Assessment of serum trace elements, lipid profile and proteins in hyperprolactinaemic female patients at a tertiary hospital in Abeokuta

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ABSTRACT

Background: Hyperprolactinemia is a frequent endocrine syndrome with varied prevalence rates among infertile women and women with other gyneacological problems. Report has also shown that prolactin exerts a wide variety of actions on metabolic profile.

Objective: To determine the serum levels of Trace Elements, Lipid Profile and Proteins in hyperprolactinaemic female patients.

Methods: A total of 100 female participants were recruited, comprising 60 hyperprolactinaemic patients and 40 healthy controls. Ethical approval was obtained from the institutional review board, and informed consent was secured from all participants. Prolactin was estimated using Chemiluminescent Microparticle Immunoassay (CMIA) and trace elements were analysed using the Flame Atomic Absorption Spectrophotometer. Lipid profile and proteins were analysed using standard methods.

Results: Trace elements showed no significant difference in cases but their mean values were decreased. Cu was slightly elevated in cases.

Significant ($p<0.05$) decrease and increase occurred in HDL and TG respectively in cases but there were no significant difference in TCHOL and LDL in cases. Albumin level was significantly ($p<0.05$) higher in cases but there were no significant difference ($p>0.05$) in total protein and globulin levels.

Conclusion: This study highlights significant metabolic alterations in hyperprolactinaemic female patients, particularly in, lipid profile, and albumin levels. These findings underscore the need for nutritional and therapeutic interventions to mitigate the metabolic impact of hyperprolactinaemia. On the levels of proteins hyperprolactinaemia caused albumin level to be significantly ($p<0.05$) increased while globulin and total protein levels were only slightly elevated in cases.

Keywords: Hyperprolactinaemia, Trace Elements, Displipideamia, Protein

Évaluation des oligo-éléments sériques, du profil lipidique et des protéines chez des patientes hyperprolactinémiques dans un hôpital tertiaire d'Abeokuta

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RÉSUMÉ

Contexte: L'hyperprolactinémie est un syndrome endocrinien fréquent dont la prévalence varie chez les femmes infertiles et celles présentant d'autres problèmes gynécologiques. Une étude a également montré que la prolactine exerce une grande variété d'actions sur le profil métabolique.

Objectif: Déterminer les taux sériques d'oligo-éléments, le profil lipidique et les protéines chez les patientes hyperprolactinémiques.

Méthodes: Au total, 100 participantes ont été recrutées, dont 60 patientes hyperprolactinémiques et 40 témoins sains. L'approbation éthique a été obtenue auprès du comité d'éthique institutionnel et le consentement éclairé de toutes les participantes. La prolactine a été estimée par dosage immunologique par microparticules chimioluminescentes (CMIA) et les oligo-éléments ont été analysés par spectrophotomètre d'absorption atomique à flamme. Le profil lipidique et les protéines ont été analysés selon des méthodes standard.

Résultats: Les oligo-éléments n'ont pas montré de différence significative entre les cas, mais leurs valeurs moyennes ont diminué. Le taux de Cu était légèrement élevé dans les cas.

Une diminution et une augmentation significatives ($p<0,05$) des HDL et des TG ont été observées respectivement dans les cas, mais aucune différence significative n'a été observée entre les TCHOL et les LDL. Le taux d'albumine était significativement plus élevé ($p<0,05$) dans les cas, mais aucune différence significative n'a été observée ($p>0,05$) dans les taux de protéines totales et de globulines.

Conclusion: Cette étude met en évidence des altérations métaboliques significatives chez les patientes hyperprolactinémiques, notamment au niveau du profil lipidique et des taux d'albumine. Ces résultats soulignent la nécessité d'interventions nutritionnelles et thérapeutiques pour atténuer l'impact métabolique de l'hyperprolactinémie . En ce qui concerne les taux de protéines, l'hyperprolactinémie a entraîné une augmentation significative ($p<0,05$) du taux d'albumine, tandis que les taux de globuline et de protéines totales n'étaient que légèrement élevés dans certains cas.

Mots clés: Hyperprolactinémie, oligoéléments, dysplipidémie, protéines

INTRODUCTION

Hyperprolactinaemia is a relatively common endocrine abnormality, it ranges from mild conditions which may not require treatment to major complications that may necessitate instant treatment. Hyperprolactinaemia is an endocrine syndrome with prevalence rates of 31.7-36.2% among infertile women and women with other gyneacological problems in North West Nigeria.[1] Another study in Rivers state, in Nigeria among infertile females reported a prevalence of 53.09 %.[2] It impacts reproduction through inhibitory effects on the pituitary gland in which amenorrehea or infertility is more commonly its presenting symptom. Report has also shown that prolactin exerts a wide variety of actions on metabolic profile in addition to the effects on gonadic function.[3] A study involving trace elements, cortisol and prolactin in transient ischemic attack (TIA) patients revealed a significant association between trace elements concentration and prolactin level.[4] Adverse effect of some drugs may also manifest as hyperprolactinaemia.[5] High prolactin levels can lead to manifestation of some menopause symptoms such as absence of menstrual periods, vaginal dryness and infertility. Hyperprolactinemia is a well-established cause of hypogonadotropic hypogonadism and this can as well result to infertility.[6,7] Other likely consequences from hyperprolactinaemia include galactorrhoea, poor erection problem in men and decreased sex drive generally in both sexes. Normal physiological conditions such as pregnancy, lactation and stress can cause hyperprolactinaemia. Pathological causes of hyperprolactinaemia are majorly diseases affecting the pituitary gland. Also, compromise in the function of other vital organs such as renal or hepatic failure can also affect the clearance of prolactin in the system leading to increased level of prolactin in the serum beyond the upper limit of reference range.[8] Disturbance in prolactin regulation is also caused by external factors such as medications,[9,10] mainly by antipsychotic and antiemetic drugs.

Trace elements are minerals usually required by adults in extremely small amounts. Some of these trace elements are nutritionally essential and some are potentially toxic. Nutritionally essential trace elements are required in our diet because the human body cannot naturally synthesize them. They contribute greatly to metabolism, growth and development and in repair of warn out tissues but despite their functions, they become toxic to the system if excessively consumed.[11] Essential trace elements of the human body include: zinc (Zn), copper (Cu), selenium (Se), manganese (Mn) and others. However, a deficiency state of these trace elements imparts negatively on the body, especially the reproductive function and digestive system.[12] Reports have established a relationship between the concentration of several trace elements and cases of infertility which has connection with hyperprolactinaemia. A study reported that subfertility was predominantly reported in women with lower selenium concentration levels.[13]

It has been documented that the hormones of anterior pituitary (including prolactin) require some enzymatic activation. The enzymes involved usually require the support of trace elements for their catalytic activities.[14] A study in hyperprolactinemic patients reported that there was a statistically significant decrease in zinc in the patients when compared with the control.[15]

Several studies have been carried out to evaluate the effect of Dopamine agonist (DA) on some metabolic parameters in the treatment of hyperprolactinaemia. Reduced Total Cholesterol (TC) and Low density Lipoproteins (LDL) levels were observed in prolactinoma patients treated with Das.[16] Another independent report on the use of DA on 20 premenopausal women with hyperprolactinaemia gave significant decrease in TC and LDL cholesterol.[17]

Serum Proteins are many but essentially emphasis is laid on Albumin and Globulin because of their percentage concentration on the whole serum protein. Albumin, which constitutes the major part of total protein is synthesized mainly from the liver. It keeps the osmotic pressure within the system balanced, transports drugs, hormones and essential nutrients needed for body growth and repair. Meanwhile, globulin, on the other hand comprises of different protein types (alpha, beta, and gamma globulin). The synthesis of globulins is shared majorly by the liver and immune system. Some globulins bind with haemoglobin in the blood to function in the transportation of oxygen and other essential nutrients in the body. Some globulin fractions transport metal ions in the blood while some are involved in fighting infection.

Research suggests that prolactin may have anabolic effect because of significant increase in serum levels of total proteins, albumin and oncotic pressure that were found in prolactinoma patients with hyperprolactinaemia.[18]

This study was aimed at investigating the pattern of serum levels of trace elements in hyperprolactinaemic female patients and the consequences of hyperprolactinaemia on lipid profile and plasma protein.

MATERIALS AND METHODS

Study area

This study was carried out at Federal Medical Centre, Idi-Aba, Abeokuta, Ogun State, Nigeria. It was a case control study in which Sixty (60) hyperprolactinaemic female patients were recruited for the study and forty (40) female patients whose prolactin levels were within normal reference range were recruited as controls. The Sixty (60) hyperprolactinaemic female patients were recruited from a total of one hundred and forty four (144) female patients who reported at the infertility clinic of the hospital over a period of 8 months.

Sites of analyses

The prolactin assay was done at the chemical pathology laboratory of federal medical center, Abeokuta.

Informed consent

Informed consent to participate in the study was obtained from all the subjects using an informed consent form to intimate each subject with the nature, procedure and scope of the study. The purpose and benefits of the study were also explained to them.

Ethical approval

Ethical approval was obtained from Ethics Committee of Federal Medical Centre, Abeokuta before the commencement of the study.

Sample size determination

The sample size was determined using the formula below:
Sample size (n): determined by the formula:

$$n = \frac{2(Z_\alpha + Z_\beta)^2 \times m(1-m)}{(P_1 - P_0)^2}$$ [19]

Where n = sample size

$Z\alpha$ = Standard normal deviation, corresponding to 2 sided α level at 5% = 1.96

$Z\beta$ = Standard normal deviation, corresponding to a β

Error of 10% (power of 90%) = 1.28

P_1 = Expected Prevalence of hyperprolactinaemia in general population = 50% = 0.5[20]

P_0 = Prevalence of hyperprolactinaemia among women with reproductive diseases = 17%= 0.17[21]

Inclusion criteria

Female patients of child bearing age (15-49years) whose prolactin values were greater than 26ng/ml were used as hyperprolactinaemic patients and female patients whose prolactin levels fell within normal reference range of 5.18-25.53 ng/ ml were used as control.

Exclusion criteria

Pregnant and breastfeeding women, women with chronic debilitating illness (hypertension, diabetes, chronic liver and kidney disease) whose condition may have adverse effect on their biochemical parameters and women with uterine fibroid were excluded from the study.

Sample collection

For prolactin test, blood sample was collected about 3 hours after the patient has woken up, between 8 a.m. and 10 a.m. Patients were cautioned to avoid emotional stress and strenuous exercise before the collection of their blood samples as this may raise prolactin levels. From each patient, 5mls of whole blood was collected into plain sample bottle. The blood was allowed to clot, after which the serum was separated and stored frozen at 0℃ before analysis for prolactin estimation, trace elements (Cu, Mn Se and Zn), lipid profile and protein.

Sample analysis

4 mls of serum sample was used for the assays; 1 ml serum sample each was used for prolactin assay, trace elements (Cu, Mn, Se and Zn), lipid profile and serum proteins respectively.

Prolactin was estimated using Chemiluminescent Microparticle Immunoassay (CMIA).[22]

The Trace elements were analysed using the Flame Atomic Absorption Spectrophotometer (FAAS),[23] a simple, very rapid and robust interference-free technique.

Estimation of total cholesterol was estimated by Enzymatic Endpoint Method,[24] Triglyceride was estimated using modified Trinder Reaction,[25] HDL was estimated by precipitation method[26] and LDL was estimated by calculation.[27]

Estimation of total protein was by Biuret method[28] and serum albumin using bromocresol green colorimetric method.[29]

Statistical analysis
Data analysis was done using Statistical Package for the Social Sciences (SPSS version 21). Independent t-test was used to determine the differences between two groups of continuous variables. The level of statistical significance for all tests was set at P value < 0.05

RESULTS
All the subjects (both tests and controls) selected for this study were females whose ages span between 19 and 49 years. As shown in table 1 below, the patient group had the same demographic characteristics with the control group.

Table 1: Socio-demographic characteristics of the hyperprolactinaemic female patients (Cases) and the control group.

Socio-demographics		Participants		X^2	p-value
		Control (%)	Cases (%)		
Age (years)	≤ 36	26 (65)	39 (65)	0.000	1.000
	> 36	14 (35)	21 (35)		
Ethnic group	Yoruba	35 (87.5)	50 (83.3)	0.327	0.568
	Igbo, Hausa & Others	5 (12.5)	10 (16.7)		
Social Status	Upper class	9 (22.5)	16 (26.7)	0.222	0.637
	Middle and Lower class	31 (77.5)	44 (73.3)		
Education	No/ Primary Education	19 (47.5)	27 (45.0)	0.327	0.849
	Secondary Education	16 (40.0)	23 (38.3)		
	Tertiary Education	5 (12.5)	10 (16.7)		
Alcohol intake	Heavy/ Moderate	6 (15.0)	11 (18.3)	0.189	0.664
	Not taking alcohol	34 (85.0)	49 (81.7)		

*Significant at p<0.05

As shown in Table 2 below, the Prolactin levels in the test group varied from that of the control group and there was a statistically significant difference in the prolactin level of the test group compared to the control (p-value < 0.05)

Table 2: Prolactin Levels showing mean values and standard deviations in hyperprolactinaemic female patients (cases) and the control group

Variable	Control Mean ± S.D.	Cases Mean ± S.D.	t test	P value
Prolactin	12.500 ± 6.930	54.460 ± 23.910*	10.785	0.000

*Significant at p<0.05

The result of the trace elements in this study as shown in Table 3 revealed that the differences in the levels of Cu, Mn, Se and Zn were not statistically significant (P > 0.05) between cases and controls but Mn, Se and Zn were slightly reduced while Cu was slightly raised in cases.

Table 3: The trace elements showing the mean values and standard deviations in hyperprolactinaemic female patients and the control group

Variables	Cases (n=60)	Control (n=40)	T	p-value
Zn	80.05±23.55	85.02±24.41	-1.135	0.259
Cu	113.58±29.24	110.53±33.47	0.531	0.597
Mn	6.50±2.04	6.60±3.81	- 1.365	0.172
Se	91.93±28.63	92.65±53.49	- 1.365	0.172

*Significant at (P < 0.05)

The results of lipid profile in this study are as shown in Table 4 below. The HDL level was significantly lower and TG was significantly higher in cases compared to controls (p<0.05). However, there was no significant difference in the levels of TCHOL and LDL, although, both were slightly raised in cases (p>0.05).

Table 4: Comparison of lipid profile between hyperprolactinaemic female patients (Cases) and controls

Variables	Cases (n=60)	Controls (n=40)	T	p-value
TCHOL	171.47±42.93	164.43±40.19	0.926	0.356
HDL	41.17±15.64	51.77±15.21	-3.796	<0.001*
TRIG	190.83±213.77	89.60±41.95	-2.573	0.010*
LDL	108.44±47.48	98.41±30.98	1.333	0.185

*Significant at p<0.05

The results of serum proteins in this study are as shown below in Table 5. The albumin level was significantly higher in cases compared to controls (p<0.05) while the differences in total protein and globulin levels between cases and controls were not statistically significant (p>0.05), although, they appear slightly raised in cases.

Table 5: Protein levels in hyperprolactinaemic female patients and the control group

Variables	Cases (n=60)	Controls (n=40)	T	p-value
TP	7.27±1.05	6.96±0.75	1.865	0.065
Alb	4.40±0.47	4.21±0.36	2.549	0.012*
Glb	2.89±0.79	2.75±0.60	1.118	0.266

*Significant at p<0.05

Albumin/globulin ratio: 1.53

DISCUSSION

Several studies have given varied reports about the association between trace elements, hyperprolactinaemia and effects of hyperprolactinaemia on metabolic profile.

A total number of 60 female individuals with hyperprolactinaemia were involved in the study as case group, while 40 females with normal level of prolactin were recruited as controls.

It was observed from this study that the differences in the levels of trace elements (Cu, Se, Mn and Zn) assayed in hyperprolactinaemic samples against the control group were not statistically significant (Table 3). However, the mean values of Zn, Mn and Se were reduced in cases compared to controls. This observation of zinc decrease corroborates a previous study, which reported that the serum zinc level of hyperprolactinemic patients was significantly decreased than in apparently normal individuals.[15]

Another study stated that there is a link between hyperprolactinaemia and zinc deficiency[30] in sick patients. These two studies suggest an inverse relationship between intake of Zn and serum level of prolactin.

From Table 3, the observation that manganese was slightly low in the test group compared to the control is supported by a previous study that reported that prolactin varied with Mn exposure in adults, and that the concentration of Mn in the blood of neonates showed a significantly positive correlation to prolactin levels, and this may affect important developmental parameters in neonates.[31] However, another previous study reported that blood prolactin level is increased by Mn ion, which was linked to increased release of neurotransmitter.[32]

The concentration of selenium (Table 3) was slightly reduced in the case group in this study. This corroborates previous studies which reported that there was no significant difference in the level of selenium and prolactin in sick people and apparently healthy people. However, a reduction was reported in very critically ill patients with sepsis.[33,34] The result for Cu in this study showed slightly raised value in case than control group but not significantly different. This corroborates a previous work (Case report) in which hyperprolactinaemia was observed in a female patient of Wilson's disease, a disease associated with high copper level.[35]

For Lipid profile in this study (Table 4), the pattern of lipids in hyperprolactinaemic female individuals showed that HDL level was significantly lower in case compared to control group at $p<0.05$ while TG was significantly higher in case compared to control group ($p<0.05$). However, the difference was not significant in TCHOL and LDL levels between case and control groups ($p>0.05$) but their mean values were higher in case compared to control group. This finding corroborates what was observed in a previous study[36] among patients with breast cancer. It was observed that their prolactin level was significantly increased while their serum lipids had higher levels of VLDL and LDL cholesterol and elevated triglyceride concentrations when compared with normal healthy group.

For the protein levels in this study (Table 5), it was observed that the difference in the level of total protein between case and control groups was not statistically significant ($p>0.05$) although the mean value tend to increase in case compared with control group. However, there was a statistically significant increase in albumin ($p<0.05$). This finding is in agreement with a previous work[37] that there was a significant increase in albumin, total protein in hyperprolactinaemia due to pituitary prolactinoma in patients when compared with those of normal groups.[37] This finding may not be too surprising as it was purported that prolactin may have anabolic effects. The difference in globulin level was also not statistically significant in case when compared with control groups ($p>0.05$).

CONCLUSION

Although, this study has not shown a statistically significant pattern of trace elements studied in hyperprolactinaemia, however, the reduced levels of Mn, Se, Zn and increased Cu levels observed in hyperprolactinaemic females suggest that there might be an association between trace element levels and serum prolactin, more especially when the previous studies by other researchers support this fact. This opens an avenue for future investigations involving a larger sample size to know the various relationships between the different trace elements and hyperprolactinaemia. It is however interesting to note that hyperprolactinaemia caused a metabolic disruption in lipid profile, causing a lowered good cholesterol (HDL) and increased atherogenic factor (TG), both of which promote atherogenesis and cardiovascular disease (CVD). The effect of hyperprolactinaemia on serum protein may have a beneficial effect, as prolactin is an anabolic hormone and facilitates increase in serum albumin, which is of great clinical use in human health.

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