Serum and Seminal Resistin, Tumour Necrosis Factor – alpha Correlations with Semen Quality in Obese and Non-Obese Patients with Varicocele in Qalyubia Governorate

By


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Introduction:

Varicocele which is an abnormal dilatation of the pampiniform venous plexus in the scrotum, has an incidence of 4.4%–22.6% in the general population\(^1,2,3\).

The relationship between varicocele and body mass index (BMI) is still controversial\(^4\). Chen and Huang, \(^5\) reported that, lean men might be prone to varicocele as a result of the "nutcracker" effect of the superior mesenteric artery compressing the left renal vein over the aorta. Other studies like those done by Hassanzadeh et al., \(^6\); Gokce et al., \(^7\); Rais et al., \(^8\); Doğantekin et al., \(^9\) have shown that the occurrence of varicocele is inversely correlated with the BMI and the occurrence of varicocele may be decreased in overweight and obese men. They suggested that, in obese men excess fat around the renal vein provides a cushion protecting against the nutcracker phenomenon. In contrast, Chanc Walters et al., \(^10\) have shown no significant correlations between varicocele and BMI. In addition, Baek et al., \(^11\) showed that men with varicocele had a lower BMI.

Doğantekin et al., \(^9\) reported that the grade and severity of varicocele were inversely correlated with the increased BMI and obesity. On the contrary, Hamid and Delavar \(^12\) found that men with grade III varicocele had the highest mean of BMI compared with normal men.

Varicocele due to its adverse effects is considered to be a sort of inflammation which increases the number of activated leukocytes with increased cytokines secretion \(^13\).

The reproductive system is tightly coupled with energy balance and adipokines, pharmacologically active low molecular weight proteins that exert pleiotropic functions through several metabolic pathways, are considered to be a link between reproduction and energy metabolism and are able to regulate the functions of the hypothalamic-pituitary axis and that of the male gonads \(^14\).

Adiposity, obesity with an excessive growth of adipose tissue, is associated with increased macrophage infiltration in white adipose tissue and contributes to the chronic low-grade subclinical inflammation and the dysregulated elevated secretion of adipokines, most of
them are of the proinflammatory type as resistin, TNF-α and others. Adipokines can modify many obesity related diseases, including the reproductive functions \(^{(15)}\).

Resistin is an adipose-tissue-specific secretory factor with pro-inflammatory effects on different body cells. In humans, macrophages, monocytes and peripheral blood mononuclear cells are the key producers of resistin and its production is dramatically induced by inflammatory stimuli \(^{(16)}\).

Resistin was identified in the pituitary gland and hypothalamus of mice. Also, at the peripheral level, resistin was detected in adult rat Leydig and Sertoli cells \(^{(17)}\). The expression of this peptide is controlled by gonadotropins, demonstrating that resistin has a hormonal impact upon the testes \(^{(18)}\). Very few data are available on the presence and the implications of resistin in human seminal plasma. The physiological role of resistin, its regulation, its target tissue in seminal plasma and its association with inflammation draw the attention of andrologists to this adipokine as the variety of signaling mechanisms by which resistin exerts its biological effects are incompletely understood \(^{(19)}\).

Tumour Necrosis Factor–α (TNF-α) is a powerful proinflammatory cytokine that is made primarily by activated monocytes, macrophages, also it can be produced by a broad variety of cell types \(^{(20)}\). In male reproductive system, TNF-α is naturally occurring in human semen and is secreted by immune cells, mesenchymal cells, Sertoli cells and spermatogonia \(^{(21)}\).

The aim of this study was to evaluate the serum and seminal plasma resistin and TNF-α levels and their correlations with semen quality in obese and non-obese patients with varicocele.

**Patients and methods**

This study is a cross sectional study. It was carried out on eighty clinically and ultrasonography diagnosed varicocele patients. They were selected from those attending the Outpatient Clinic of the Dermatology & Andrology Department, Benha University Hospital during the period from January 2016 to December 2016. All patients were above 18 years old.

**Exclusion criteria:**

Any patient presented with any of the following conditions was excluded from this study

- Diabetes mellitus or hypertension
- Hepatic and/or renal impairment
- Any endocrinal diseases
- History of surgical repair of varicocele
• History of intake of anti-hyperlipidemic drugs within one year prior to the study

All patients were divided into 2 groups:

**Group 1**: Forty non-obese patients with varicocele of any grade and their BMI were <25 kg/m².

**Group 2**: Forty obese patients with varicocele of any grade and their BMI were >30 kg/m².

**Methods:**

Patients were subjected to:

1. **Written informed consent**
2. **Complete history taking**
3. **Local examination**
4. **Determination of obesity-associated markers**
5. **Scrotal Doppler**
6. **Semen analysis**: Semen samples were obtained by masturbation after 3–5 days of sexual abstinence and collected into sterile nontoxic plastic closed containers. Each semen sample was subjected to:
   a) **Evaluation of semen parameters** Manual evaluation of semen parameters including volume (ml), pH, liquefaction time (minutes), total sperm count (millions/ejaculate), sperm concentration (millions/ml), motility, abnormal forms percentage and pus cells / HPF were done according to *World Health Organization guidelines*, (22).
   b) **Determination of resistin and TNF-α concentrations in seminal plasma** by a commercially available human resistin (RETN) enzyme-linked ELISA kit and human TNF-α ELISA kit. The procedure was done following the manufacturer's instructions.

7. **Blood samples** were collected for determination of serum resistin and TNF-α concentrations by a commercially available human resistin (RETN) ELISA kit and human TNF-α ELISA kit. The procedure was done following the manufacturer's instructions.

**Statistical analysis**

The collected data were summarized in terms of mean ± Standard Deviation (SD) and range for quantitative data and frequency and percentage for qualitative data. Comparisons between the different study groups were carried out using the Chi-square test ($\chi^2$) and Fisher’s Exact Test (FET) to compare differences between proportions as appropriate. The Student’s T-test ($t$) and the Mann-Whitney (Z) test were used to test differences between two groups regarding parametric and non-parametric data respectively. The One-way Analysis Of Variance (ANOVA; F) and the Kruskal Wallis ($\chi^2$) test were used to compare more than two groups as
appropriate. Spearman correlation coefficient (rho; ρ) was used to examine the correlation of resistin and TNFα levels and estimated parameters in studied groups.

After the calculation of each of the test statistics, the corresponding distribution tables were consulted to get the “P” (probability value). Statistical significance was accepted at P value <0.05 (S). A P value <0.001 was considered highly significant (HS) while a P value >0.05 was considered non-significant.

All statistical analyses were carried out in STATA/SE version 11.2 for Windows (STATA Corporation, College Station, Texas).

Results

In this study, age and BMI were significantly higher in obese than non-obese patients (P=0.001 & P<0.001) respectively. Left varicocele was found in all the eighty patients. Right varicocele was reported in twenty five out of forty non-obese patients and fifteen out of forty obese patients. Differences regarding varicocele grades showed non significant difference.

Differences between non-obese and obese varicocele patients as regards the seminal volume, total sperm count, sperm concentration, percentage of sperms with abnormal forms, pus cells percentage and type of motility were found to be of no significance.

As regards the serum and seminal plasma resistin and TNF-α measurements, it was found that, in non-obese patients, the mean levels of resistin in seminal plasma were significantly higher than in serum (9.25±3.9 vs. 3.16±4.01; P<0.001). In obese patients, the mean levels of resistin in seminal plasma were significantly higher (P=0.006) than in serum (13.46±7.22 vs. 12.53±24.82; P=0.006). Seminal plasma resistin levels were significantly higher in obese patients than that measured in non-obese patients (13.46±7.22 vs. 9.25±3.9; P=0.02) while the serum resistin levels showed no significant difference (12.53±24.82 vs. 3.16±4.01; P=0.11) between both groups (Table 1).

Table 1: Comparison between non-obese and obese patients as regards serum and seminal plasma resistin levels

<table>
<thead>
<tr>
<th>Variable</th>
<th>Serum resistin (ng/ml) N=40</th>
<th>Seminal plasma resistin (ng/ml) N=40</th>
<th>Wilcoxon signed-rank test(z)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (non-obese)</td>
<td>3.16 ± 4.01</td>
<td>9.25 ± 3.9</td>
<td>4.88</td>
<td>&lt;0.001 (S)</td>
</tr>
<tr>
<td>Group 2 (obese)</td>
<td>12.53 ± 24.82</td>
<td>13.46 ± 7.22</td>
<td>2.75</td>
<td>0.006 (S)</td>
</tr>
<tr>
<td>Mann-Whitney test (z)</td>
<td>1.58</td>
<td>2.33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.11</td>
<td>0.02 (S)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
In non-obese group, there was a positive significant correlation between seminal plasma resistin levels and both serum and seminal plasma TNF-α levels (rho=0.34; P=0.03 & rho=0.54; P<0.001) respectively (Figures 1, 2).

**Figure 1: Correlation between seminal plasma resistin and serum TNF-α levels in non-obese patients**

![Correlation chart for non-obese patients](image1)

In obese group, significant positive correlations were observed between seminal plasma resistin levels and seminal plasma TNF-α levels (rho=0.44; P=0.005) (Figure 3).

**Figure 3: Correlation between seminal plasma resistin and seminal plasma TNF-α levels in obese patients**

![Correlation chart for obese patients](image3)
Semen analysis showed that twenty nine patients (36.25%) out of eighty had pus cells in their semen samples. Seminal plasma resistin levels were significantly higher in pus positive than pus negative patients (13.67±5.89 vs. 8.47±3.75; P<0.001). Moreover, seminal plasma TNF-α levels were significantly higher in pus positive than pus negative patients (676.68±1053.28 vs. 79.13±122.21; P<0.001) (Table 2).

Table 2: Comparison between seminal plasma resistin and TNF-α levels in pus positive and pus negative patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pus positive</th>
<th>Pus negative</th>
<th>Mann-Whitney Test (z)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seminal plasma resistin</td>
<td>13.67 ± 5.89</td>
<td>8.47 ± 3.75</td>
<td>4.34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(ng/ml)</td>
<td></td>
<td></td>
<td></td>
<td>(S)</td>
</tr>
<tr>
<td>Seminal plasma TNF-α</td>
<td>676.68 ± 1053.28</td>
<td>79.13 ± 122.21</td>
<td>4.54</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(ng/l)</td>
<td></td>
<td></td>
<td></td>
<td>(S)</td>
</tr>
</tbody>
</table>

S: significant (P<0.05)
Positive: pus cells count ≥ 10 / HPF
Negative: pus cells count <10 / HPF

Out of eighty patients thirty three (41.25%) were smokers. Seminal plasma resistin levels were significantly higher in smokers than non-smokers (12.97±6.52 vs. 8.52±3.06; P<0.001) (Table 3).

Table 3: Comparison between smokers and non-smokers as regards seminal plasma resistin and TNF-α levels

<table>
<thead>
<tr>
<th>Variable</th>
<th>Smoker n=33</th>
<th>Non-smoker n=47</th>
<th>Mann-Whitney Test (z)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seminal plasma resistin</td>
<td>12.97 ± 6.52</td>
<td>8.52 ± 3.06</td>
<td>3.38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(ng/ml)</td>
<td></td>
<td></td>
<td></td>
<td>(S)</td>
</tr>
<tr>
<td>Seminal plasma TNF-α</td>
<td>541.82 ± 1029.42</td>
<td>122.97 ± 154.57</td>
<td>0.84</td>
<td>0.40</td>
</tr>
<tr>
<td>(ng/l)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

S: significant (P<0.05)

Out of eighty patients thirty five (43.75%) had poor sperm progressive motility. Seminal plasma resistin levels were significantly higher in patients having poor sperm progressive motility than those with good sperm progressive motility (11.88±5.41 vs. 9.17±4.85; P=0.03) (Table 4).
Table 4: Comparison between patients with good and poor sperm progressive motility as regards seminal plasma resistin and TNF-α levels

<table>
<thead>
<tr>
<th>Variable</th>
<th>Good progressive motility n=45</th>
<th>Poor progressive motility n=35</th>
<th>Mann-Whitney Test (z)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seminal plasma resistin (ng/ml)</td>
<td>9.17 ± 4.85</td>
<td>11.88 ± 5.41</td>
<td>2.13</td>
<td>0.03 (S)</td>
</tr>
<tr>
<td>Seminal plasma TNF-α (ng/l)</td>
<td>206.36 ± 620.33</td>
<td>410.66 ± 779.47</td>
<td>1.02</td>
<td>0.31</td>
</tr>
</tbody>
</table>

**Good progressive motility**: ≥ 32%
**Poor progressive motility**: < 32%
S: significant (P<0.05)

Discussion:

Adiposity is usually associated with elevated levels of adipocytokines in peripheral blood (23, 24) and these proteins could be involved in the molecular mechanisms of obesity-related male infertility in the form of impaired semen quality (25). The mechanisms of how adipokines influence sperm function and how they coordinately regulate obesity-related inflammation is not clearly understood (26, 14).

Resistin is a kind of adipokines and has been found to be involved in inflammation and regulation of other cytokines as well. On the other hand, some proinflammatory cytokines can induce its expression (16). It is strictly related to the proinflammatory cytokine pathway and is expressed primarily in inflammatory cells (27,28,29). The physiological role of resistin, its regulation and its target tissue in male genital tract is unknown and still under debate.

Resistin is found in the pituitary gland and hypothalamus of mice and at the peripheral level, it was detected in adult rat Leydig and Sertoli cells. It appears to control the testosterone secretion in an animal model (17). In humans, serum resistin concentrations are associated with testosterone in either obese or lean children and adolescents male. The modulation of resistin expression by gonadotropins demonstrating that it has a hormonal impact upon the testes (18) and its association with inflammation draw the attention of andrologists to this adipocytokine (30).

Qian et al., (21) reported that, TNF-α and some of its soluble receptors are naturally occur in human semen and are secreted by immune cells, mesenchymal cells, sertoli cells and spermatogonia. In male genital tract, TNF-α plays a role in directing germ cells to apoptosis, promotes the germ cell survival during spermatogenesis, acts on the androgenic receptor regulating steroiogenesis, Sertoli and Leydig cell secretory functions, testosterone activity and together with testosterone have the capacity to regulate spermatogenesis (31,32).

To the best of our knowledge, till date, there have been only three studies investigating the seminal plasma resistin levels and semen quality in different groups of patients (30, 19, 33).
Thomas et al., (19) studied the association between age and BMI in normal weight and overweight/obese men and reported that the normal weight men were significantly younger than the overweight and obese men. The results of this study were consistent with that finding as the age was significantly higher in obese than non-obese patients. The possible explanation of the strong association between obesity and its increase with age is the fact that obesity is a result of imbalance between food intake and caloric requirements which is usually disturbed by age as a result of lifestyle changes (34).

The results of this study showed that obesity had no effect on sperm parameters. In agreement with this result, two other studies that failed to find any detrimental effect of obesity on sperm functions and quality (35, 36). Shayeb et al., (37) found that high BMI was related to low semen volume and had no effect on other sperm parameters. In contrast, a negative correlation between BMI and semen parameters was reported by Stewart et al., (38); Fariello et al., (39); Thomas et al., (19); Belloc et al., (40) and Tsao et al., (41). The discrepancies observed between the different results support the hypothesis that increased adiposity may not be the sole cause of impaired semen parameters in obese males (42). To the best of our knowledge, despite many evidences suggest that obesity might affect semen quality, the pathogenesis of this putative interaction remains unclear.

Guo et al., (43) reported that, the effect of obesity on the sperm parameters is multifactorial and the proposed pathophysiological mechanisms underlying these sophisticated relationships have been raised from endocrinology to psychology. Besides, obesity is a metabolic disorder phenomenon, a proper understanding of small molecule metabolites in human seminal plasma will provide biological information on mechanism underlying spermatogenesis.

To study the association of obesity and resistin levels in patients enrolled in this study, estimation of the levels of resistin in both serum and seminal plasma were done in obese and non-obese groups.

As regards the levels of serum resistin and BMI, it was found that, the serum resistin levels were four folds higher in obese than in non-obese patients (12.53±24.82 vs. 3.16±4.01 respectively). This finding comes in line with that reported by Azuma et al., (44) who found that serum resistin level was significantly higher in obese (BMI 32.9 ± 5.6) nondiabetic subjects taking no medication than lean (BMI 21.1 ± 1.3) volunteers. Utzschneider et al., (45) measured plasma resistin levels in seventy five non-diabetic males with different measurements of BMI and found that serum resistin levels correlated with the BMI of their study population. Thomas et al., (19) also reported that the serum levels of resistin were higher in obese than non-obese patients. Lutz and Quinn, (46) and Małgorzewicz et al., (47) also, reported that resistin RNA is expressed at higher levels in visceral fat than in non-abdominal subcutaneous fat and its serum levels are higher in obese than in lean subject.
Regarding the levels of seminal plasma resistin in association with BMI, the results of this study showed that seminal plasma resistin levels were higher in obese than non-obese patients (13.46±7.22 vs. 9.25±3.9; P=0.02). These results are supported by that reported by Thomas et al., (19) who enrolled ninety six male volunteers in their study and found that seminal plasma resistin levels were significantly higher in obese than non-obese (13.8±34.6 vs. 11.9±22.2 respectively). They concluded that the BMI had a significant positive correlation with the seminal plasma resistin concentrations.

Contradictory results were reported by Kratzsch et al., (30) who measured BMI and the resistin concentrations in human seminal plasma of seventy-two men, fifty-four male partners of infertile couples and eighteen vasectomized patients. They found non significant relationship in the concentrations of resistin in seminal plasma and BMI.

In this study, by comparing the serum and seminal plasma resistin levels, it was found that resistin level was four folds higher in serum of obese than non-obese but with no significant differences and its level in seminal plasma was significantly higher in obese than non-obese varicocele patients. These differences may be attributed to the presence of varicocele rather than the presence of obesity alone. This explanation is supported by that reported by Mohammadi et al., (13) who found that varicocele has adverse effects as a source of inflammation. Michalakis et al., (18) reported that the resultant inflammation increases the number of activated macrophages and monocytes which are the main source and the key producers of resistin in humans.

The higher levels of resistin in seminal plasma point to specific physiologic functions of this adipokine in this body fluid, confirm its local production and reinforce the hypothesis that resistin is involved in the cytokine network during local inflammation which may be due to varicocele aggravated by obesity or any other cause.

The results of this study that showed that the levels of resistin were higher in seminal plasma than serum level whether the patient was obese or non-obese were in agreement with that reported by Thomas et al., (19) and Moretti et al., (2014) who found that the mean level of resistin in semen was significantly higher than that measured in serum (13.8±34.6 vs. 11.9±22.2 and 2.4±2.0 vs. 1.08±0.58) respectively.

In contrast, Kratzsch et al., (30) found that the resistin concentration in seminal plasma was lower than its concentration in the serum. The differences between the results may be due to variations in patients selection or the method although all studies were done using ELISA or materials supplied by different manufacturers used for resistin determination.

In this study, TNF-α was detected in all serum and seminal plasma of all patients with a higher levels in serum and seminal plasma of obese than non-obese patients but with no significant differences. This difference may be attributed to the fact that obesity is associated with a chronic inflammation known as the pro-inflammatory state (14, 48). It was reported that
hypoxia of adipose tissue is characterized by the production of abnormal amounts of adipocytokines, as TNF-α, resistin, leptin, visfatin, plasminogen activator inhibitor-1 and others (25,49,50,51).

Correlating the seminal plasma levels of resistin with that of TNF-α in both groups revealed that, there was a positive significant correlation between resistin and TNF-α levels in the seminal plasma of all patients either non-obese (rho=0.54; P<0.001) or obese (rho=0.44; P=0.005). This result is in agreement with that reported by Moretti et al., (33) who found that in seminal plasma, resistin levels showed a positive correlation with TNF-α levels (rho=0.42; P<0.001). This finding draws the attention to consider the association between resistin and TNF-α in the seminal fluid and supports the concept that resistin function as a proinflammatory cytokine. So close to our observation that was reported by Kratzsch et al. (30) who found an association between resistin and elastase and IL-6 as markers of inflammation in human seminal plasma and its concentrations were correlated well with these inflammatory markers.

Nehus et al., (52); Ghaffari et al., (53); Demirci et al., (16) reported an increased level of resistin in various inflammation-related conditions. Moreover, they showed that resistin levels were positively correlated with markers of inflammation as the C-reactive protein, TNF-α and the inflammatory cytokines in the serum of patients suffering from any inflammatory conditions associated with leucocyte infiltrations or activation.

Lutz and Quinn, (46); Małgorzewicz et al., (47) and Jiang and Wang (54) reported that the inflammatory activity is usually attributed to resistin, TNF-α and other cytokines. Resistin induces TNF-α and IL-6 proinflammatory cytokines via the NF-κB-dependent pathway secretion by human blood leukocytes and, in turn, resistin expression is induced by IL-1, TNF-α and IL-6, suggesting a potential feed-forward loop of pro-inflammatory cytokines.

The correlations done in this study concerning the semen parameters and both serum and seminal plasma resistin levels in obese and non-obese patients are consistent with that reported by Kratzsch et al., (30) who found that there were no significant differences between either serum or seminal plasma resistin levels in the semen samples with normal spermiogram parameters and those with abnormal spermiogram parameters.

Concerning the comparisons done between the levels of seminal plasma resistin and the progressive sperm motility in all patients, it was found that resistin was significantly higher in all patients with poor progressive motility than those with good progressive motility. Adding the BMI to this comparison, it was found that obese patients having poor sperm progressive motility have significantly higher levels of seminal plasma resistin compared to those with good sperm progressive motility (P=0.02) and no differences between seminal plasma resistin levels and sperm progressive motility either good or poor in non-obese patients.
Since the seminal plasma resistin levels were significantly higher in obese than non-obese patients, the resistin could be linked to poor progressive motility.

In this study, seminal plasma TNF-α was higher in patients with poor progressive motility regardless of their BMI but with no significance. To the best of our knowledge no previous data were reported regarding this relationship and further studies should be done.

As regards resistin levels in patients having pus cells in their semen samples, it was found that seminal plasma resistin levels were significantly higher in pus positive patients than those having no pus cells in their semen analysis (P=<0.001). This result is consistent with that reported by Moretti et al., (33) and confirms the fact that resistin is a proinflammatory cytokine and its production is stimulated mainly by infection or inflammation.

In this study, both seminal plasma resistin and TNF-α levels were significantly higher (P=<0.001) in pus positive than pus negative patients regardless of their BMI. These results confirm the link between resistin and TNF-α both being proinflammatory cytokines produced in the seminal plasma.

In non-obese patients, seminal plasma resistin and TNF-α levels were significantly higher in pus positive than negative patients (P=0.003 & P=0.02) respectively. In obese patients seminal plasma resistin and TNF-α levels were significantly higher in pus positive than negative patients (P=0.001 & P=<0.001) respectively.

Taking into consideration the above data, seminal plasma resistin and TNF-α levels were increased due to leukocytospermia and this finding comes in line with that reported by Moretti et al., (33) who demonstrated that human semen samples with leukocytospermia showed increased levels of resistin which was associated with elevated levels of IL-6 and TNF-α. This result is similar to that found in this study when measuring the serum resistin and TNF-α levels in patients having pus cells in their semen samples, both were found to be higher in pus positive compared to pus negative patients. The presence of leukocytes in semen and increasing levels of resistin and other cytokines could indicate a typical inflammation profile. Pilatz et al., (55) in their study supported the link between the resistin and TNF-α proinflammatory cytokines and reinforced the hypothesis that resistin is involved in the cytokine network during inflammation.

Moretti et al., (33) observed a significant increase in resistin, and TNF-α concentrations in semen samples of cigarette smokers compared with non-smokers.

In the current study, concerning the influence of smoking on seminal plasma resistin and TNF-α in all patients, it was found that seminal plasma resistin levels are higher in smokers than non-smokers regardless the BMI.
In non-obese patients, it was found that both levels of seminal plasma resistin and TNF-α are higher in smokers than non-smokers but with no significant differences. In obese patients, both levels of resistin and TNF-α were significantly higher in smokers than non-smokers (P<0.001 & P=0.03). This finding may suggest that obesity may aggravate the effects of smoking on the proinflammatory cytokines resulting in higher local production of resistin and TNF-α. This observation needs further studies to clarify this mechanism.

Conclusion:

The existence of higher levels of both resistin and TNF-α in the seminal plasma of patients having leukocytospermia either obese or non-obese support the link between resistin, TNF-α and inflammation and suggest that resistin and TNF-α are potential regulators of inflammation in the male reproductive system and could be considered as local markers of inflammation.

The association which was found between the increased levels of seminal plasma resistin and factors known to be associated with inflammation as varicocele, obesity, smoking and the presence of pus cells in patient’s semen add more support to the link between resistin and inflammation and suggest that resistin is a potential regulator of inflammation rather than having just a metabolic role in humans.

Although both serum and seminal plasma resistin levels are higher in obese than in non-obese varicocele patients, the relation between resistin and obesity may be related to inflammation induced by obesity as macrophages rather than adipocytes are the major source of resistin production in humans.

The presence of resistin in higher levels in seminal plasma than in serum whether the patients were obese or non-obese points to the suggestion that obesity is not the only determinant of resistin production but other factor as varicocele could be incriminated in that issue.

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