Original Article

Status of Serum Prolactin Levels among Male Cohort in Infertile Couples

Kinikanwo I. Green, Collins Amadi[1,2]

Departments of Obstetrics and Gynecology and [1]Chemical Pathology, University of Port Harcourt Teaching Hospital, Port Harcourt, [2]Department of Chemical Pathology, Rivers State University, Rivers State, Nigeria

Abstract

Background: Abnormalities of serum prolactin adversely impact the reproductive functions among infertile men. Hence, this study was aimed to determine the influence of prolactin abnormalities on gonadal functions of male cohorts of infertile unions in Port Harcourt, Nigeria. **Methods:** This was a retrospective survey of 1845 males of infertile unions who presented in a health-care facility for reproductive endocrine evaluation following abnormal semen parameters between 2007 and 2018. The demographic, clinical, and laboratory variables were evaluated among study cohorts. **Results:** Hyperprolactinemia was observed in 16.7% of the study cohorts with 9.6%, 5.0%, and 2.1% of mild, moderate, and severe grades, respectively. The hyperprolactinemic cohorts had depressed levels of follicle-stimulating hormone (FSH), luteinizing hormones (LH), and total testosterone (TT) which worsened further with worsening grades of hyperprolactinemia. Inverse relationship of prolactin levels existed with FSH (crude β: −0.651; $P < 0.001$; adjusted β: −0.666; $P < 0.001$), LH (crude β: −0.481; $P < 0.001$; adjusted β: −0.536; $P < 0.001$), and TT (crude β: −0.525; $P < 0.001$; adjusted β: −0.546; $P < 0.001$) in crude analysis and amplified on age and body mass index (BMI) adjustment. The greatest risk of depressive impact of hyperprolactinemia was on serum TT (crude hazard ratio [HR]: 35.185; $P < 0.001$; age and BMI-adjusted HR: 35.086; $P < 0.001$). Erectile dysfunction (ED) was the single most isolated sexual abnormality ($n = 111$; 35.6%) recorded among the general hyperprolactinemics; however, the ED was specifically more prevalent ($n = 15$; 38.5%) among the severely hyperprolactinemics. **Conclusion:** The present study revealed a high frequency of hyperprolactinemia among studied participants. Since the hyperprolactinemia was associated with a large number of cases with other endocrine and sexual dysfunctions, diagnostic and treatment protocols should include prolactin measurement and management during infertility evaluation in males.

Keywords: *Male hyperprolactinemia, male infertility, Nigeria*

Introduction

Infertility of couples, defined as the inability to achieve pregnancy following at least 12 months of regular and unprotected sexual intercourse, is a very common reproductive condition confronting couples worldwide.[1] It affects between 5% and 8% couples in the developed countries and between 5.8% and 44.2% couples in developing nations.[2] Regarding the etiological factors, both couples contribute about 30%, females contribute about 30%, males contribute about 30%, whereas 10% of cases are of unknown etiology.[3] Male etiological factors include social, infective, structural, genetic, biochemical, and endocrine abnormalities.[4]

An often missed endocrine etiologic factor of male infertility is the role played by the disorders of the prolactin hormone.[5,6] The contributions of the hormone in female reproduction are well appreciated, whereas its function in male physiology remains relatively unclear.[5] However, an aberration of the hormone, termed hyperprolactinemia, is antagonistic to the normal hypothalamic-pituitary-gonadal (HPG) endocrine functions in reproductive males with untoward adverse health consequences inclusive erectile dysfunctions (EDs) and abnormal semen qualities leading to infertility.[5,6]

This antagonistic action on the male gonadal functions diminishes the pulsatile release of gonadotropin-releasing hormone (GnRH), thereby depressing the secretion of follicle-stimulating hormone (FSH), luteinizing hormones (LH) which ultimately impacts negatively on the synthesis and release of serum total testosterone (TT).[5,6]

While the clinical features of hyperprolactinemia among the females

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Address for correspondence:
Dr. Collins Amadi, Department of Chemical Pathology, Rivers State University, Port Harcourt, Nigeria.
E-mail: collins338@yahoo.com

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presenting with infertility are well pronounced, the clinical manifestations among their male counterparts are usually vague and ill-defined.[5,7] This positions male hyperprolactinemic condition as an under-reported and neglected contributing etiological factor in male infertility.[5]

Studies seem to indicate that a high proportion of undiagnosed male infertility could be related to the subtle derangements in the status of prolactin hormone.[6,8]

Despite the overwhelming evidence of the detrimental consequences of deranged prolactin status on reproductive males,[9-11] there remains a paucity of clinical data on the status of prolactin hormone among males of infertile couples around our region.

Hence, this study was conducted with the primary aim to investigate the status of serum prolactin hormone and its relationship with other reproductive characteristics among male cohorts of infertile unions in Port Harcourt, Nigeria.

Methods

Study design and site

This was a retrospective, cross-sectional hospital-based survey conducted in the Department of Chemical Pathology of the University of Port Harcourt Teaching Hospital (UPTH). UPTH is an adequately equipped and specialist-staffed third-level health-care center located in the Niger Delta region of Nigeria. The hospital harbors various departments where couples with infertility issues are properly managed. During the evaluation of infertile couples in the hospital, male partners of infertile couples are usually evaluated first on presentation through basic semen analysis conducted either within the hospital or other laboratories outside the hospital. Thereafter, among those with abnormal semen analysis, the results are usually subjected further to an endocrine evaluation in the Department of Chemical Pathology.

Ethical considerations

Research approval was obtained from the Institutional (UPTH) Ethical Research Committee with approval reference UPTH/ADM/90/S.11/VOL.X1/724. Written or oral informed consent was not deemed necessary owing to the retrospective and anonymized data-based design of the study. However, permission was sort from the heads of various relevant departments, and all the data were anonymized and treated with the utmost confidentiality in accordance with the 1975 Declaration of Helsinki and its subsequent revision in 2000.

Study population

The study population consists of 1845 male cohorts of primary and secondary infertile unions who had presented in the Department of Chemical Pathology of UPTH for reproductive endocrine evaluation following abnormal semen analysis parameters.

Eligibility criteria

The inclusion criteria were medical and laboratory records of male partners of infertile couples presenting for an endocrine evaluation following abnormal semen findings between the January 1, 2007 and December 31, 2018.

The criteria for exclusion included the records of those with incomplete data, those on any medications (neuroleptics: haloperidol and phenothiazines; anti-hypertensives: calcium-channel blockers; psychotropic agents: tricyclic antidepressants; anti-ulcer agents: histamine-2 receptor blockers; and dopamine-depleting agents: reserpine, alpha-methyldopa, and opiates) known to influence serum prolactin levels through dopamine antagonism or its depletion, those with reproductive genetic disorders, chronic renal diseases, liver diseases, disorders of thyroid axis especially primary hypothyroidism, those with anatomic abnormality of the external genitalia, those who are diabetics, and those addicted to smoking/alcohol.

Data acquisition

Data acquired from the medical and laboratory records were: Infertility class (primary or secondary infertility), age (years), sexual dysfunctions, body mass index (BMI), serum prolactin in μg/l (reference interval: 3.0–14.7 μg/L), serum FSH in IU/L (reference interval: 1.4–15.4 IU/L), serum LH in IU/L (reference interval: 1.2–7.8 IU/L), and serum TT in nmol/L (reference interval: 9–38 nmol/L). The aforementioned reference intervals were based on study site reference values.

Specimen collection and laboratory protocols

During the study period, fasted venous whole blood specimens were usually drawn in the morning between 9 a.m. and 10 a.m. daily, after at least 10–12 h overnight fast, from all males with abnormal semen analysis on the presentation. The drawn specimen, collected under standard protocols, were usually transferred into plain containers devoid of anticoagulants, processed accordingly to obtain supernatant sera, and the obtained sera normally stored frozen at –20°C pending analysis.

Participants were usually rested for 60 min before specimen collection. In the study center, fasted morning specimens were deemed necessary to offset the effect of meal intake and diurnal variations on serum prolactin levels.[9]

Serum prolactin, FSH, LH, and TT were determined using the enzyme-linked immunosorbent assay (ELISA) methodology. Analytical procedures were monitored for precision with the use of three levels of commercial internal quality control sera. ELISA reagents and the commercial control sera were all procured from Monoblind Incorporated, USA through their distributors in Nigeria (Nums Diagnostics).

Patients with mildly elevated serum prolactin levels of between 20 and 50 μg/L with accompanying

clinical signs/symptoms of hyperprolactinemia are usually subjected to repeat serum prolactin estimation a week later. While those samples with marked elevation of serum prolactin levels above 100 µg/L without accompanying clinical signs/symptoms of hyperprolactinemia were suspected of macroprolactin presence and were usually mixed in equal dilution with polyethylene glycol, centrifuged, and the supernatant re-assayed for monomeric prolactin hormone.

Data definitions and stratifications

Hyperprolactinemia was defined as serum prolactin levels ≥20 µg/L, whereas normoprolactinemia was taken as serum prolactin levels <20 µg/L as previously outlined.[12] Hyperprolactinemia was further categorized as mild (serum prolactin levels of <50 µg/L), moderate (serum prolactin levels between 50 and 100 µg/L), and severe (serum prolactin levels >100 µg/L) grades as described by the Canadian Medical Association.[13] Age was arbitrarily dichotomized as young (≤40 years) and old (>40 years). Patients with serum prolactin above 200 µg/l are usually sent for brain magnetic resonance imaging for further evaluation.

Serum FSH, LH, and TT were arbitrarily dichotomized as follows: FSH as optimal (≥1.4 IU/L) or depressed (<1.4 IU/L), LH as optimal (≥1.2 IU/L) or depressed (<1.2 IU/L), and TT was dichotomized based on the guidelines established by the American Urology Association as optimal (≥10.4 nmol/L) or depressed (<10.4 nmol/L).[14]

Primary infertile couples were defined as the couples with no previous successful conception, whereas secondary infertile couples were defined as couples with at least one previous successful conception irrespective of the outcome.

Data management and analyses

Statistical analysis was done using the Statistical Package for the Social Sciences software version 21 (IBM Corp., Armonk, NY, USA).

The continuous variables were initially tested for skewed distribution using the Shapiro–Wilk test. The skewed data were log-transformed before analysis. The continuous variables were presented as mean ± standard deviations and compared with the independent Student's *t*-test if only two continuous variables are involved or compared with the analysis of variance if more than two variables are involved.

The categorical variables were presented in numbers and percentages and compared with the Chi-square test or Fisher's test when the frequency distribution is <5. Both linear and Cox-proportional regression models were used to evaluate the direction and magnitude of relationships between the study variables. A two-tailed $P < 0.05$ was considered statistically significant.

Results

During the 12-year (2007–2018) period under the survey, 2336 males had presented to the department of chemical pathology for reproductive endocrine evaluation following abnormal findings on semen analyses. Following a detailed review of medical and laboratory records of these 2336 males, 1845 records of male partners of infertile couples met the inclusion criteria and were acquired and enrolled for the study. The enrolled 1845 study populations consisted of 687 (37.2%) and 1158 (62.8%) subpopulations of primary and secondary infertile male cohorts in infertile couples, respectively.

Depicted in Table 1, the frequency of hyperprolactinemia was observed in 16.7% (n = 309) of the entire study cohorts (n = 1845) with 9.6% (n = 177), 5.0% (n = 93), and 2.1% (n = 39) of mild, moderate, and severe grades, respectively ($P < 0.001$).

Depicted in Table 2, no age difference was observed between the normoprolactinemic and hyperprolactinemic cohorts (P = 0.166). The hyperprolactinemics had significantly lower serum levels of FSH ($P < 0.001$), LH ($P < 0001$), TT ($P < 0.001$), and BMI (<0.011) compared to the normoprolactinemic cohorts [Table 2].

Most of the normoprolactinemics (n = 1392; 90.6%; $P < 0.001$) presented without sexual dysfunctions [Table 2]. However, few of the hyperprolactinemic cohorts (n = 15; 4.9%) were devoid of any sexual dysfunctions, which imply that the majority (n = 294; 95.1%) of the hyperprolactinemic cohorts had various degrees of sexual dysfunctions [Table 2].

The most pronounced sexual abnormality documented among the hyperprolactinemics was ED which occurred mostly in isolation (n = 111; 35.6%; P = 0.007) of other sexual abnormalities and in the company of reduced libido (n = 33; 10.7%), reduced libido/galactorrhea (n = 18; 5.8%), and reduced libido/gynecomastia (n = 21; 6.8%), respectively [Table 2].

In Table 3, age and BMI did not differ among cohorts with mild, moderate, and severe grades of hyperprolactinemia. However, there was a progressive statistically significant ($P < 0.001$) decrease of serum FSH, LH, and

Table 1: Serum prolactin status/hyperprolactinemic grades among studied cohorts (n=1845)

Variables	*n* (%)	*P*
Serum prolactin status		
Normoprolactinemia	1536 (83.3)	<0.001*
Hyperprolactinemia	309 (16.7)	
Grades of hyperprolactinemia (n=309)		
Mild	177 (9.6)	<0.001*
Moderate	93 (5.0)	
Severe	39 (2.1)	

*Statistically significant

Table 2: Comparison of the study variables based on serum prolactin status

Variables	Normoprolactinemia (*n*=1536)	Hyperprolactinemia (*n*=309)	*P*
Clinical/laboratory data, mean±SD			
Age (years)	38.22±4.09	38.83±4.09	0.166
FSH (IU/L)	6.96±2.80	3.03±1.43	<0.001*
LH (IU/L)	4.29±2.02	2.46±1.34	<0.001*
TT (nmol/L)	13.05±2.66	8.10±2.14	<0.001*
Prolactin (µg/l)	9.34±4.04	58.54±8.37	<0.001*
BMI (kg/m^2)	28.71±4.57	27.52±2.43	0.011*
Sexual dysfunctions, *n* (%)			
No sexual dysfunction	1392 (90.6)	15 (4.9)	<0.001*
RL	72 (4.7)	72 (24.3)	0.805
EDs	72 (4.7)	111 (35.6)	0.007*
Gynecomastia	Nil	12 (3.9)	NA
RL + ED	Nil	33 (10.7)	NA
RL + gynecomastia	Nil	21 (6.8)	NA
RL + galactorrhea	Nil	6 (1.9)	NA
RL + ED + galactorrhea	Nil	18 (5.8)	NA
RL + ED + gynecomastia	Nil	21 (6.8)	NA

*Statistically significant; SD: Standard deviation; FSH: Follicle-stimulating hormone; LH: Luteinizing hormone; TT: Total testosterone; SD: Standard deviation; IU/L: International unit per liter; nmol/L: Nanomole per liter; µg/l: Microgram per liter; RL: Reduced libido; ED: Erectile dysfunction; BMI: Body mass index

Table 3: Comparison of study variables based on hyperprolactinemic grades

Variables	Mild HPL (*n*=177)	Moderate HPL (*n*=93)	Severe HPL (*n*=39)	*P*
Clinical/laboratory data (mean±SD)				
Age (years)	38.76±4.32	37.94±4.66	41.30±2.50	0.060
FSH (IU/L)	3.77±1.37	2.25±0.72	1.54±0.52	<0.001*
LH (IU/L)	2.95±1.44	2.02±0.88	1.31±0.38	<0.001*
TT (nmol/L)	8.78±1.86	7.82±1.84	5.46±1.52	<0.001*
Prolactin (µg/l)	38.65±6.83	70.27±7.60	116.87±10.00	<0.001*
BMI (kg/m^2)	27.26±2.10	28.99±3.03	27.59±2.26	0.394
Sexual dysfunctions, *n* (%)				
No dysfunctions	12 (6.8)	3 (3.2)	Nil	<0.001*
RL	60 (33.9)	12 (12.9)	Nil	<0.001*
EDs	63 (35.6)	33 (35.5)	15 (38.5)	<0.001*
Gynecomastia	3 (1.7)	6 (6.5)	3 (7.7)	0.472
RL + ED	18 (10.2)	15 (16.1)	Nil	0.004*
RL + gynecomastia	12 (6.8)	9 (9.7)	Nil	0.513
RL + galactorrhea	Nil	3 (3.2)	3 (7.7)	1.000
RL + ED + galactorrhea	Nil	6 (6.5)	12 (30.8)	0.157
RL + ED + gynecomastia	9 (5.1)	6 (6.5)	6 (15.4)	0.651

*Statistically significant; FSH: Follicle stimulating hormone; LH: Luteinizing hormone; TT: Total testosterone; SD: Standard deviation: IU/L: International unit per liter; nmol/L: Nanomole per liter; µg/l: Microgram per liter; RL: Reduced libido; ED: Erectile dysfunction; HPL: Hyperprolactinemia; BMI: Body mass index

TT as the hyperprolactinemic status worsens from the mild to moderate and to severe status. ED was more pronounced among the cohorts with severe hyperprolactinemia (n = 15; 38.5%; $P < 0.001$) compared to those with mild/moderate hyperprolactinemic status [Table 3].

Among the normoprolactinemics, positive linear relationship only existed between prolactin and TT in both the crude (β: 0.220; standard error [SE]: 0.059; $P < 0.001$) and age-adjusted (β: 0.220; SE: 0.059; <0.001) regression models [Table 4], but no positive linear relationship existed between prolactin and FSH ($P > 0.05$) and between prolactin and LH ($P > 0.05$) levels in both the crude and adjusted models among the normoprolactinemics [Table 4].

Among the hyperprolactinemic cohorts, an inverse relationship existed between prolactin and FSH (β: −0.651; SE: 1.477; $P < 0.001$), between prolactin and LH (β: −0.481; SE: 1.827; $P < 0.001$), and between prolactin and TT (β: −0.525; SE: 1.133; $P < 0.001$) on crude linear logistic model [Model 1; Table 4]. These inverse relationships, observed among the hyperprolactinemic

cohorts in crude linear regression model, was amplified following the adjusted linear regression model between prolactin and FSH (β: −0.666; SE: 1.480; $P < 0.001$), between prolactin and LH (β: −0.536; SE: 1.841; $P < 0.001$), and between prolactin and TT (β: −0.546; SE: 1.146; $P < 0.001$) [Model 2; Table 4].

Table 5 summarizes the magnitude of the risk, determined using Cox-proportional regression model hazard ratios (HRs), of hyperprolactinemic-associated depressive impact on the serum FSH, LH, and TT levels. The greatest risk was observed on serum TT in both crude (HR: 35.185; 95% confidence interval [CI]: 23.707–53.221; $P < 0.001$) and adjusted (HR: 35.086; 95% CI: 23.630–52.097; $P < 0.001$) Cox-proportional regression models [Table 5].

Discussion

In the present study, we explored the status of prolactin among male cohorts in infertile unions and documented a 16.7% frequency of hyperprolactinemia of varied grades. The 16.7% frequency approximate the 15.4% rate documented by Oladosu *et al*.[15] in a prospective study reported from the North Central part of Nigeria among males seeking infertility evaluation. However, other authors had document contrasting frequencies in the literature.[16-22] Lower frequencies of 5.1%, 9.4%, 11%, 12.2%, and 12.5% had been reported by Ozoemena *et al*.,[16] Hasan and Wijesingle,[17] Masud *et al*.,[18] Soler Fernández *et al*.,[19] and Geidam *et al*.,[20] respectively. Higher frequencies of 30% and 90.1% were recently documented by Aljabri *et al*. and Ahmed and Ahmed, respectively.[21,22]

The discrepancies in the reported frequencies could be related to the differences between the studies, including population characteristics, measurement methods, and diagnostic metrics used in defining hyperprolactinemia.[16-22] For instance, Masud *et al*. had evaluated only azoospermic/oligospermic infertile males, assessed serum prolactin with radioimmunoassay method, and defined hyperprolactinemia using twice normal prolactin levels.[18] While Ahmed and Ahmed had defined hyperprolactinemia among infertile males using serum prolactin cutoff of 17 ug/l (375 mIU/L).[22]

The hyperprolactinemics in the present study had the depressed levels of FSH, LH, and TT compared to the normoprolactinemics ($P < 0.001$) with further depression observed with increasing grades and worsening of their hyperprolactinemic status. This finding is in congruence with the report by Benjamin *et al*.,[23] who also reported the depressed levels of FSH, LH, and TT levels ($P < 0.001$) among Nigerian infertile males presenting with hyperprolactinemia associated with hypogonadotropic hypogonadism compared to the normoprolactinemic infertile men and normal controls.

However, in contrast, Soler Fernández *et al*.[19] reported no change in serum FSH, LH, and TT among infertile males with hyperprolactinemia in a similar study.

Table 4: Linear logistic regression analyses between serum prolactin levels and serum follicle-stimulating hormone, luteinizing hormone, and total testosterone

	Normoprolactinemic cohorts (*n*=1536)			Hyperprolactinemic cohorts (*n*=306)		
	β	SE	*P*	β	SE	*P*
Model 1						
FSH	0.006	0.064	0.896	−0.651	1.477	<0.001*
LH	−0.038	0.088	0.400	−0.481	1.827	<0.001*
TT	0.220	0.059	<0.001*	−0.525	1.133	<0.001*
Model 2						
FSH	0.005	0.064	0.920	−0.666	1.480	<0.001*
LH	−0.040	0.088	0.367	−0.536	1.841	<0.001*
TT	0.228	0.059	<0.001*	−0.546	1.146	<0.001*

Model 1: Crude; Model 2: Adjusted for age and BMI. *Statistically significant. FSH: Follicle-stimulating hormone; LH: Luteinizing hormone; TT: Total testosterone; BMI: Body mass index; SE: Standard error

Table 5: Association between hyperprolactinemia and serum levels of follicle-stimulating hormone, luteinizing hormone, and total testosterone

	Hyperprolactinemic cohorts (n=309)					
	Model 1			Model 2		
	HR	95% CI	*P*	HR	95% CI	*P*
FSH (IU/L)						
Optimal[a]	1.0			1.0		
Depressed[b]	4.745	3.391-6.639	<0.001*	4.273	3.048-5.990	<0.001*
LH (IU/L)						
Optimal[a]	1.0			1.0		
Depressed[b]	4.322	3.089-6.049	<0.001*	3.787	2.702-5.307	<0.001*
TT (nmol/L)						
Optimal[a]	1.0			1.0		
Depressed[b]	35.185	23.707-52.221	<0.001*	35.086	23.630-52.097	<0.001*

*Statistically significant; [a]Values within or above the upper limit of the reference interval (reference); [b]Values below the lower limit of the reference interval (depressed). Model 1: Crude; Model 2: Adjusted for age and BMI. FSH: Follicle-stimulating hormone; LH: Luteinizing hormone; TT: Total testosterone; HR: Hazard ratio; CI: Confidence interval; BMI: Body Mass Index

The existence of an inverse relationship between prolactin levels and FSH, LH, and total TT was also observed among the hyperprolactinemics. The inverse relationships, observed in the present study, further reinforces evidence of the negative influence of hyperprolactinemia on the HPG axis among infertile males as previously documented.[15-18] Conversely, positive relationship existed between serum prolactin and serum TT among normoprolactinemics which is in agreement with the findings that emphasized modulation of LH receptors and upregulation of steroidogenic enzymes in Leydig cells by optimal serum levels of prolactin thereby promoting enhanced TT synthesis.[24]

In the present study, the most profound negative impact of hyperprolactinemia was observed to be on serum TT. This finding is consistent with a report from a prospective study by Hasan and Wijesingle[17] In that study by Hasan *et al*., though the magnitude of the impact was not assessed, Hasan and Wijesingle documented markedly depressed levels of serum TT, relative to FSH and LH, among the majority (26/28; 92.9%) of infertile males diagnosed with hyperprolactinemia.[17] These findings had previously been suggested by various investigators to be indicative of the depressive and negative impact of hyperprolactinemia on the HPG axis.[5-8]

The present study revealed a high proportion of the hyperprolactinemics presenting with various degrees of sexual dysfunctions compared with the normoprolactinemics. The most pronounced sexual dysfunction documented among the hyperprolactinemic cohorts is ED which was observed in isolation among the majority (n = 111; 35.6%) of the hyperprolactinemics and in association with reduced libido, gynecomastia, and galactorrhea among a substantial number of the hyperprolactinemic cohorts.

Furthermore, among the hyperprolactinemics, the frequencies of these sexual dysfunctions notably ED were more prevalent among the cohorts with severe hyperprolactinemia.

These observations had previously been documented in the literature.[7-10] Buvat[7] had reviewed the literature on the effect of hyperprolactinemia on male sexual functions and concluded that ED, generally associated with reduced sexual desire (low libido) and sometimes with organismic or ejaculatory dysfunction, was the most revealing clinical feature of hyperprolactinemia

Recently, Corona *et al*.[25] had documented that severe hyperprolactinemia, but not mild hyperprolactinemia, was a determinant of sexual dysfunctions among male cohorts consulting for sexual dysfunctions. The ED preponderance among the severely hyperprolatinemics may be a consequence of other nonneuroendocrine effects of hyperprolactinemia on erectile function respectively documented by Xu *et al*.,[10] Devoto and Aravena,[11] and Badal *et al*.[26]

The mechanisms underlying the suppressive impact of hyperprolactinemia on the gonadal axis of reproductive males have extensively been documented and are closely related to the induction of low TT levels.[17,18] Hyperprolactinemia depresses the pulsatile secretion of GnRH, which diminishes the secretion of FSH and LH with consequent reduction of TT synthesis and secretion.[17,18]

Hyperprolactinemia also inhibits the binding of LH on the LH receptors on Leydig cells which diminishes the synthesis and secretion of TT.[7] Dabbous and Atkin[6] had recently reported that hyperprolactinemia induces the synthesis and secretion of abnormally high levels of adrenal steroids which further depresses the serum TT levels.

Furthermore, Badal *et al*.[26] had given evidence of the adverse impact of hyperprolactinemia on down-regulating dopamine receptors and acting independently of depressed GnRH, FSH, LH, and TT levels to influence gonadal functions in a male presenting with persistent ED secondary to hyperprolactinemia.

Hence, the ultimate resultant effect of hyperprolactinemia in male fertility is the depressed gonadal function with low TT (hypogonadism) which clinically manifests as sexual dysfunctions with a reduction in the quality and quantity of semen parameters leading finally to infertility.[5-8,17,18,22,26] This evidence, therefore, highlights the need to factor the routine determination of prolactin status among males presenting for infertility evaluation by all concerned clinicians.[8]

The strength of this current study lies in its large sample size; however, its limitations must be considered as well. First, it is a retrospective hospital-based study conducted in a single center. Hence, its findings might not necessarily be representative of the entire population within the study region. Second, being also a retrospective designed study, a follow-up of the study cohorts was not conducted owing to limited resources. The third limitation was the confining of this study to only those men who had semen abnormalities. A comparison with men with normal semen parameters could have yielded more understanding of the role of hyperprolactinemia on male infertility.

Conclusion

The present study revealed a high frequency of hyperprolactinemia among the studied male cohorts in infertile couples with significant negative impacts on evaluated endocrine parameters and sexual functions. These negative impacts were significantly associated with worsening grades and the severity of hyperprolactinemia.

Since the hyperprolactinemia was significantly associated with a large number of cases with endocrine (depressed FSH, LH, and TT) and sexual dysfunctions, diagnostic

and treatment protocols should include the prolactin measurement and management of its disorders during infertility evaluation in males.

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Conflicts of interest

There are no conflicts of interest.

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