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IN PATIENTS WITH THYROID DYSFUNCTION**



**Priyanka Kumari, Nagraj Soni\* and G G Kaushik**

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## RESEARCH ARTICLE

# STUDY OF SERUM OSTEOPONTIN AND OTHER PARAMETERS IN PATIENTS WITH THYROID DYSFUNCTION

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### ABSTRACT

**Background:** Osteopontin (OPN) is a glycoprotein. It is found in several biological fluids. OPN can be detected in plasma or serum, was found to be upregulated in several patients with hyperthyroidism and down regulated in hypothyroid patients so it may represent a new biomarker. **Objective:** The objective of this study was designed to investigate the evaluation of serum osteopontin levels with clinical parameters of thyroid hormone dysfunction. **Materials and Methods:** The present study was conducted on 50 hypothyroid (Group II) and 50 hyperthyroid (Group III) patients attending the Medical OPD and Radio Immuno Assay (RIA) Laboratory of the Biochemistry Department of JLN Medical College & Hospital, Ajmer. The results of patients were compared with 50 healthy control (Group I) subjects of either sex of age group (15-55 years). Serum levels of FT3, FT4 and OPN were measured by ELISA and TSH was measured by RIA method, after taking approval from ethical committee. **Results:** The mean serum Osteopontin (OPN) level was observed statistically highly significant increase ( $p$  value  $< 0.0001$ ) in hyperthyroid subjects and statistically highly significant decrease ( $p$  value  $< 0.0001$ ) in hypothyroid subjects when compared with healthy controls. **Conclusions:** This study indicates that osteopontin might be useful as a novel prognostic biomarker in patients with thyroid dysfunction.

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### INTRODUCTION

The thyroid gland is one of the largest endocrine glands in the body. The function of normal thyroid gland is to control metabolism, growth, development and maintenance of the internal environment of the body. It produces two main hormones triiodothyronine ( $T_3$ ) and thyroxine ( $T_4$ ) [3]. Both of these hormones are under the control of thyroid stimulating hormone (TSH) released by anterior lobe of the pituitary gland and in turn it is controlled by thyrotrophin releasing hormone (TRH) of hypothalamus. The spectrum of thyroid dysfunction ranges from hypothyroidism (under production) to hyperthyroidism (over production). Thyroid disorders may affect individuals belonging to any age and gender, but its occurrence is different in different geographical areas and in different age and sex groups. Thyroid dysfunction is the most commonly encountered endocrinopathies in the clinical and endocrinology laboratories [11].

Osteopontin (OPN) is a molecule first identified in 1986 in osteoblasts and is known to be involved in the formation and calcification of bone [10]. The prefix of the word "osteopontin" indicates that the protein is expressed in bone and the suffix "pontin" is derived from "pons," the Latin word for bridge, and signifies osteopontin's role as a linking protein. Osteopontin is a negatively charged phosphoglycoprotein

which is composed of 300 amino acids and contain an arginine-glycine-aspartic acid cell binding sequence. It is located on the long arm of chromosome 4 region 13 (4q13) [14] and is found in different forms in the body i.e. full length osteopontin (OPN-FL), OPN-R elicited in various immune responses [12,16]. Osteopontin has important roles in normal physiological as well as pathological processes [1]. It is suggested that osteopontin plays a role in many diseases such as chronic inflammation, including Crohn's disease [18], several types of cancer [4,5,17], autoimmune diseases [20,21] i.e. Grave's disease [2], obesity [6,9], atherosclerosis [6,8,9] and cardiac fibrosis [9]. Osteopontin has multiple biological functions based on its structural modification and the environment in which it is expressed [14]. More information is required to understand the function of osteopontin in different disease states. Keeping this in mind we investigated changes in serum osteopontin with thyroid hormones and TSH levels induced by thyroid function disorders. In our study we aimed to demonstrate that serum osteopontin levels strongly correlate with clinical parameters of thyroid hormone dysfunction.

### MATERIALS AND METHODS

The present study was conducted on 50 hypothyroid (Group II) and 50 hyperthyroid (Group III) patients attending the Medical OPD and Radio Immuno Assay (RIA) Laboratory of the

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Biochemistry Department of JLN Medical College & Hospital, Ajmer. The results of patients were compared with 50 healthy control (Group I) subjects of either sex of age group(15-55years). Blood samples were collected by venipuncture by aseptic technique. The serum separated from the samples were analyzed for following biochemical parameters. Anthropometric measurements including age, weight (KG), height (meters) and body mass index (BMI) was calculated according to the formula: weight (KG) /height (M<sup>2</sup>). Serum levels of FT<sub>3</sub>, FT<sub>4</sub> and OPN were measured by ELISA and TSH was measured by RIA method, after taking approval from ethical committee. SPSS.13/win statistical software was used for analyzing the data. Data were presented as mean±standard deviation. A parametric independent sample t-test was used to compare differences between two groups. Level of statistical significance was set at p<0.05.

## RESULTS

**Table 1** Comparison between three groups as regard to age, height, weight & body mass index (BMI).

| Parameters                  | GROUP-I<br>MEAN±S.D | GROUP-II<br>MEAN±S.D | GROUP-III<br>MEAN±S.D. |
|-----------------------------|---------------------|----------------------|------------------------|
| AGE (in years)              | 38.8±8.3            | 40.8±9.4             | 37.1±8.7               |
| HEIGHT (in cms.)            | 175±10              | 172±9                | 175± 12                |
| WEIGHT (in kg.)             | 68±6                | 80±8                 | 58±5                   |
| BMI (in Kg/m <sup>2</sup> ) | 22.4±2.1            | 27.2±4.2             | 19.1±3.5               |

Subject's characteristics and anthropometric parameters are summarized in table 1. The common age group of having thyroid dysfunction was 30–45 years in our study population and the body mass index calculated for hypothyroid patients was more than the other two groups.

**Table 2** Thyroid status of the study groups; p<0.05 is considered significant.

| Tests                  | GROUP-I<br>MEAN±S.D. | GROUP-II<br>MEAN±S.D | GROUP-III<br>MEAN±S.D. | NORMAL<br>RANGE  |
|------------------------|----------------------|----------------------|------------------------|------------------|
| FT <sub>3</sub> pmol/l | 5.80±0.80            | 1.40±0.30            | 12.10±3.10             | 2.10-8.10 pmol/l |
| FT <sub>4</sub> pmol/l | 20.10±1.30           | 5.40±0.90            | 39.20±6.80             | 10.2-25.7 pmol/l |
| TSH µIU/ml             | 1.80±0.70            | 46.90±6.0            | 0.22±0.15              | 0.4–4.05 µIU/ml  |

[Table-2] shows the serum TSH and the Free thyroid hormone levels of the 3 groups. As compared to the controls, the mean TSH level was significantly higher with lower T<sub>3</sub> and T<sub>4</sub> values in the Group-II patients and vice versa in the Group-III patients.

**Table 3** Comparison of Osteopontin in the subjects studied.

| Tests                  | GROUP-I<br>MEAN±S.D. | GROUP-II<br>MEAN±S.D | GROUP-III<br>MEAN±S.D. | T-test | P-value         |
|------------------------|----------------------|----------------------|------------------------|--------|-----------------|
|                        | 4.6±0.7              | 1.1±0.2              | -                      | 3.88   | P<0.001<br>(HS) |
| Osteopontin<br>(ng/ml) | 4.6±0.7              | -                    | 14.5±1.2               | 10.13  | P<0.001<br>(HS) |
|                        | -                    | 1.1±0.2              | 14.5±1.2               | 15.01  | P<0.001<br>(HS) |

\*\*p-value < 0.001 Highly Significant (HS).

[Table-3] has compared the serum Osteopontin concentration of the study groups. The increase in serum OPN level was observed statistically highly significant (p<0.001) in Group III

and vice versa in the Group II subjects when compared with healthy control subjects. As compared to the Group-II, the mean OPN level was significantly higher in the Group-III patients.

## DISCUSSION

The thyroid dysfunctions are the most common afflictions involving the endocrine system. Diagnosis and therapy are firmly based on the principles of thyroid hormone physiology and biochemistry. Thyroid diseases are usually present as a spectrum of clinical and metabolic features of varying severity. Although primary diseases of the thyroid gland are the most common, secondary disorder due to hypothalamic pituitary insufficiency can also give rise dysfunctional state. Many other factors, both exogenous and endogenous may affect the thyroid hormone, biosynthesis, secretion, transport in the circulation and metabolism which offer numerous targets for drug interaction. In hyperthyroid group had lower body mass index (BMI) than the other groups, and this explained by marked loss of weight due to hyper catabolic state of thyrotoxicosis. Hypothyroid gland had higher BMI than other group and this may be due to weight gain as a result of deposition of glycosamino glycans in intra cellular spaces in skin and muscle, and hypo catabolic state of hypothyroidism.

Osteopontin (OPN) is phosphorylated sialic acid-rich non-collagenous bone matrix protein. OPN is found in several biological fluids including human plasma, serum, breast milk and urine. The pattern of change in serum osteopontin levels observed in our study i.e. elevated in hyperthyroidism and decreased in hypothyroidism, may be due to these various cell processes going on in the thyroid gland under the influence of osteopontin, yet the exact function of osteopontin in thyroid dysfunction has not been determined. Our results are comparable with the study on patients with Grave's disease in Chinese population [2]. According to this study in patients with Grave's disease, serum OPN levels were elevated which coincided with an increase in OPN receptor coexpression and enhancement in proinflammatory cytokine and chemokine production. Significant difference observed in serum osteopontin levels between normal and hyperthyroid patients in this study was due to the fact that OPN promotes pathogenesis of autoimmune diseases by inducing immune cell activation and migration and inflammatory cytokine production.

Liou YM *et al* (2005) demonstrated about the pathological impact of Osteopontin(OPN) with thyroid dysfunction. OPN was not only found to be involved in the formation and calcification of bone, but also in processes like inflammation, cell adhesion and migration and prevention of apoptosis because of its expression by various other tissues of the body. The pattern of change in serum OPN levels observed in study i.e. elevated in hyperthyroidism and decreased in hypothyroidism may be due to these various cell processes going on in the thyroid gland under the influence of osteopontin.

Another study done by Xu L *et al*, 2011 reported that that the levels of osteopontin were significantly higher in patients with

graves disease than control group. These results and our findings are explained by intact osteopontin promotes pathogenesis of graves disease and other autoimmune diseases by an increase in osteopontin receptors coexpression and subsequent enhancement of its gene, that lead to stimulation and induction of immune cells (T1 helper and T2 helper). TH1 and TH2 and its activation lead to inflammatory cytokine and chemo kin production (Gianou kakis *et al*, 2008).

In the present study, the mean of serum OPN level in hypothyroid subjects was  $1.1 \pm 0.2$  ng/ml and in hyperthyroid subjects it was  $14.5 \pm 1.2$  ng/ml. The mean value correlates with that of Sara Reza (2013) whose mean serum OPN level was  $1.48 \pm 0.16$  ng/ml and in hyperthyroid subjects it was  $15.76 \pm 0.25$  ng/ml. Sara Reza *et al* (2013) states that osteopontin is positively correlated with T<sub>3</sub> and T<sub>4</sub> while it is negatively correlated with thyroid stimulating hormone showing a significant correlation. They suggest that osteopontin might be useful as a novel prognostic biomarker in patients with impaired thyroid function.

## CONCLUSIONS

This study indicates that osteopontin might be useful as a novel prognostic biomarker in patients with thyroid dysfunction.

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### ABSTRACT

**Background:** Osteopontin (OPN) is a glycoprotein. It is found in several biological fluids. OPN can be detected in plasma or serum, was found to be upregulated in several patients with hyperthyroidism and down regulated in hypothyroid patients so it may represent a new biomarker. **Objective:** The objective of this study was designed to investigate the evaluation of serum osteopontin levels with clinical parameters of thyroid hormone dysfunction. **Materials and Methods:** The present study was conducted on 50 hypothyroid (Group II) and 50 hyperthyroid (Group III) patients attending the Medical OPD and Radio Immuno Assay (RIA) Laboratory of the Biochemistry Department of JLN Medical College & Hospital, Ajmer. The results of patients were compared with 50 healthy control (Group I) subjects of either sex of age group (15-55 years). Serum levels of FT3, FT4 and OPN were measured by ELISA and TSH was measured by RIA method, after taking approval from ethical committee. **Results:** The mean serum Osteopontin (OPN) level was observed statistically highly significant increase ( $p$  value  $< 0.0001$ ) in hyperthyroid subjects and statistically highly significant decrease ( $p$  value  $< 0.0001$ ) in hypothyroid subjects when compared with healthy controls. **Conclusions:** This study indicates that osteopontin might be useful as a novel prognostic biomarker in patients with thyroid dysfunction.

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## INTRODUCTION

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## RESULTS

**Table 1** Comparison between three groups as regard to age, height, weight & body mass index (BMI).

| Parameters                  | GROUP-I<br>MEAN±S.D | GROUP-II<br>MEAN±S.D | GROUP-III<br>MEAN±S.D. |
|-----------------------------|---------------------|----------------------|------------------------|
| AGE (in years)              | 38.8±8.3            | 40.8±9.4             | 37.1±8.7               |
| HEIGHT (in cms.)            | 175±10              | 172±9                | 175± 12                |
| WEIGHT (in kg.)             | 68±6                | 80±8                 | 58±5                   |
| BMI (in Kg/m <sup>2</sup> ) | 22.4±2.1            | 27.2±4.2             | 19.1±3.5               |

Subject's characteristics and anthropometric parameters are summarized in table 1. The common age group of having thyroid dysfunction was 30–45 years in our study population and the body mass index calculated for hypothyroid patients was more than the other two groups.

**Table 2** Thyroid status of the study groups; p<0.05 is considered significant.

| Tests                  | GROUP-I<br>MEAN±S.D. | GROUP-II<br>MEAN±S.D | GROUP-III<br>MEAN±S.D. | NORMAL<br>RANGE  |
|------------------------|----------------------|----------------------|------------------------|------------------|
| FT <sub>3</sub> pmol/l | 5.80±0.80            | 1.40±0.30            | 12.10±3.10             | 2.10-8.10 pmol/l |
| FT <sub>4</sub> pmol/l | 20.10±1.30           | 5.40±0.90            | 39.20±6.80             | 10.2-25.7 pmol/l |
| TSH µIU/ml             | 1.80±0.70            | 46.90±6.0            | 0.22±0.15              | 0.4–4.05 µIU/ml  |

[Table-2] shows the serum TSH and the Free thyroid hormone levels of the 3 groups. As compared to the controls, the mean TSH level was significantly higher with lower T<sub>3</sub> and T<sub>4</sub> values in the Group-II patients and vice versa in the Group-III patients.

**Table 3** Comparison of Osteopontin in the subjects studied.

| Tests                  | GROUP-I<br>MEAN±S.D. | GROUP-II<br>MEAN±S.D | GROUP-III<br>MEAN±S.D. | T-test | P-value         |
|------------------------|----------------------|----------------------|------------------------|--------|-----------------|
|                        | 4.6±0.7              | 1.1±0.2              | -                      | 3.88   | P<0.001<br>(HS) |
| Osteopontin<br>(ng/ml) | 4.6±0.7              | -                    | 14.5±1.2               | 10.13  | P<0.001<br>(HS) |
|                        | -                    | 1.1±0.2              | 14.5±1.2               | 15.01  | P<0.001<br>(HS) |

\*\*p-value < 0.001 Highly Significant (HS).

[Table-3] has compared the serum Osteopontin concentration of the study groups. The increase in serum OPN level was observed statistically highly significant (p<0.001) in Group III

and vice versa in the Group II subjects when compared with healthy control subjects. As compared to the Group-II, the mean OPN level was significantly higher in the Group-III patients.

## DISCUSSION

The thyroid dysfunctions are the most common afflictions involving the endocrine system. Diagnosis and therapy are firmly based on the principles of thyroid hormone physiology and biochemistry. Thyroid diseases are usually present as a spectrum of clinical and metabolic features of varying severity. Although primary diseases of the thyroid gland are the most common, secondary disorder due to hypothalamic pituitary insufficiency can also give rise dysfunctional state. Many other factors, both exogenous and endogenous may affect the thyroid hormone, biosynthesis, secretion, transport in the circulation and metabolism which offer numerous targets for drug interaction. In hyperthyroid group had lower body mass index (BMI) than the other groups, and this explained by marked loss of weight due to hyper catabolic state of thyrotoxicosis. Hypothyroid gland had higher BMI than other group and this may be due to weight gain as a result of deposition of glycosamino glycans in intra cellular spaces in skin and muscle, and hypo catabolic state of hypothyroidism.

Osteopontin (OPN) is phosphorylated sialic acid-rich non-collagenous bone matrix protein. OPN is found in several biological fluids including human plasma, serum, breast milk and urine. The pattern of change in serum osteopontin levels observed in our study i.e. elevated in hyperthyroidism and decreased in hypothyroidism, may be due to these various cell processes going on in the thyroid gland under the influence of osteopontin, yet the exact function of osteopontin in thyroid dysfunction has not been determined. Our results are comparable with the study on patients with Grave's disease in Chinese population [2]. According to this study in patients with Grave's disease, serum OPN levels were elevated which coincided with an increase in OPN receptor coexpression and enhancement in proinflammatory cytokine and chemokine production. Significant difference observed in serum osteopontin levels between normal and hyperthyroid patients in this study was due to the fact that OPN promotes pathogenesis of autoimmune diseases by inducing immune cell activation and migration and inflammatory cytokine production.

Liou YM *et al* (2005) demonstrated about the pathological impact of Osteopontin(OPN) with thyroid dysfunction. OPN was not only found to be involved in the formation and calcification of bone, but also in processes like inflammation, cell adhesion and migration and prevention of apoptosis because of its expression by various other tissues of the body. The pattern of change in serum OPN levels observed in study i.e. elevated in hyperthyroidism and decreased in hypothyroidism may be due to these various cell processes going on in the thyroid gland under the influence of osteopontin.

Another study done by Xu L *et al*, 2011 reported that that the levels of osteopontin were significantly higher in patients with

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In the present study, the mean of serum OPN level in hypothyroid subjects was  $1.1 \pm 0.2$  ng/ml and in hyperthyroid subjects it was  $14.5 \pm 1.2$  ng/ml. The mean value correlates with that of Sara Reza (2013) whose mean serum OPN level was  $1.48 \pm 0.16$  ng/ml and in hyperthyroid subjects it was  $15.76 \pm 0.25$  ng/ml. Sara Reza *et al* (2013) states that osteopontin is positively correlated with T<sub>3</sub> and T<sub>4</sub> while it is negatively correlated with thyroid stimulating hormone showing a significant correlation. They suggest that osteopontin might be useful as a novel prognostic biomarker in patients with impaired thyroid function.

## CONCLUSIONS

This study indicates that osteopontin might be useful as a novel prognostic biomarker in patients with thyroid dysfunction.

## References

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