Association of Serum Prolactin Levels with Diabetes Mellitus A Cross Sectional Study

(Dr. A. G. Kulkarni Associate professor, Dr. Sachin D. Chate Jr, Dr. Kanchan Devde Jr)

Abstract

Prolactin (PRL) is a pituitary hormone known to control the initiation and maintenance of lactation. However, as the PRL receptor is expressed in various tissues and cells such as endometrium, the prostate, pancreatic islets, and adipocytes, PRL is also involved in various other physiological functions including metabolism. Experimental studies indicated that PRL has effects on food intake, body weight gain, and insulin resistance via inhibiting adiponectin and IL-6 production. This cross-sectional study was conducted among 113 patients with hyperprolactinaemia, which had been diagnosed at Department of General Medicine Mean serum prolactin level was found to be higher in non-diabetic subjects as compared to diabetic patients. This difference was found to be statistically significant (p=0.001). The mean HbA1C (%) values tends to decrease with increasing serum prolactin quartiles. The difference between the serum prolactin quartiles was found to be statistically significant.

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I. Introduction

Prolactin is a polypeptide originally known as a pituitary hormone and named for its ability to promote lactation in response to the suckling stimulus of hungry young mammals. Prolactin plays important role in the reproduction, growth and development, metabolism, immune regulation, brain function, and behavior. However, as the PRL receptor is expressed in various tissues and cells such as endometrium, the prostate, pancreatic islets, and adipocytes, PRL is also involved in various other physiological functions including metabolism. Experimental studies indicated that PRL has effects on food intake, body weight gain, and insulin resistance via inhibiting adiponectin and IL-6 production. This cross-sectional study was conducted among 113 patients with hyperprolactinaemia, which had been diagnosed at Department of General Medicine Mean serum prolactin level was found to be higher in non-diabetic subjects as compared to diabetic patients. This difference was found to be statistically significant (p=0.001). The mean HbA1C (%) values tend to decrease with increasing serum prolactin quartiles. The difference between the serum prolactin quartiles was found to be statistically significant.

II. Material And Methods

- **Study Setting:** Study was done at MGM’s Medical College & Hospital, Aurangabad, Maharashtra, India.
- **Study design:** It was a cross-sectional study conducted at Department of General Medicine, MGM’s Medical College & Hospital, Aurangabad, Maharashtra, India.
- **Study subject:** Study has been included patients with hyperprolactinaemia, which had been diagnosed at Department of General Medicine, MGM’s Medical College & Hospital, Aurangabad, Maharashtra, India.
- **Inclusion criteria:**
  - All patients of type 2 diabetes mellitus.
  - Prediabetes i.e. Subjects with impaired fasting glucose and impaired glucose tolerance.
  - Normal glycaemic status
  - Age ≥18 yrs
  - Patients giving written consent for study
  - Both gender

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Exclusion criteria:
- Pre-menopausal women and individuals with elevated prolactin levels (outside the normal range) such as Prolactinoma patients
- Thyroid disorders on thyroid related medications.
- Patients on any medication known to affect serum prolactin levels such as metoclopramide, oestrogen, tricyclic antidepressants eg reserpine, methyl dopa, oral contraceptives.
- Chronic medical illnesses such as chronic kidney disease, hypertension, metabolic syndrome
- Age <30yrs
- Patients not capable of giving consent (psychiatric patients).
- Patients not willing to participate in the study (who refused to consent).

Sampling Technique: Simple Random sampling

Sampling size:
Sample size calculated is 113.

III. Result
Significance of association between diabetes patients and serum prolactin levels (n = 113)

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>Serum Prolactin level</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hyperprolactinemia</td>
<td>Normal levels</td>
</tr>
<tr>
<td>Non diabetics</td>
<td>31 (54.4%)</td>
<td>26 (45.6%)</td>
</tr>
<tr>
<td>Diabetics</td>
<td>19 (33.9%)</td>
<td>37 (66.1%)</td>
</tr>
<tr>
<td>Total</td>
<td>50 (44.2%)</td>
<td>63 (55.8%)</td>
</tr>
</tbody>
</table>

$X^2 = 4.7, df=1, p\ value: 0.028$

The proportion of serum hyperprolactinaemia was higher in non-diabetic subjects as compared to diabetic patients. This difference was found to be statistically significant (p=0.028)

IV. Discussion
- The present study is a hospital-based study to find out the association between prolactin levels in prediabetes and diabetes. In this study, 56 type 2 diabetic patients and 57 non-diabetic control subjects were included.
- The role prolactin might be playing in regulating metabolic homeostasis, in particular, glycemic status, under non-lactating conditions has not received much attention. Most of the knowledge on prolactin in this area comes from studies conducted in vitro and on rodents. Except for the research conducted in prolactinoma patients, limited information is available in this aspect in humans. Bromocriptine, a dopamine agonist, has been approved for diabetes mellitus type 2. The efficacy of bromocriptine has been shown to correlate with its potency to decrease prolactin levels, but in few epidemiological studies it has been observed that increased prolactin levels are associated with lower fasting plasma glucose and HbA1c. The present study was carried out to investigate this discrepancy.
- It has been observed that prolactin increases the levels and activity of glucose sensors in β-cells i.e. glucokinase, hexokinase, and glucose transporter 2 thereby reducing the threshold of glucose stimulated insulin release, in addition to inducing insulin gene transcription. Prolactin up-regulates a cluster of genes associated with cell-cycle regulation while down-regulating apoptosis-related genes. The best characterized molecular pathway through which prolactin brings into motion these effects has been the activation of JAK2/STAT5. However, it has been shown in subsequent research that STAT5 is not essential for prolactin to act. Prolactin also regulates islet structure and function by inducing phosphorylation of insulin receptor kinase substrate-1 and 2 via PI3K activation, and it also activates the MAPK pathway.
- Studies have discovered that human adipose tissue produces prolactin and also expresses prolactin receptors. Prolactin down regulates lipoprotein lipase and fatty acid synthase. It has been demonstrated to increase leptin synthesis and secretion.
- On the other end, chronically high prolactin levels induce central leptin resistance and inhibit adiponectin production. Collectively, these studies raise the prospect that prolactin affects lipid metabolism and insulin sensitivity through its action as an adipokine.

V. Conclusion
- In the current study, we revealed that physiologically high serum prolactin was associated with a favourable glucose metabolic profile, including lower levels of HbA1C.
- It was also found that lower prolactin levels were associated with diabetes as compared to control group. There was no significant difference between various quartile with respect to BMI and lipid profile parameters.
Our findings lend support to the postulation that the variation of serum prolactin levels associates with glucose metabolism changes in humans outside pregnancy, suggesting that prolactin may be a mediator in the pathogenesis of impaired glucose metabolism. Future studies are warranted to clarify the potential contribution of prolactin to the development of diabetes.

References:

[7]. Freemark M, Driscoll P, Maaskant R, Petryk A, Kelly PA. Ontogenesis of prolactin receptors in the human fetus in early gestation. Implications for tissue differentiation