramps and the duration of cramps ($p<0.05$).

**Table 7.** The relation between the exposure to the Sun and Vit D level

| Veiling (n= 62) | Not Veiling (n=33) | P value |
|---|---|---|
| **8,50 ± 0,64** | 11,56 ± 1,8 | 0,1347 |

A statistical meaning could not be found between the groups ($p<0.05$).

**Table 8.** The relation with the Vit D level as per the blood medicine usage

| Blood medicine (n= 79) | No blood medicine (n=16) | P value |
|---|---|---|
| **9,94 ± 0,92** | 7,66 ± 0,94 | 0,3417 |

A statistical meaning could not be found among the groups ($p<0.05$).

**Table 9.** The relation with the Vit D levels as per the Vit D usage

| Using Vit D (n= 24) | Not using Vit D (n=71) | P value |
|---|---|---|
| **15,14 ± 2,53** | 7,67 ± 0,45 | 0,0001* |

A statistical meaning was found between the users and non-users of 25-OH Vitamin D ($p<0.05$).

**Table 10.** The relation with the Vit D level as per the Vitamin usage

| Using vitamin (n= 73) | Not using vitamin (n=22) | P value |
|---|---|---|
| **10,34 ± 0,98** | 6,97 ± 0,75 | 0,0297* |

A statistical meaning was found between the users and non-users of vitamin ($p<0.05$).

**Table 11.** The relation between the night cramps and the Vit D level

| No (n=50) | 1-3 times (n=22) | 3-5 times (n=9) | More than 10 times (n=3) | P value |
|---|---|---|---|---|
| **9,12 ± 0,90** | 8,87 ± 0,73 | 7,47 ± 11,41 | 6,80 ± 4,0 | 0,0308 |

A statistical meaning was found between the groups ($p<0.05$).

**Table 12. The relation with the Vit D level as per when the cramps occur**

| While moving (n= 38) | While resting (n=57) | P value |
|---|---|---|
| **9,81 ± 1,63** | 9,39 ± 0,75 | 0,5263 |

A statistical meaning could not be found between the groups ($p<0.05$).

## Discussion

Since 25(OH)D plays an active role in many metabolic processes, deficiencies may be related to leg cramps as well as other illnesses like pre-eclampsia. A previous study found that the pre-eclampsia risk was 5.41 times higher among pregnant women with insufficient 25(OH)D levels (10). Another study reported that women with low 25(OH)D levels gave birth to lower weight babies (11). Other reports have indicated that women who took supplemental 25(OH)D during pregnancy had higher calcium levels and less birth pain (12, 13). Therefore, 25(OH)D is an important nutrient, and its deficiency is related to several pathological conditions in addition to leg cramps.

In a randomized, controlled, double blind study conducted on 126 pregnant women who were 18 to 24 years old, the study group was provided supplemental 25(OH)D for six weeks, but no difference in cramp frequency, intensity, and duration was observed compared to the control group (1). We found that many of the pregnant women in our study already had low 25(OH)D levels, suggesting that supplemental 25(OH)D may need to be administered in higher doses during pregnancy or may even need to be started before pregnancy to prevent leg cramps. Within the outpatient clinic control group in our study, a significant difference was found between 25(OH)D levels and cramp intensity among the pregnant women who regularly took supplemental 25(OH)D on the advice of their doctors ($p < 0.029$). In addition, there was a significant difference between the cramp intensity and the number of cramps. Therefore, we conclude that the number of cramps indirectly increases cramp intensity.

## Conclusion

We found that supplemental 25(OH)D increased 25(OH)D levels in pregnant women; however, these levels were still within the deficiency range. To fully investigate the effects of 25(OH)D levels on pregnancy-related leg cramps, supplemental 25(OH)D should be provided in higher doses and preferably before the start of pregnancy. More significant findings might have been made in this study if we could have compared pregnant women who had low 25(OH)D levels with women who had normal 25(OH)D levels because they had previously taken supplemental 25(OH)D. This demonstrates a shortfall in our study. Further research is needed employing supplemental 25(OH)D for a longer period and at a higher dose, both during and pre-pregnancy, to provide an effective comparison with patients who have never taken supplemental 25(OH)D.

**Conflict of Interest:** The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Author's Contributions: PK:** Research concept and design; patient examination, data collecting, analysis and interpretation of data**.** Preparation of article. All authors approved the final version of the manuscript.

**Ethical issues:** All Authors declare, Originality and ethical approval of research. Responsibilities of research, responsibilities against local ethics commission are under the Authors responsibilities. The study was conducted under defined rules by the Local Ethics Commission guidelines and audits.

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# Is ultrasound-guided transversus abdominis plane block in providing analgesia in pediatric cases safe and efficient?: A retrospective study

**Orhan Binici[1]*, Osman Hakan Kocaman[2], Evren Buyukfirat[1], Mahmut Alp Karahan[1], Nuray Altay[1]**

## Abstract

**Objective:** The use of high or insufficient doses of analgesics in pediatric cases unfavorably affects the patient's health in the postoperative period. Ultrasound-guided transversus abdominis plane (TAP) block is used in the management of postoperative pain in pediatric cases. The present study aims to evaluate the efficacy of ultrasound-guided TAP block in pediatric patients using a mixture of lidocaine and bupivacaine.

**Methods:** The medical records of cases, who underwent surgery for the repair of the inguinal hernia and undescended testis using ultrasound-guided TAP block in the department of pediatric surgery, were retrospectively reviewed (28 cases). The study included ASA I-II pediatric cases aged 2-12 years. The amount of drug administered while performing USG-guided TAP block, time to first analgesic use in the postoperative period, pain score and the amount of first analgesic administration were recorded. The satisfaction of the surgeon and patient's companion was evaluated.

**Results:** A p-value <0.05 was considered statistically significant. The findings showed that pain score was the lowest in the group with the highest patient's companion and physician satisfaction score, and the highest in group with the lowest satisfaction score and the difference was statistically significant (p<0.001). The satisfaction of the physicians (p=0.010) and the patient's companion (p=0.027) increased with increasing drug volume.

**Conclusions:** The volume of 0.4 ml.kg-1 (50:50 1% lidocaine and 2.5% bupivacaine) achieved the best physician and patient's companion satisfaction and the longest duration of analgesia in pediatric cases undergoing surgery for the repair of the inguinal hernia and undescended testis. The lack of any complications in the present study suggests that USG-guided TAP block is a safe procedure in pediatric patients in experienced hands. Further studies are required.

**Keywords:** Transversus abdominis plane, Ultrasound-guided, Pediatric cases.

## Introduction

Postoperative pain management has a growing importance for the patient's quality of life and response to therapy. TAP block involves administration of local anesthetics into anatomic neuro fascial space between internal oblique and transversus abdominis muscles in the antero-lateral region of the abdomen to block anterior branches of the thoracic intercostal (T7-T12) and first lumbar (L1) nerves (1). Although this block was previously performed, Hebbard et al. were the first to describe ultrasound (USG)-guided TAP block technique (2). This technique has made the procedure easier to perform, and USG-guided TAP block was widely used with scarcely any complications, if any. Nowadays, TAP block is an auxiliary analgesic method often used to reduce opioid use in the intraoperative period or reduce systemic analgesic use in the postoperative pain management, thereby reducing the use of high doses of analgesic or eliminating the need for using IV or IM analgesics after procedures that may be extremely painful.

The use of high or insufficient doses of analgesics in pediatric cases unfavorably affects the patient health in the postoperative period. Today, the use of ultrasound-guided transversus abdominis plane (TAP) block has become a popular procedure for postoperative pain control in pediatric cases (3).

The aim of the present study is to retrospectively evaluate the efficacy of USG-guided TAP block in ASA I-II patients who underwent inguinal hernia or undescended testis repair under elective conditions.

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## Materials and Methods

After obtaining approval of the ethics committee on 15.10.2017, the medical records of cases, who underwent surgery for the repair of the inguinal hernia and undescended testis using ultrasound-guided TAP block in the department of pediatric surgery at Harran University Faculty of Medicine between January 15.10.2017 and September 2017, were retrospectively reviewed. The study included ASA I-II 28 pediatric cases aged 2-12 years. Patients with a history of opioid use or allergy to local anesthetics and patients with infections at the injection site and those with coagulation disorders were excluded. The data retained by the departments of surgery and anesthesiology, data of intelligence technologies department, and medical charts of the patients were reviewed. The patients underwent electrocardiography (EKG), heart rate monitoring (HRM), non-invasive blood pressure (NIBP) monitoring and peripheral oxygen saturation (SpO2) monitoring in the pre-anesthesia preparation room. Patients who underwent surgery received general anesthesia. After induction of anesthesia using a routine protocol involving propofol 2.5-3 mg.kg-1, fentanyl 2 µgr.kg-1, and rocuronium0.6 mg.kg-1, anesthesia was maintained using 50%/50% O2/air, sevoflurane 2-3%, and remifentanil infusion at a rate of 0.05-0.1 µgr.kg-1.min-1. While performing ultrasound-guided (Esaote MyLab 30 Gold, Italy) TAP block, abdominal cavity was scanned laterally with the probe (Figure 1); the drug was injected by passing the 50 mm 22 G nerve needle (Pajunk, SonoPlex STIM, Germany) through subcutaneous tissues, external oblique muscle, and internal oblique muscle. (Figure 2) TAP block was performed in ultrasound guidance using 0.2-0.3 or 0.4 ml.kg-1 50:50 mixture of lidocaine 1% and bupivacaine 0.25%. The face, legs, activity, cry, consolability scale or numeric pain scale (0-10) were used to evaluate postoperative pain in patients aged three years who are deemed suitable. Patients who achieved >4 points on the scale received paracetamol 10-15 mg.kg-1 for pain relief.

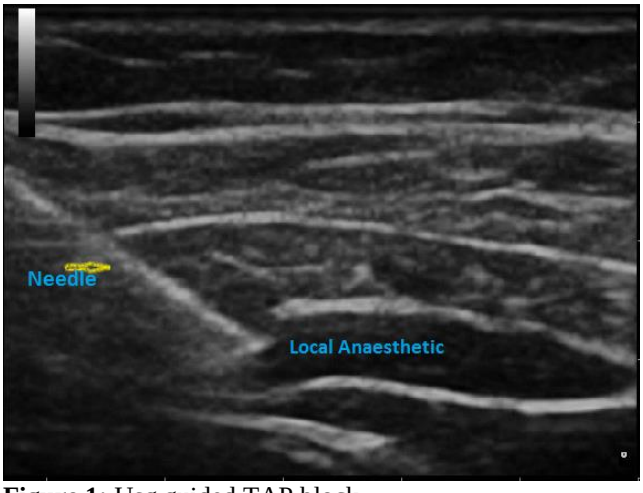


**Figure 1:** Usg guided TAP block

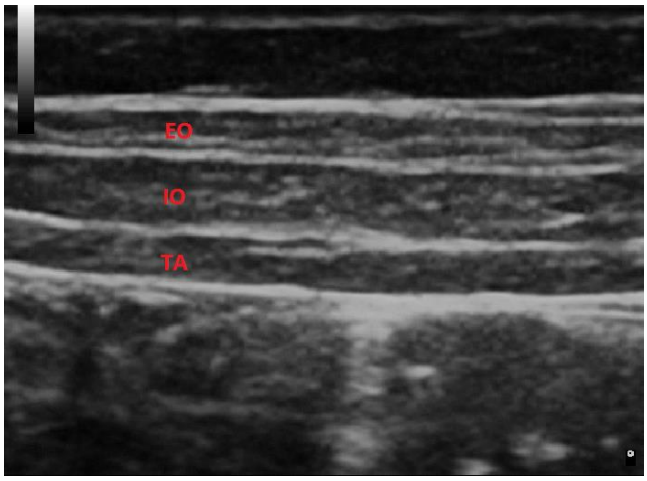


**Figure 2:** EO: External oblique, IO: Internal oblique, TA: Transversus abdominis

Demographic data of the patients, blood pressures at the entrance and with 5-minute intervals during surgery, peripheral oxygen saturation, heart rate and operation time were recorded. Specific diagnosis leading to surgery, uni or bilateral surgery, time to perform TAP block and the amount of drug administered was examined. The time to first analgesic use in the postoperative period, pain score and the amount of first analgesic administration were examined. The satisfaction of the surgeon and patient's companion was examined after surgery (poor: 1, moderate: 2, good: 3). The patients were monitored for postoperative complications, such as nausea, vomiting, urinary retention, femoral nerve paresthesia, hematoma, and organ and tissue injury.

### Statistical Analysis

The data were analyzed using SPSS for Windows version 23.0. Descriptive statistics for continuous variables included mean and standard deviation and categorical variables were expressed as a percentage. The Mann-Whitney test was used in the comparison of paired groups without normal distribution, and Kruskal Wallis test was used to compare multiple groups. Chi-square test was used to compare the categorical variables. The Spearman's rank correlation coefficient was calculated to evaluate the correlation between continuous variables. A p-value $<0.05$ was considered statistically significant.

## Results

Demographic data are presented in Table 1.

The scores in pain scale (PS) were highest in patient's companions that were dissatisfied the most, and pain scores were lowest in patient's companions that were satisfied the most ($p<0.001$). The duration of postoperative analgesia was the lowest in dissatisfied patient's companions and the highest in satisfied patient's companions ($p<0.001$) (Table 2).

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The physician satisfaction score (p=0.010) and patient's companion satisfaction score (p=0.027) increased with increasing drug volume, and the highest satisfaction score was observed with a volume of 0.4 ml.kg-1 (Table 3 and Table 4).

The score on PS was the lowest in physicians with the highest satisfaction score and the highest in physicians with the lowest satisfaction score (p<0.001). The duration of postoperative analgesia was the highest in physicians with the highest satisfaction score and the lowest in physicians with the lowest satisfaction score (p<0.001).

The time to perform TAP block, patient age and the number of postoperative analgesics were similar at all physician satisfaction levels (Table 5).

There was a strong negative correlation between the duration of postoperative analgesia and the score on PS (r=0.835, p<0.001). The score on PS decreased with increasing duration of postoperative analgesia.

**Table 1:** Types of surgery operations

| | Unilateralhernia | | Bilateralhernia | | Undescended testis | | P |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | |
| **Sex** | | | | | | | |
| **Male** | 11 | 68,8% | 2 | 40,0% | 7 | 100,0% | **0,239** |
| **Female** | 5 | 31,3% | 3 | 60,0% | | | |
| **Block location** | | | | | | | |
| **Lateral** | 8 | 50,0% | | | 2 | 28,6% | |
| **Right** | 8 | 50,0% | | | 3 | 42,9% | **0,046** |
| **Bilateral** | | | 5 | 100,0% | 2 | 28,6% | |

**Table 2:** Postop: postoperative, PS: pain scala

| | Poor | | Moderate | | Good | | p |
|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD | |
| **Age** | 6,71 | 2,93 | 3,44 | 1,01 | 6,67 | 3,28 | **0,009** |
| **PS** | 5,86 | 1,21 | 2,11 | 1,9 | 0,92 | 0,67 | **<0,001** |
| **Postop analgesia duration (hour)** | 1 | 0 | 7,56 | 3,21 | 10,25 | 1,22 | **<0,001** |
| **Amount of postop analgesia (paracetamol mg.kg$^{-1}$)** | 9,71 | 0,76 | 9,78 | 0,67 | 9,67 | 0,78 | 0,939 |
| **Application block time (minute)** | 4 | 0,58 | 5 | 1,5 | 5,5 | 1,45 | 0,051 |

**Table 3:** Satisfaction of physician

| | | Satisfaction of physician | | | | | | P |
|---|---|---|---|---|---|---|---|---|
| | | Poor (n=4) | | Moderate (n=7) | | Good (n=17) | | |
| | | n | % | n | % | n | % | |
| **Sex** | **Male** | 3 | 15,0% | 6 | 30,0% | 11 | 55,0% | **0,422** |
| | **Female** | 1 | 12,5% | 1 | 12,5% | 6 | 75,0% | |
| **Drug Volume(ml kg$^{-1}$)** | **0,2** | 3 | 37,5% | 2 | 25,0% | 3 | 37,5% | **0,010** |
| | **0,3** | 1 | 10,0% | 4 | 40,0% | 5 | 50,0% | |
| | **0,4** | 0 | 0,0% | 1 | 10,0% | 9 | 90,0% | |

**Table 4:** Satisfaction of patient's companion

| | | Satisfaction of patient's companion | | | | | | P |
|---|---|---|---|---|---|---|---|---|
| | | Poor | | Moderate | | Good | | |
| | | n | % | n | % | n | % | |
| **Age** | **Male** | 6 | 30,0% | 6 | 30,0% | 8 | 40,0% | **0,470** |
| | **Female** | 1 | 12,5% | 3 | 37,5% | 4 | 50,0% | |
| **Volume(ml kg$^{-1}$)** | **0,2** | 4 | 50,0% | 2 | 25,0% | 2 | 25,0% | **0,027** |
| | **0,3** | 2 | 20,0% | 5 | 50,0% | 3 | 30,0% | |
| | **0,4** | 1 | 10,0% | 2 | 20,0% | 7 | 70,0% | |

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**Table 5:** Postop: postoperative, PS: painscala

| | Satisfaction of physician | | | | | | |
|---|---|---|---|---|---|---|---|
| | Poor (n=4) | | Moderate (n=7) | | Good (n=17) | | p |
| | Mean | SD | Mean | SD | Mean | SD | |
| **Age** | 6,75 | 3,3 | 4,57 | 2,64 | 5,82 | 3,11 | 0,340 |
| **Ps** | 6,25 | 1,5 | 4,43 | 1,4 | 0,88 | 0,7 | **<0,001** |
| **Postop analgesia time (hour)** | 1 | 0 | 3 | 2,24 | 10,18 | 1,19 | **<0,001** |
| **Amount of postop analgesia (paracetamol mg.kg$^{-1}$)** | 10 | 0 | 9,43 | 0,98 | 9,76 | 0,66 | 0,396 |
| **Application block time (minute)** | 4 | 0,82 | 4,57 | 1,51 | 5,35 | 1,37 | 0,072 |

## Discussion

The studies have indicated that 25% to 67% of patients receive insufficient therapy for pain. Insufficient pain control results in cardiac problems, such as cardiac hypertension, arrhythmia, and myocardial ischemia, pulmonary complications, are associated with insufficient cough and reduced respiratory movements, such as atelectasia, and prolongs the duration of hospital stay by reducing the response to therapy (4-5). Opioids possess side effects, including sedation, respiratory depression, pruritus, and nausea-vomiting, while neuro axial methods may result in complications like paraplegia or hemorrhage. USG-guided TAP block is used for analgesic purposes in patients undergoing lower abdominal surgery.

USG-guided TAP block can be performed before the induction of anesthesia or immediately before closure of the incision (6-7). In the present study, TAP block was performed before closure of the incision, as this gives a longer duration of postoperative analgesia.

Although TAP block could be performed using various anesthetic agents, such as ropivacaine, bupivacaine, levobupivacaine, chirocaine, and lidocaine, the present study used a mixture of lidocaine and bupivacaine due to the rapid onset of action for lidocaine and better safety profile of bupivacaine (8,9-10).

The finding that the scores on NPS were significantly higher in the group with the highest patient's companion and physician satisfaction score suggests that patients with lower postoperative pain score result in higher level of satisfaction in patient's companions and physicians. The finding that the duration of postoperative analgesia was significantly higher in physicians and patient's companions with the highest satisfaction score suggests that increasing duration of analgesia increased the level of satisfaction.

There is research that evaluated the optimal dose in pediatric cases and reported that levobupivacaine 0.2 ml.kg-1 provided the highest level of analgesia (11). One study that evaluated ilio-inguinal block versus TAP block in pediatric cases undergoing inguinal surgery used 0.3 ml.kg-1 lidocaine 1% added in equal volume to ropivacaine 1%.

Research on infants used 0.1 ml.kg-1 0.25% levobupivacaine 0.25% (12). In the study conducted by Sahin et al., 0.5 ml.kg-1 levobupivacaine 0.25% was found to be the most appropriate dose providing prolonged analgesia in patients undergoing inguinal hernia repair with USG-guided TAP block (13). In the present study, TAP block was performed at doses of 0.2, 0.3 and 0.4 ml.kg-1 (50:50, lidocaine 1% and bupivacaine 0.25%) and the satisfaction score of patient's companions and physicians increased with increasing drug volume, and this finding was statistically significant. The highest satisfaction score was observed with a drug volume of 0.4 ml.kg-1. A postoperative PS score of <4 was most commonly observed in patients who received a dose of 0.4 ml.kg-1. The lack of complications, such as nausea, vomiting, urinary retention, femoral nerve paresthesia, hematoma, and organ and tissue injury, in patients receiving TAP block indicates that ultrasound-guided TAP block is a safe procedure in pediatric cases.

## Conclusion

Postoperative pain control has a growing importance in pediatric cases. Despite the use of various drug volumes, the highest satisfaction scores in physicians and patient's companions and the longest duration of analgesia were achieved using a drug volume of 0.4 ml.kg-1 (lidocaine 1% and bupivacaine 0.25%) in pediatric cases undergoing inguinal hernia and undescended testis repair. The lack of any postoperative complications in the present study suggests that USG-guided TAP block could be a safe method for providing analgesia in pediatric patients in experienced hands. Further controlled studies are required to provide valuable insights into the relevant literature.

**Conflict of Interest:** The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Author's Contributions: OB, OHK, EB, MAK, NA:** Research concept and design; patient examination, data collecting, analysis and interpretation of data**. OB:** Preparation of article, Revisions. All authors approved the final version of the manuscript.

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# The effect of emotional intelligence on anger management among anesthesiologists, surgeons and internal medicine physicians

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## Abstract

**Objective:** Anger management among health professionals can lead to chaos in the hospital or operating room if administered poorly. Aim of the study is to investigate the effect of emotional intelligence level on anger control in physicians.

**Material and Methods:** Emotional intelligence (Reuven Bar-On) and anger control questionnaire (Spielberger) were performed on the voluntary physicians.

**Results:** The 188 voluntary physicians (internal medicine physicians n = 67, surgeons n = 64, anesthesiologists n = 57) were included in the study. Emotional intelligence and continuous anger scales did not differ between the three groups whereas the scores of external anger in surgeons and internal anger (repressed anger) in anesthesiologists were higher. Stress endurance in the surgical group, problem-solving and empathy in anesthesiologists and social responsibility in the internal physicians group were prominent. A positive correlation was observed between emotional intelligence and age, hobbies, physical activity and anger control, while there was negative correlation with external anger scores. Total group was divided into two groups in terms of age. In the group over 35 years old, the scores of continuous anger and external anger were lower, whereas the emotional intelligence was higher.

**Conclusion:** We conclude that emotional intelligence is effective in anger management. Higher age, more occupational experience, being more activities and having hobbies may be associated with better emotional intelligence and anger management in anesthesiologists and surgeons under stress in the operating room and internal physicians as well.

**Keywords:** Emotional intelligence, Anger management, Anesthesiologists, Surgeons, Physicians

## Introduction

Emotional intelligence (EI) is the ability to understand the feelings of the person himself and the people around him and manage them appropriately (1). Psychologist and author Daniel Goleman (2) popularized EI in the 1990s. He found that successful Fortune 500 leaders were distinguished by high EI. High EI persons seemed to perform better on the job and were effective leaders.

They also have higher mental health and less burnout scores. Goleman defined EI by five components: motivation, empathy, self-awareness, self-control and social skills (2).

Successful physicians should not only have high intelligence quotient, but must be able to successfully apply the information in patient care and, also work in harmony with their team and colleagues. This is possible with the development of emotional intelligence (1).

Aristoteles said that 'Anybody can become angry - that is easy, but to be angry with the right person and to the right degree and at the right time and for the right purpose - that is not within everybody's power and is not easy.'

As known, anger is a normal emotion but can cause chaos if administered poorly in the operation room. It is well known recognized that patient safety and quality of care depend on good communication and teamwork. Among surgeons and anesthesiologists anger management has gained great importance in recent years (3).

The aim of our study is to determine association of emotional intelligence in physicians working in different specialties with anger management. We also hypothesize that emotional intelligence may be associated with age, hobbies, physical activity and marital status.

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## Material and Methods

After the approval of the ethics committee (12.05.2017-E.27933) , emotional intelligence and anger control questionnaire was performed on the voluntary physicians (surgeon, anesthesiologist, and internal medicine) who work at university and state hospital in our city. Physicians who completed the study questionnaire were assigned to groups according to the specialties. Physicians who had worked general surgery, urology, obstetrics and gynecology, otorhinolaryngology, ophthalmology, orthopedics, neurosurgery, thoracic surgery and cardiovascular surgery were included in surgery group. Pulmonary diseases, cardiology, nephrology, public health, family medicine, dermatology, and oncology physicians were chosen as the internal medicine group. The last physician group was anesthesiologists. For the emotional intelligence questionnaire, emotional intelligence inventory developed by Reuven Bar-On (4) was adapted to Turkish by Acar (5). The Bar-On EQ scale consists of 133 questions. During adaptation study Acar et al. (5) reduced question number to 88 due to cultural differences. The 5-point Likert scale was used to evaluate up. (1 = Absolutely not, 5 = Absolutely agree). Mean scores of Likert scale was used for assessment of each parameter. Cronbach's Alpha internal consistency reliability coefficient $\alpha = 0.92$. Scores were given on the following 5 composite scales comprising 15 subscale scores (4-6).

The Cronbach-alpha reliability scores of "Continuous Anger and Anger Expression Scale" developed by Spielberger (7) and also adapted to Turkish by Özer (8) were determined between 0.73 and 0.84. Anger expression scale was collected in 3 topics; Internal anger (repressed anger) , external anger and anger control ".

### Statistical analysis

The Kolmogorov-Smirnov test was used to assess the normality of numeric variables. For the numeric variables that were normally distributed, comparison between groups was made by independent samples t test and one way ANOVA, and descriptive statistics are presented as mean±standard deviation.

For the numeric variables that were not normally distributed, comparison between two groups was made by Kruskal Wallis test and descriptive statistics are presented as median (minimum-maximum values). To analyze the categorical data, a chi-square test was used and descriptive statistics are presented as frequency (%).The Spearman's rank correlation looked for a relationship between total EQ and age, hobbies, physical activity, continuous anger, internal anger and external anger scores. The p values below 0.05 were considered statistically significant.

## Results

Questionnaire forms were given to 205 physicians.14 physicians did not want to fill out the questionnaire, and 3 physicians's in completed the questionnaire and they were extracted. Emotional intelligence and anger control questionnaire performed on the 188 voluntary physicians (internal medicine physicians n = 67, surgeons n = 64, anesthesiologists n = 57). Both residents and specialist physicians were participated in the questionnaire. Gender, marital status, hobby and physical activity were different in three physician groups. Emotional intelligence and continuous anger scales did not differ between the three groups. The scores of external anger in the surgical group and the scores of internal anger in anesthesiologist group were highest (Table 1 and 2). Stress endurance in the surgical group, problem-solving and empathy in anesthesia group and social responsibility in the internal physicians group were more (Table 2).

A positive correlation was observed between EI and age, hobbies, physical activity, and anger control while there was negative correlation with external anger scores ($p= 0.024$, $p=0.044$, $p=0.041$, $p=0.001$, and $p=0.037$ with respectively).

The 188 volunteers were also divided into two groups, over and under 35 years of age. In the group over 35 years old, the scores of continuous anger and external anger were lower, but the emotional intelligence was higher (Table 3).

**Table 1.** Emotional intelligence, demographics and social features of anesthesiologists, surgeons, and internal medicine physicians.

| | Anesthesiologists (n=57) | Surgeon (n=64) | Internal medicine physicians (n=67) | P value |
|---|---|---|---|---|
| Gender; Female | 52.6 | 25 | 34.3 | 0.001 |
| Male % | 47.6 | 75 | 65.7 | |
| Hobby; Absent | 8.8 | 29.7 | 25.4 | 0.014 |
| Present % | 91.2 | 70.3 | 74.6 | |
| Marital status | | | | |
| Single | 21.1 | 32.8 | 44.8 | 0.019 |
| Married % | 78.9 | 67.2 | 55.2 | |
| Physical activity | | | | |
| Absent | 31.1 | 39.1 | 37.2 | 0.07 |
| Present% | 78.9 | 60.9 | 62.7 | |
| Age (year) | 37.8 ±8 .6 | 36.8 ±9 .6 | 34.0 ±8 .9 | 0.056 |
| Years in the occupation | 13.8 ±8 .8 | 11.7 ±9.8 | 9.7 ±9 .1 | 0.125 |
| Emotional intelligence | 241.3 ±20 .8 | 239.8 ±19.7 | 242.7 ±22 .1 | 0.782 |

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**Table 2.** Empathy, stress tolerance, problem-solving, social responsibility, and anger scores of the anesthesiologist, surgeon, and internal medicine physicians

| | Anesthesiologists (n=57) | Surgeons (n=64) | Internal medicine physicians (n=67) | P value |
|---|---|---|---|---|
| Empathy | 14(9-19) | 12 (3-18) | 13 (5-18) | 0.041 |
| Problem solving | 12 (9-54) | 11 (5-16) | 11 (8-16) | 0.035 |
| Stress tolerance | 19 (11-25) | 22 (6-56) | 18 (10-26) | 0.017 |
| Social responsibility | 15 (6-19) | 15 (3-18) | 17 (11-21) | 0.028 |
| Continuous anger | 19 (11-36) | 20 (12-40) | 19 (10-37) | 0.052 |
| Inner anger* | 17 (12-28) | 15 (12-23) | 15 (11-24) | 0.044 |
| External anger* | 15 (8-22) | 18 (11-26) | 15 (10- 22) | 0.023 |
| Anger control* | 18 (11-23) | 16 (15-23) | 18 (12- 22) | 0.033 |

Scores are presented as median (minimum-maximum).

**Table 3.** Emotional intelligence, anger scores, demographics and social features in physicians over or under 35 years of age

| | Under 35 years (n=96) | Over 35 years (n=92) | P value |
|---|---|---|---|
| Gender Female | 53.1 | 42.4 | 0.148 |
| Male % | 46.9 | 57.6 | |
| Hobby Absent | 22.9 | 20.7 | 0.727 |
| Present % | 77.1 | 79.3 | |
| Marital status | | | |
| Single | 52.1 | 14.1 | 0.001 |
| Married % | 47.9 | 85.9 | |
| Physical activity | | | |
| Absent | 36.5 | 29.3 | 0.353 |
| Present % | 63.5 | 70.7 | |
| Emotional intelligence | 232.7 ±21 .5 | 242.6 ±19.3 | 0.039 |
| Continuous anger* | 20 (10-41) | 18 (12-36) | 0.037 |
| Inner anger* | 17 (14-28) | 16 (12-28) | 0.204 |
| External anger * | 16 (11-26) | 14 (8-22) | 0.001 |

*Scores are presented as median (minimum-maximum).

## Discussion

We concluded that the level of emotional intelligence positive correlated with age, anger control, having hobbies, and physical activity. Emotional intelligence and continuous anger scores did not differ between the three groups whereas the scores of external anger in surgeons and the scores of internal anger in anesthesiologists were highest.

Studies in the healthcare industry have suggested that high EI can lead to improved doctor–patient relationships, empathy, teamwork and communication skills (1,9,10) In a study of internal medicine residents, it was observed that EI improved after an academic year, resulting in better performance and lower burnout scores [11]. Tomar et al.(12) suggested that "experience is the best teacher". Physicians become more empathic, acknowledged, problem solving, good listener, and have patience and also improve their communication skills. These qualities enrich their emotional intelligence. In accordance with the literature, there was an increase in emotional intelligence in older physicians compared to younger in our study.

Our results indicate that total EI scores is not directly affected by gender, as noted in previous studies (13-15).

We observed that physicians' physical activity and having hobbies increases their level of emotional intelligence. Exercise on a regular basis may provide emotional benefits such as self-confidence and assertiveness, more positive body image, fewer phobias, reduced anxiety, less anger, and lower levels of depression. Many psychologists and physicians suggest exercise in addition to main treatment for emotional difficulties (16). Hobbies provide experience and success outside of medicine. Hobbies can lead to creativity. Furthermore hobbies encourage interaction with other people and provide some social opportunities. Hobbies allow our brain to focus on a task and help to calm down. When we learn something and gain a new skill, we improve our self-confidence (17).

The operating room is a stressful environment which includes time pressures, rapid changing conditions and hierarchical structure. Emotional intelligence combines, protects and enriches to the operation team.

Two single-institution studies found that EI scores were above or below average for general surgery and orthopedic residents, respectively, when compared to national norms (18,19). A study conducted by Stanton et al (20) in 2011 concluded that there was no overall difference in the emotional intelligence scores when compared psychiatrists with surgeons. The study found that psychiatrists scored higher in the areas of emotional self-awareness, empathy, impulse control and social responsibility. Jensen et al. also (21) conclude that surgical residents may score higher norm for stress tolerance, because surgeons are faced with more stress factors in their workplace than in the normal population. In their study, the surgical group scored higher in the areas of self-regard, stress tolerance and optimism. Similar to these result surgeons had more stress tolerance in according to our study.

The social responsibility scores in surgeons and anesthesiologists were lower compared to the internal medicine physicians in our study. As surgeons and anesthesiologists, it may be easy to get caught up in the operating room's busy schedule and miss many social and family activities (21).

Empathy involves understanding another person's perspectives and the capacity to communicate and understanding. In our study, empathy scores were higher in the anesthesiologists compared to others groups. Anesthesiologists' have interpersonal good communication skills such as emphaty create a positive impression on surgical colleagues and patients. A communication done with empathy can act as a vocal anxiolytic (22). Hojat et al. (23) found that women were more empathic than men. In our study there were more female physicians in anesthesiology group. Higher empathy score in anesthesiologists in our study may be relevant by these factors.

Anesthesiologists and surgeons are likely to have more anger level because of closed working conditions with stressful patients for long hours. In our study, there were more external reflected anger scores in surgeons, while anesthesiologists had more inner anger scores.

Rosenstein and O'Daniel (24) investigated implications of disruptive behavior in the perioperative arena. They conclude that disruptive behavior by anesthesiologists was lower than surgeons. They mention that: 'Some surgeons seem to believe that they have the right to be rude, verbally abusive, and disrespectful to non-physicians.'

Inner anger has been associated with many physical disorders such as hypertension, coronary artery disease, cancer. Long working hours and stressful job and the psychological dynamics may have influence on depression. Indeed anesthesia specialists are higher risk among the specialists in terms of prevalence of burnout (25).

The limitation of our study was that our study group was not homogeneous in terms of specialty areas, gender and occupational year.

## Conclusion

We conclude that emotional intelligence is effective in anger management. Higher age, more occupational experience, being more active and having hobbies may be associated with better emotional intelligence and anger management in anesthesiologists and surgeons under stress in the operating room and internal physicians as well.

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**Conflict of Interest:** The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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**Ethical issues:** All Authors declare, Originality and ethical approval of research. Responsibilities of research, responsibilities against local ethics commission are under the Authors responsibilities. The study was conducted under defined rules by the Local Ethics Commission guidelines and audits.

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# Impact of menopause on quality of life: A cross sectional study in menopausal females'

**Lama Al-Mehaisen[1*], Oqba Al-kuran[2]**

## Abstract

**Objective:** Menopause can severely effects the somatic, urogenital and psychological aspects of life, our aim is to find out the Health Related Quality of Life in female patients with menopause in a tertiary care hospital.

**Methods**: A cross-sectional, observational study was conducted in the Gynecology out-patient department. All female patients with menopause attending the Gynecology OPD of tertiary care hospital for various complaints were included in the study. After obtaining written informed consent, demographics, relevant medical and surgical history was noted and they were then administered validated questionnaire 'Health related Quality of Life Questionnaire: Menopause Rating Scale' (HRQoL).

**Results:** The overall population sample size was 409. The mean age of menopause was 48.91± 4.76 years. Hot flushes and sweating (somatic symptom) were the commonest symptom (86.31%), followed by anxiety (psychological symptom) in 76.53%. Maximum score was attributed to psychological symptoms, while urogenital domain had the minimum score. The association between the duration of menopause (early versus late post-menopause) and severity of symptom complex was found to be significant in psychological symptoms only. Frequency of psychological symptoms decreased as the duration since onset of menopause increased. Occurrence of somatic and urogenital symptoms is not significantly associated with duration of menopause.

**Conclusion:** Menopausal symptoms commonly affect a large number of early and late post-menopausal women and adversely affect health related quality of life. Menopausal symptoms are common in postmenopausal women and except psychological symptoms there is minimal difference in the frequency and severity of other symptoms with duration.

**Keywords:** Menopause, Quality of life questionnaire, Menopause Rating Scale, Quality of life

## Introduction

Menopause is a universal phenomenon for women. It is a biologic process, characterized by fall in estradiol and progesterone levels, increases in follicle stimulating hormone, as well as a life stage, characterized by changing roles such as the end of childbearing potential and children leaving home. While the biologic impact of menopause is well characterized, the impacts of menopause on a woman's function and well-being, or quality of life, are less clear. The interest of clinical research in aging women increased in recent years and thereby the interest to measure health-related quality of life (HRQoL) and symptoms (1).

These hallmark symptoms of menopause are caused in part by changes in reproductive hormone levels. Early in the menopause, most women experience hot flashes, which can persist for more than 5 years.

Symptoms experienced with the menopausal transition and early postmenopause are varied and span both physical and psychological domains. Anovulatory cycles and ovarian failure may be accompanied by a multiplicity of physical symptoms. Vasomotor symptoms, including hot flashes and night sweats, sleep disturbances, vaginal dryness, urinary incontinence, and weight gain, are common physical conditions experienced by women in the transition through menopause and during menopause.

Psychological symptoms frequently associated with menopause include fatigue, irritability, and anxiety. Not all women who experience hot flashes, however, report them as bothersome. In the later stages of menopause and persisting until death, women can experience vaginal dryness; bother associated with vaginal dryness has not been well studied (2)

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Some studies have shown that the early menopause and late menopause negatively impacts HRQoL, while others have found no impact of menopausal status alone, but rather an impact of menopausal symptoms on HRQoL. Few empirical studies, however, have examined the interrelated nature of symptoms associated with the menopausal transition and early post-menopause and the effects of those symptom groups on quality of life. In some chronic diseases, symptoms may have greater impact when they co-occur in distinct clusters; this impact is referred to as 'symptom experience'. It is important to understand symptom experience during the transition through menopause and early post-menopause because of the large number of symptoms that may co-occur (3)

Studies find that most women experience at least one or more of these symptoms as they transition through the postmenopausal stage of life. Recently, the Study of Women's Health Across the Nation (SWAN), a community-based sample of women across the menopausal transition, found a negative impact of menopausal symptoms on HRQoL and much less of an impact of menopausal status (4). Overall, studies that draw from populations of women seeking care for menopausal symptoms have shown a negative impact of later menopausal stage on HRQoL, while general population studies have either reported a negative impact only of menopausal symptoms, but not status, on HRQoL or failed to find any impact of menopause at all (5)

Quality of life is a broad, multidimensional concept that lacks a precise definition in the medical literature. The World Health Organization has defined quality of life as 'Individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns. Quality of life tends to decline in older women, and there is a need to determine what role, if any, symptoms commonly associated with early and post-menopause play in this phenomenon. Quality of life is an important outcome measure of health care, and understanding the impact of menopause on quality of life is a critically important part of the care of symptomatic postmenopausal women (6)

Symptom experience includes perception of, evaluation of, and response to a symptom. Symptom evaluation occurs when individuals make a judgment about the severity, cause, treatability, and effects of a particular symptom on their life. Understanding symptom experience is important in the evaluation and mitigation of negative effects on health and quality of life. Symptom experience may be influenced by the fact that women often report experiencing multiple symptoms associated with menopause (7)

The Menopause Rating Scale (MRS) is a health-related quality of life scale (HRQoL) and was developed in response to the lack of standardized scales to measure the severity of aging-symptoms and their impact on the HRQoL (8)

Understanding the impact of menopause on HRQoL is important as our population ages. Despite a majority of women experiencing multiple symptoms, the literature still presents a gap on whether clusters of symptoms consistently occur and what effect symptom clusters have on quality of life. In this study of menopausal patients in a tertiary care setting, we examine overall frequency of symptoms and the impact of menopausal status alone, or in the context of menopausal symptoms, on HRQoL.

## Materials and methods

**Study design:** This was a cross-sectional, observational study conducted in the Gynecology out-patient department (OPD) of tertiary care hospital, from ___September 2013 to sept 2014.

**Ethics:** Ethics Committee permission was obtained prior to commencement of the study. Written informed consent was obtained from all the women prior to their inclusion in the study.

**Study population:** All clinically diagnosed menopausal women, attending the Gynecology OPD of –Jordan University of science and technology teaching hospital for various complaints were included in the study. After obtaining written informed consent, demographics, relevant medical and surgical history was noted. They were then administered a validated questionnaire 'The Menopause Rating Scale' which is a Health Related Quality of Life Questionnaire' (HRQoL) by the same medical person.

**HRQoL Questionnaire:** 'The Menopause Rating Scale' (MRS) is a patient reported HRQoL questionnaire (9). It was divided into 3 subscales with a total of 21 items pertaining to the symptoms of urinary incontinence:

1) Psychological symptoms: 0 to 16 scoring points ( 4 symptoms: depressed, irritable, anxious, exhausted)

2) Somato-vegetative symptoms: 0 to 16 points (4 symptoms: sweating/flush, cardiac complaints, sleeping disorders, joint & muscle complaints)

3) Urogenital symptoms: 0 to 12 points (3 symptoms: sexual problems, urinary complaints, vaginal dryness).

**Scoring by HRQoL:** Each item was to be scored on a 5-point Likert scale of 0 (not at all) to 4 (very severe). A median score for each subscale is calculated (averaging the scores as well as a total score for all 11 items (sum of all subscale scores). The score increases point by point with increasing severity of subjectively perceived complaints in each of the 11 items. The total score of the MRS ranges between 0 (asymptomatic) and 44 (highest degree of complaints).

**Interpretation of HRQoL:** For all items, higher scores indicated higher impact of menopausal symptoms on quality of life.

**Statistical analysis:** Categorical variables were described using frequencies and percentages; continuous variables were described using mean and standard deviation (SD) if normal, and range and median if non-normal. Comparison of groups and categorical variables (cross-tabulation) was conducted using chi square if the variable was binomial. An

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α of 0.05 was considered statistically significant. All statistical analysis was conducted using IBM SPSS Statistics 19.0 (IBM, Chicago, IL) using 2-tailed tests.

**Sample size:** No formal sample size was calculated for this study. All menopausal women visiting the Gynecology OPD were sequentially enrolled in the study with no previous medical or surgical illnesses causing such complaints

## Results

Total number of women studied was 409. The age-wise distribution of post-menopausal women is outlined in Table1. The mean age at which menopause was attained was 48.91 years, with an SD of 4.76 years.

**Table 1:** Age-wise distribution of the post-menopausal women

| Age (years) | No. of women |
|---|---|
| **40 and below** | 4 |
| **41-60** | 269 |
| **61-80** | 134 |
| **81 and above** | 2 |
| **Total** | **409** |

Women were classified as per the time since menopause, as early postmenopausal (if their last menstrual period [LMP] was between 12 months and 5 years ago) and late post-menopausal (if their LMP was 5 or more years ago.

The number of women having early menopause were 124 whereas 285 women had late post-menopause.

Symptoms of menopause were experienced by women. The frequency of these symptoms is shown in Table 2. Hot flushes and sweating (somatic symptom) were the commonest symptom (86.31%), followed by anxiety (psychological symptom) in 76.53%.

The median grade of each of the symptoms and the sum-score of the domain is also shown in Table 2. Maximum score was attributed to psychological symptoms, while urogenital domain had the minimum score.

It was analyzed whether the presence or absence of symptoms from various domains was associated with the duration of menopause.

The association between duration of menopause and somatic symptoms is shown in Table 3. The p-value obtained was 0.0806, indicating that occurrence of somatic symptoms is not significantly associated with duration of menopause.

The association between duration of menopause and psychological symptoms is shown in Table 4. The p-value obtained was 0.04, indicating that there is significant association between occurrence of psychological symptoms and duration of menopause.

As per Table 4, we found that the frequency of psychological symptoms decreased as the duration since onset of menopause increased

**Table 2:** Frequency and scores of menopausal symptoms

| Domain | Menopausal symptoms | No. of women | Percentage | Median score (Range) | Sum-score |
|---|---|---|---|---|---|
| Somatic | Hot flushes, sweating | 353 | 86.31 | 4 (0-4) | 8 |
| | Heart discomfort | 193 | 47.19 | 0 (0-4) | |
| | Sleep problems | 251 | 61.37 | 2 (0-4) | |
| | Joint and muscular discomfort | 249 | 60.88 | 2 (0-4) | |
| Psychological | Depressive mood | 258 | 63.08 | 2 (0-4) | 10 |
| | Irritability | 290 | 70.90 | 2 (0-4) | |
| | Anxiety | 313 | 76.53 | 3 (0-4) | |
| | Physical and mental exhaustion | 288 | 70.42 | 3 (0-4) | |
| Urogenital | Sexual problem | 92 | 22.49 | 0 (0-4) | 4 |
| | Bladder problem | 206 | 50.37 | 1 (0-4) | |
| | Dryness of vagina | 261 | 63.81 | 3 (0-4) | |

**Table 3:** Association between duration of menopause and somatic symptoms

| | At least one somatic symptom present | Somatic symptoms absent | Total |
|---|---|---|---|
| Early post-menopausal | 22 | 102 | 124 |
| Late post-menopausal | 75 | 210 | 285 |
| Total | 97 | 312 | 409 |
| p=0.0806, using chi-square test. There is no significant association between duration of menopause and the number of postmenopausal women who experience at least one somatic symptom | | | |

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**Table 4:** Association between duration of menopause and psychological symptoms

| | At least one psychologic symptoms present | Psychologic symptoms absent | Total |
|---|---|---|---|
| Early post-menopausal | 63 | 61 | 124 |
| Late post-menopausal | 112 | 173 | 285 |
| Total | 175 | 234 | 409 |
| p=0.04, using chi-square test. There is significant association between the duration of menopause and number of women experiencing psychological symptoms | | | |

**Table 5:** Association between duration of menopause and urogenital symptoms

| | At least one urogenital symptom present | Urogenital symptoms absent | Total |
|---|---|---|---|
| Early post-menopausal | 19 | 105 | 124 |
| Late post-menopausal | 37 | 248 | 285 |
| Total | 56 | 353 | 409 |
| p=0.6339, using chi-square test. There is no significant association between duration of menopause and the number of postmenopausal women who experience at least one urogenital symptom | | | |

The association between duration of menopause and urogenital symptoms is shown in Table 5. The p-value obtained was 0.6339, indicating that occurrence of urogenital symptoms is not significantly associated with duration of menopause.

## Discussion

Menopause which is defined as complete cessation of menstruation for twelve months or more is a normal physiological change experienced by middle age women. Some of menopausal symptoms experienced by these women can be severe enough to affect their normal daily activities. Unfortunately majority of these women are not aware of the changes brought about by menopause (10).

The assessment tool that we used in our study was based on Menopause Rating Scale (MRS) questionnaire. Although in menopausal symptoms studies few assessment tools were available, we used the Menopause Rating Scale (MRS) questionnaires, these questionnaires has been widely used in many epidemiological and clinical research when investigating the menopausal symptoms, These questionnaires has been validated and translated in many languages, although it is a self-administrated questionnaires, it's used were not only meant to assess the menopausal symptoms but also its severity, however, in our study, modification has to be done on the scaling of the original MRS because we noted that the respondents had difficulties in rating the scales, this could be explained by the fact that nearly half of the respondent studied never had formal education or only studied at primary level, and to minimize the reporting error, face to face interviewed were used instead of self administered by the respondents (11)

In this study hot flushes and sweating (somatic symptom) were the commonest symptom (86.31%).

The association between the duration of menopause and severity of symptom complex was found to be significant in psychological domain. Frequency of psychological symptoms decreased as the duration since onset of menopause increased. Occurrence of somatic and urogenital symptoms was not significantly associated with duration of menopause.

The duration, severity and impact of menopausal symptoms vary greatly from person to person and population to population. Some population-based surveys, largely conducted among Caucasian subjects, have reported a high prevalence of menopausal symptoms at between 40% and 70% (12). Conversely, studies of Asian women from differing ethnic backgrounds have reported lower symptom prevalence of between 10% and 50% (13)

Rather than imply that the physiologic changes of menopause are intrinsically causing a decrement in HRQoL, we interpret these data as evidence that other changes that may occur concurrent to menopause, beyond hot flashes and vaginal dryness, and need to be examined. In this study several potentially important variables that can change with aging were not examined such as changes in intimate relationships (e.g., changes in sexual activity due to self or partner functioning), alterations in sleep patterns, changes in caregiving responsibilities, and severity of chronic medical conditions (e.g., worsening of pulmonary disease, progression of arthritis). Nonetheless, the decrement in HRQoL associated with menopausal status in our study is similar to decrements seen with other health conditions.14 While some of the decrement is related to hot flashes, which may improve, the vaginal dryness associated with the menopausal transition does not spontaneously resolve.

Physicians and patients should be attentive to the declines in HRQoL in menopausal women, and not just expect that they will get better when hot flashes resolve. Practitioners and patients should continue to examine to other aspects of women's lives beyond menopausal symptoms that occur simultaneously and may be amenable to intervention.

These analyses have a number of limitations that deserve mention. Our study participants were enrolled from a single tertiary care practice. While tertiary care is not menopause-specific care, it may not represent the broader population including women who chose not to access private health care.

The MRS scale is a standardized HRQoL scale with good psychometric characteristics. Among women accessing tertiary care, transitioning into the menopause, regardless of the presence of its hallmark symptoms of hot flashes and vaginal dryness, is associated with a decrement in HRQoL. Clinicians and women should be aware of this impact and work to improve HRQoL, as opposed to expecting HRQoL to spontaneously improve when symptoms resolve. Researchers need to look beyond the classic menopausal symptoms to a more comprehensive biopsychosocial model in order to better understand decline in HRQoL during the menopause.

## Conclusion

To conclude menopausal symptoms commonly affect a large number of early and post-menopausal women and adversely affect health related quality of life. Menopausal symptoms are common in postmenopausal women and except psychological symptoms there is minimal difference in the frequency and severity of other symptoms with duration.

**Conflict of Interest:** The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Author's Contributions: LA, OA:** Protocol or project development, Data collection or management **LA:** Data analysis Manuscript editing or writing, Revisions. All authors approved the final version of the manuscript.

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# Relationship of Total Antioxidant Capacity and Endothelin-1 levels in prehypertensive individuals among population attaining a sedentary lifestyle in central India

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## Abstract

**Objective:** As known, hypertension has relation with increased peripheral vascular resistance. Vascular tone is regulated by multiple mediators; among them is Endothelin-1. Endothelin-1 (ET-1) is one of the most potent vasoconstrictors known to date. While its plasma /serum concentrations are elevated in some forms of hypertension. Prehypertension is one step towards hypertension, hence the same factor is involved in it. Oxidative stress is also found to be involved in pathogenesis of hypertension .Therefore our present study is designed to find the relationship between ET-1 levels and Total antioxidant capacity (TAC) in Prehypertension.

**Methods:** Total 100 prehypertensive cases and 100 sex matched controls were enrolled in this study. Inclusion criteria include patients with systolic blood pressure (SBP) in the range of 120 to 139 mmHg and diastolic blood pressure (DBP) in the range 80-90 mmHg, while patients with BP ⩾140/90 mmHg, diabetes mellitus (DM), Stroke, coronary artery disease (CAD) and myocardial infarction (MI) were excluded. Plasma ET -1 and plasma total antioxidant capacity were measured .We estimated ET -1 levels and TAC levels in Prehypertensive cases and Normotensive controls. Students T test were used for statistical analyses.

**Results:** Plasma ET -1 levels were found significantly (p:0.001) higher in prehypertensive cases as compared to normotensive controls. In contrary to this, Plasma Total Antioxidant capacity was found extremely significantly lower in prehypertensive cases as compared to normotensive controls($p<0.0001$).

**Conclusion:** The study demonstrated that in Prehypertensives, there is an inverse relationship between Endothelin -1 and Total antioxidant capacity.

**Keywords:** Endothelin-1, Total Antioxidant Capacity, DBP, SBP

## Introduction

Recently, the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (1) suggested a new classification for borderline blood pressure levels, the "pre-hypertension". The new classification describes people with blood pressures between 120 and 139mmHg systolic or between 80 and 89mmHg diastolic blood pressures. This "new" category between normal blood pressure and established hypertension includes a population at high risk for developing hypertension and in which lifestyle modifications are needed (2).

Despite the high prevalence and intense efforts, understanding of the pathogenesis of essential hypertension is still limited (3). Among other mechanisms, hypertension has been associated with increased peripheral vascular resistance. Vascular tone is regulated by multiple mediators, among them endothelin-1(4).

Endothelin-1 is a 21-amino-acid peptide that is produced by vascular endothelial and smooth muscle cells. Endothelin-1 (ET-1) has potent vasopressor effects (5,6) and may therefore play a part in the regulation of blood pressure (BP) and in the pathogenesis of hypertension. An association between elevated circulating ET-1 levels and

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essential hypertension has been noted in several (7,8,9) but not in all studies (10).

The determination of total antioxidant capacity is now considered as a tool in medical diagnosis and treatment of several diseases, including cardiovascular disease, cancer, diabetes mellitus and aging 11.Total antioxidant capacity (TAC) considers the cumulative action of all the antioxidants present in plasma and body fluids and provides an integrated parameter rather than the simple sum of measurable antioxidants. There is now a wide range of evidence indicating the importance of TAC in plasma and tissues and its modification during oxidative stress development, as well as its feasibility as a tool for investigating the association between diet and oxidative stress12.Therefore the aim of our present study was to determine the relationship between Endothelin 1 levels and total antioxidant capacity in prehypertensive subjects.

## Materials and methods

This observational case control study was undertaken in the Department of Medical Biochemistry, Gandhi Medical College, Bhopal (M.P.) in association with Department of Medicine, Hamidia Hospital, Bhopal (M.P.), between January 2013 and December 2014 after approval from institutional ethical committee for biomedical research. The study included 100 prehypertensive patients diagnosed on the basis of clinical findings and having blood pressure in the range of 120 to 139 mmHg and DBP in the range 80-90 mmHg. The control group included 100 healthy normotensive individuals of both sexes. Fasting Blood samples were collected before giving any antioxidant drug/anti hypertensive treatment for the last 12 hrs for the estimation of TAC& Endothelin -1 levels. All the volunteers were well informed about the experimentation and their written consent was obtained, while patients with BP ⩾140/90 mmHg , DM, stroke, CAD and MI were excluded.

**Measurement of blood pressure:** Each subject was seated in a quiet and comfortable position for five minutes and BP was measured, five minutes apart with a mercury sphygmomanometer (cuff size 12.5X40 cm) with auscultator method of BP measurement.

**Sample collection:** Fasting blood samples were obtained by vein puncture of anticubital vein .5 ml of blood was taken in plain vials. The blood samples were centrifuged at 3000 RPM for 10 min .After which the serum was separated for the estimation of Total antioxidant capacity and Endothelin-1 level.

**Determination of Total Antioxidant Capacity (D. Koracevic et al method, 2001)(13).**

A standardized solution of Fe–EDTA complex reacts with hydrogen peroxide by a Fenton type reaction, leading to the formation of hydroxyl radicals (OH*).These ROS degrade benzoate ,resulting in the release of Thiobarbituric Acid Reactive Substances .

Antioxidants from the added sample of human fluid cause suppression of production of TBARS .This reaction can be measured spectrophotometrically at 530 nm and the inhibition of color development defined as AOA.

Reagents- Sodium phosphate buffer :100 mmol/l, pH7.4,Sodium benzoate:10 mmol/l, Na OH ; 50 mmol/l, EDTA (Solution), Fe $(NH_4)_2SO_4$:2mmol/l, Fe-EDTA complex (prepared freshly $H_2O_2$: 10mmol/l, Acetic acid:20%, Thiobarbituric acid (TBA):0.8% (w/v) in 50 mmol/l NaOH, Uric acid :1 mmol/l in 5 mmol/l NaOH. (all the above chemicals are supplied by thermofisher scientific).

Incubate for 10 min at 100˚C (in boiling water bath) then cooled in an ice bath, measure absorbance at 532 against deionized water.

**Calculation:** TAC (mmol)= [CUA x (K-A) ]/(K-UA)

Where, K=absorbance of control ($K_1$-$K_0$), A=absorbance of sample ($A_1$-$A_0$), UA=absorbance of uric acid solution ($UA_1$-$UA_0$), CUA=concentration of uric acid (in mmol/l)

Pipette into tubes (in milliliters) as follows:

| | $A_1$ | $A_0$ | $K_1$ | $K_0$ | $UA_1$ | $UA_0$ |
|---|---|---|---|---|---|---|
| Serum | 0.01 | 0.01 | - | - | - | - |
| Uric acid | - | - | - | - | 0.01 | 0.01 |
| Buffer | 0.49 | 0.49 | 0.50 | 0.50 | 0.49 | 0.49 |
| Na benzoate | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 |
| Acetic acid | - | 1.00 | - | 1.00 | - | 1.00 |
| Fe EDTA | 0.20 | 0.20 | 0.20 | 0.20 | 0.20 | 0.20 |
| $H_2O_2$ | 0.20 | 0.20 | 0.20 | 0.20 | 0.20 | 0.20 |
| Incubate for 10 minutes at 100˚C (in boiling water bath) then cooled | | | | | | |
| Acetic acid | 1.00 | - | 1.00 | - | 1.00 | - |
| TBA | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |

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**Estimation of Endothelin -1 levels by ELISA Method**

The Endothelin-1 ELISA Kit is a solid-phase sandwich Enzyme-Linked Immunosorbent Assay (ELISA). This assay is designed to detect and quantify the level of endothelin-1 in serum, EDTA and heparin plasma.Endothelin-1 (ET-1) is a pleiotropic molecule of 21 amino acid residues involved in cardiac and vascular function, and inflammatory responses. It is highly expressed in the vascular endothelium, and also produced by leukocytes, smooth muscle cells, mesangial cells, cardiac myocytes, and astrocytes.

**Statistical analysis:** Statistical Analysis was carried out by using student's unpaired't' test .The $p<0.0001$ was extremely considered significant.

**Limitation of the study:** Test samples were collected from patients who attended the OPD of Medicine and diagnosed as prehypertensives. This study was subjected to 100 prehypertensive cases within 30-60 years of age. The laboratory of biochemistry department is well equipped with ELISA, Semiautoanalyser, colorimeter and spectrophotometer. All investigation methods used in this study are standardized in our laboratory.

## Results

**Table 1:** shows the classification of hypertension, which is classified into Prehypertension and Hypertension. According to the JNC VII hypertension is classified as Prehypertension, stage 1 and stage 2.

| | Systolic (mm Hg) | Diastolic (mm Hg) |
|---|---|---|
| **Normal** | <120 | <80 |
| **Prehypertension** | 120-139 | 80-89 |
| **Stage 1 hypertension** | 140-159 | 90-99 |
| **Stage 2 hypertension** | ≥160 | ≥100 |

**Table 2:** Shows demographic and anthropometric parameters of study population

| Variables | Normotensives (n=100) | Prehypertensives (n=100) | P value |
|---|---|---|---|
| | 32.96±6.12 | 42.52±8.74 | <0.0001** |
| **Sex (M/F)** | 55/45 | 53/47 | --- |
| **Weight (kg)** | 67.57±7.39 | 71.23±5.95 | <0.001* |
| **Height (cm)** | 166.70±6.23 | 162.47±4.51 | <0.0001** |
| **BMI (kg/m$^2$)** | 24.20±1.47 | 25.43±1.62 | <0.0001** |
| **Waist-Hip ratio** | 0.91±0.02 | 0.92±0.02 | <0.001* |
| **Obesity (%)** | 61% | 65% | --- |
| **SBP** | 118.7±4.89 | 128.46±6.04 | <0.0001** |
| **DBP** | 77.67±5.94 | 83.26±3.06 | <0.0001** |

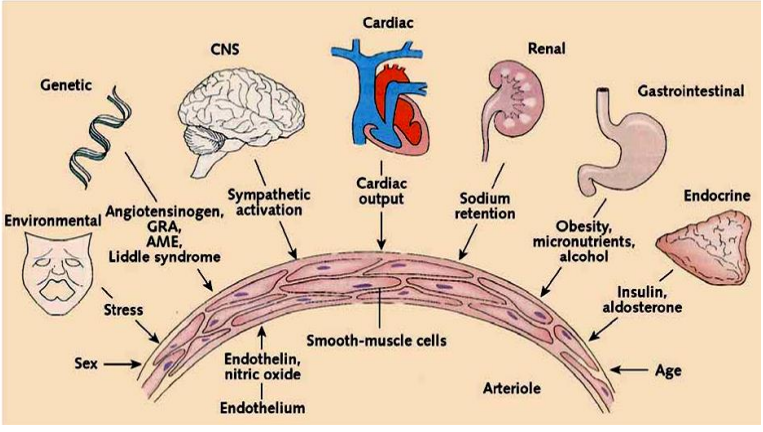
(** depicts extremely statistically significant,*depicts statistically significant)

**Table 3:** shows Endothelin -1 levels and Total Antioxidant Capacity in study population

| Variables | Normotensives(n=100) | Prehypertensives (n=100) | P value |
|---|---|---|---|
| | 3.50 ± 1.78 | 4.52 _±2.29 | <0.001* |
| | 1.94±1.35 | 1.32±0.51 | <0.0001** |

(** depicts extremely statistically significant,*depicts statistically significant)

**Figure 1:** shows the role of Endothelin in pathogenesis of hypertension**.**



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ET-1 a peptide isolated from the media of cultured vascular endothelial cells exerts marked vasomodulatory, with mainly vasoconstrictive effects (5) and may represent a major factor in the regulation of BP. The presence in plasma of ET-1 raises the possibility that an excess in production of this substance may play a role in the development or maintenance of hypertension (14).

The sex-specific distribution of several demographic and anthropometric parameters is presented in Table II.We observed that normotensive subjects were at extremely statistically significantly younger age as compared to prehypertensives and hypertensives (p<0.0001).Among 100 prehypertensive subjects 53 were men and 47 were women. Moreover pre-hypertensive participants were more frequently obese as compared to normotensive. Systolic blood pressure of normotensive individuals was found 118.7+4.89 mmHg while in prehypertensives it was 128.46+6.04 mmHg which was extremely statistically significantly (p<0001) higher. Similarly, Mean Diastolic blood pressure of normotensive individuals was found 77.67+5.94 mmHg while in prehypertensives it was mean 83.26+3.06mmHg which was extremely statistically significantly (p<0001) higher.

Comparison of Total Antioxidant Capacity and Endothelin-1 levels were shown in Table 3. It was also cleared by Figure 2 that ET-1 levels in prehypertensives (4.52±2.29 ) were statistically significantly higher than normotensives (3.50±1.78). In contrary to this, TAC was found lower in prehypertensives

(1.32±0.51) as compared to normotensives (1.94±1.35). Difference found was extremely statistically significant (p<0.001). Therefore,it can be illustrated that there is an inverse relationship between Endothelin 1 levels and Total antioxidant capacity. An association was found between hypertension status, total antioxidant capacity and Endothelin 1 levels.

## Discussion

Since the discovery of endothelium –dependent relaxation of vascular smooth muscle (15) vascular endothelium has been recognized as an important functional unit involved in the regulation of vascular smooth-muscle tone. Relaxation results from release of a labile endothelium derived relaxing factor probably identical to nitric oxide(16,17). In addition to endothelium derived vasoconstriction factors, with a characteristically slow onset and long duration of action have also recently been demonstrated (17,18,19,20).

In this work we revealed the differences in the levels of Endothelin-1 which has potent vasopressor effect and oxidative stress markers between prehypertensive subjects and normotensive subjects, without any clinical evidence of cardiovascular and metabolic disorders. The data that emerged from our study demonstrated that in prehypertensives the serum Endothelin levels were significantly increased respect to normotensives.While Total antioxidant capacity was found extremely significantly decreased in prehypertensives compared to normotensives.Moreover we found a negative correlation between ET-1 levels and TAC in patients with prehypertension.

Due to our results, normotensive controls and in prehypertensive cases were similar to those reported by previous investigators (9,10,20). In our study, TAC was found 1.32±0.51 mmol/l among prehypertensive cases. It was hypothesized that high blood pressure which is the clinical manifestation of hypertensive, is associated with loss of balance between per oxidation and various antioxidant factors which are reactive oxygen species (Krouf et al., 2003) (23). The difference was statically highly significant when compared to controls S.C. Onuoha et al (2012) reported it as 1.70±0.05 mmol/l (25).

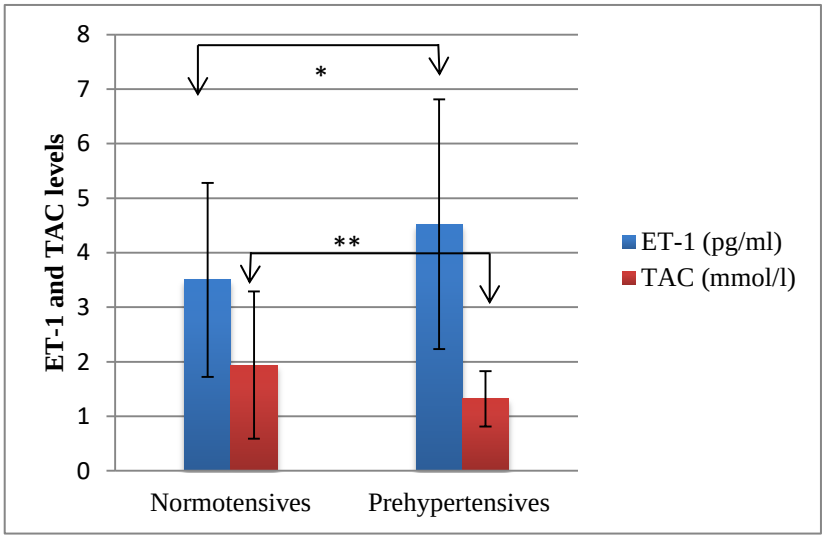


**Figure 2:** The comparision of Endothelin -1 levels and Total Antioxidant Capacity in Normotensives and Prehypertensives.

In hypertensive patients, the relative increase of forearm blood flow in response to nonselective endothelin-1 antagonists appears to be larger when compared with prehypertensive patients. Previous studies have shown an increase in forearm blood flow of 65% to 80% from baseline after endothelin-1 antagonism in hypertensive patients, whereas in prehypertensive subjects, increases of about 30% were demonstrated in the study presented by Weil et al. (7,8,16). These results suggest that prehypertension might be a less pronounced, intermediate stage of endothelial dysfunction.In our study, ET-1 levels were found to be 4.52 ±2.29 pg/ml in prehypertensives where as Letizia et al (1997) reported it as 10.4±3.4 pg/ml in hypertensives (25).

## Conclusion

We revealed a relationship between pre-hypertension status, Endothelin-1 levels

and oxidative markers among cardiovascular disease free adults, independently of other coexisting risk factors or sedentary lifestyle behaviors. This evidence may suggest that excessive production of oxidative markers could be an early event in the pathogenesis of hypertension, preceding excess rise in blood pressure levels and could also be an element that contributes to vascular injury. However, the opposite relationship of Endothelin levels and total antioxidant capacity also be supported. Since endothelial dysfunction is a well-known predictor of cardiovascular events, the confirmation of its existence in prehypertensive subjects emphasizes that prehypertension is not a benign condition. Furthermore, increased levels of endothelin-1 can lead to increased arterial stiffness and vascular remodeling via induction of vascular smooth muscle proliferation (21,22). Thus, enhanced activity of endothelin-1 in prehypertensive patients not only may result in increased vascular tone but also may be involved in the structural changes. Therefore in this present study it is conceivable that in prehypertensives with low antioxidant capacity increased Endothelin levels may induce hypertension.

In conclusion, the result of this work demonstrates an inverse relationship of Endothelin-1 levels and Total antioxidant capacity which may play a role in the pathogenesis of hypertension.

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