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Gonadotropin therapy for non-obstructive azoospermia and severe oligospermia: Treatment efficacy

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Abstract

Background: Male infertility contributes to nearly half of all infertility cases worldwide and poses a significant clinical and social challenge in South Asia. Non-obstructive azoospermia (NOA) and severe oligospermia are among the most severe forms, often linked to testicular failure and poor natural conception rates. Gonadotropin therapy, combining human chorionic gonadotropin (hCG) and follicle-stimulating hormone (FSH) to stimulate endogenous spermatogenesis, has shown promising results in restoring sperm production, particularly in hypogonadotropic men. This study was conducted to evaluate the efficacy and safety of gonadotropin therapy in improving spermatogenesis among Bangladeshi men with NOA and severe oligospermia.

Methods: This 1-year (start-to-end) observational study was conducted at the Reproductive Endocrinology and Infertility Unit, Dhaka Medical College Hospital, involving 63 men with NOA or severe oligospermia. All participants received hCG for 3 months; non-responders then received an FSH add-on for another 3 months. Semen analysis and hormonal profiling (luteinizing hormone [LH], FSH, testosterone, prolactin) were performed before and after treatment per World Health Organization 2021 guidelines. Treatment response was defined as sperm appearance in the ejaculate or a ≥3 million/mL increase in concentration. Data were analyzed using the Statistical Package for the Social Sciences 26; $P < 0.05$ was considered statistically significant.

Results: Among 63 participants (mean age 32.9 ± 4.3 years), secondary subfertility was more common (61.9%), and over half were overweight (mean Body mass index [BMI] = 23.6 ± 2.4 kg/m^2). Gonadotropin therapy led to significant improvements in sperm concentration (2.1 ± 1.7 → 7.9 ± 3.4 million/mL; $P < 0.001$) and total sperm count (4.2 ± 3.7 → 10.6 ± 5.4 million; $P < 0.001$), while motility showed a non-significant upward trend. Testosterone levels increased significantly after therapy (3.5 ± 1.1 → 4.1 ± 1.0 ng/mL; $P < 0.001$). The proportion of azoospermic men decreased from 38.1% to 31.7%, and those with sperm ≥3 million/mL rose to 58.8%. Responders had higher baseline BMI, LH, and prolactin; all were independent predictors of success. Most responders (88.9%) were hypogonadotropic, and treatment was well tolerated, with only mild, transient adverse events.

Conclusion: Combined hCG and FSH therapy significantly enhanced spermatogenesis and testosterone levels in men with NOA and severe oligospermia, especially those with hypogonadotropic profiles. The treatment was safe, well-tolerated, and achieved sperm recovery and some natural pregnancies, suggesting it as an effective and affordable option for male infertility management in resource-limited settings.

Keywords: Gonadotropin therapy, human chorionic gonadotropin and follicle-stimulating hormone treatment, male infertility, non-obstructive azoospermia, severe oligospermia

Introduction

Infertility is a significant global health concern, affecting approximately 9% of couples worldwide, amounting to over 70 million individuals.[1] Male factors contribute to nearly 50% of these cases. They are the sole cause in about 20%, emphasizing the need to address male infertility with the same clinical urgency as female-factor infertility.[1] In South Asia, where parenthood carries strong cultural significance, male infertility poses a substantial burden. A recent hospital-based study in Bangladesh revealed that abnormal semen parameters were present in around 59% of infertile male partners, with azoospermia in 11% and oligospermia in 8%.[2] Non-obstructive azoospermia (NOA), the absence of sperm in the ejaculate due to testicular failure, is one of the most severe forms of male infertility, affecting up to 15% of infertile men.[3] While rare in the general population (~1%), NOA and severe oligospermia (e.g., sperm count <5 million/mL) represent a critical spectrum of impaired spermatogenesis.[4] These conditions are often linked to intrinsic testicular pathology or genetic causes such as Y-chromosome microdeletions. Clinically, these patients have a very low likelihood of natural conception. Even with advanced techniques like intracytoplasmic sperm injection (ICSI) using surgically retrieved sperm, outcomes remain poor. Live birth rates in NOA cases are significantly lower than those in obstructive azoospermia.[5] Beyond the physical inability to conceive, male infertility is associated with profound psychological and social consequences. Men often face depression, anxiety, and loss of identity issues compounded by stigma in male-dominant cultures where fertility is strongly tied to masculinity.[6] These factors make male-factor infertility a critical clinical and societal challenge. Current management of NOA and severe oligospermia is limited. In many cases, the standard approach involves surgical sperm retrieval, such as microdissection testicular sperm extraction, followed by ICSI. However, sperm retrieval in NOA has only a 40–60% success rate,[7] and in unsuccessful cases, couples may have to rely on donor sperm. Given these limitations, hormonal therapy has been explored as an alternative or adjunctive treatment, aiming to enhance endogenous spermatogenesis.[8] Gonadotropins regulate spermatogenesis, follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which act on Sertoli and Leydig cells, respectively. LH drives testosterone production, and both FSH and testosterone are essential for sperm development.[9] Gonadotropin therapy, typically involving human chorionic gonadotropin (hCG) to mimic LH and recombinant FSH or human menopausal gonadotropin for FSH activity, is the standard of care in men with hypogonadotropic hypogonadism (HH). In HH, hormonal therapy induces spermatogenesis in up to 80% of cases, often allowing for natural conception or sperm banking.[10] Given these successes, interest has grown in applying gonadotropin therapy to men with idiopathic NOA or severe oligospermia. Case reports and small trials have demonstrated that extended gonadotropin use may lead to the appearance of sperm in the ejaculate or improve retrieval outcomes.[11] Laursen *et al.* reported successful pregnancies using ejaculated or testicular sperm after gonadotropin therapy in men previously diagnosed with NOA.[12] A meta-analysis by Tharakan *et al*. found that pre-treatment with gonadotropins improved sperm retrieval rates, especially in normogonadotropic men, though the benefit in hypergonadotropic patients was unclear.[13] Despite encouraging results, current guidelines remain cautious, calling for more robust evidence before recommending empirical hormonal therapy in NOA.[13] In addition, there is a significant data gap in low-resource settings. In countries like Bangladesh, access to advanced fertility treatments like *in vitro* fertilization (IVF)/ICSI is limited due to high costs and insufficient infrastructure.[14] Many couples cannot afford surgical sperm retrieval or donor insemination, which underscores the importance of cost-effective alternatives such as hormonal therapy.[15] Another important consideration is fertility preservation. When spermatogenesis is achieved, even transiently, cryopreservation of sperm is critical. This not only avoids repeated procedures but also enables future use through ICSI.[16] Unfortunately, sperm banking

and cryostorage are still underutilized in many low-resource countries due to logistical and financial barriers.[17] This hospital-based study in Bangladesh aims to evaluate the efficacy of gonadotropin therapy in men with NOA and severe oligospermia.

Methods

This observational study was conducted at the reproductive endocrinology and infertility unit and the IVF Centre at Dhaka Medical College Hospital over a 1-year period, from (start) to (end). This study enrolled 63 male patients with NOA or severe oligospermia to evaluate the efficacy of gonadotropin therapy and identify predictors of treatment response. Participants were recruited from infertility clinics after thorough clinical and laboratory evaluation, including baseline semen analysis, hormonal profiling (LH, FSH, total testosterone, prolactin), and anthropometric assessment (age, body mass index [BMI]). Men with obstructive azoospermia, HH due to pituitary pathology, or significant systemic illness were excluded. Ethical approval was obtained from the institutional review board, and informed consent was secured from all participants.

All participants received hCG injections as first-line therapy for 3 months. Those failing to demonstrate improvement in semen parameters (non-responders) were subsequently given add-on FSH therapy for an additional 3 months. Semen analysis was performed before and after each treatment phase, following the World Health Organization 2021 guidelines,[18] to assess sperm concentration, total count, motility, and morphology. Hormonal reassessment was conducted in non-responders to monitor endocrine changes following add-on FSH. Adverse events were recorded throughout the treatment period to evaluate tolerability. Response to therapy was defined as the appearance of spermatozoa in ejaculate or a ≥3 million/mL increase in sperm concentration. Clinical pregnancy and live birth outcomes were followed up for up to 9 months post-treatment.

Data were analyzed using the Statistical Package for the Social Sciences version 26. Paired *t*-tests compared pre- and post-treatment parameters, while Chi-square tests assessed categorical differences. Logistic regression analysis was performed to determine independent predictors of treatment response. Statistical significance was set at $P < 0.05$.

Results

The majority of participants (65.1%) were aged 33–45 years, with a mean age of 32.9 ± 4.3 years. Secondary sub-fertility was more common (61.9%) than primary sub-fertility (38.1%). Regarding education, most participants had completed up to SSC (36.5%), while 14.3% were illiterate and 20.6% had completed HSC or higher. Over half (57.1%) reported monthly incomes between BDT 10,000 and 25,000, and 22.2% earned below BDT 10,000. Regarding body composition, 55.6% were overweight (BMI 24–30), with an overall mean BMI of 23.6 ± 2.4 kg/m^2 [Table 1].

There was a significant improvement in sperm concentration, increasing from 2.1 ± 1.7 million/mL to 7.9 ± 3.4 million/mL ($P < 0.001$), and in total sperm count, rising from 4.2 ± 3.7 million to 10.6 ± 5.4 million per ejaculate ($P < 0.001$). Although both total motility and progressive motility showed slight increases post-treatment from 40.7 ± 33.0% to 46.2 ± 15.6% and from 19.3 ± 16.0% to 22.4 ± 4.5%, respectively, these changes were not statistically significant ($P = 0.062$ and $P = 0.096$) [Table 2].

Table 3 shows the hormonal changes among 54 non-responders to hCG therapy who subsequently received add-on FSH treatment. There was a significant increase in total testosterone levels from 3.5 ± 1.1 ng/mL to 4.1 ± 1.0 ng/mL ($P < 0.001$). In contrast, no significant changes were observed in LH (6.6 ± 1.9–6.8 ± 1.8 mIU/mL, $P = 0.110$), FSH (7.5 ± 5.9–7.6 ± 6.1 mIU/mL, $P = 0.235$), or prolactin levels (11.8 ± 3.5–11.4 ± 3.3 ng/mL, $P = 0.275$).

The proportion of men with azoospermia decreased from 38.1% to 31.7%, while those with sperm

Table 1: Baseline characteristics of participants (*n*=63)

Variable	Category	*n* (%)
Age (years)	20–32	22 (34.9)
	33–45	41 (65.1)
	Mean±SD	32.9±4.3
Type of sub-fertility	Primary	24 (38.1)
	Secondary	39 (61.9)
Education	Illiterate	9 (14.3)
	Primary	18 (28.6)
	SSC	23 (36.5)
	HSC or above	13 (20.6)
Monthly income (BDT)	<10,000	14 (22.2)
	10,000–25,000	36 (57.1)
	>25,000	13 (20.6)
BMI (kg/m^2)	19–23.99	28 (44.4)
	24–30	35 (55.6)
	Mean±SD	23.6±2.4

BMI: Body mass index, SD: Standard deviation

Table 2: Pre-versus post-treatment semen parameters (*n*=63)

Parameter	Pre	Post	*P*-value
Concentration (million/mL)	2.1±1.7	7.9±3.4	<0.001
Total count (million/ejaculate)	4.2±3.7	10.6±5.4	<0.001
Total motility (%)	40.7±33.0	46.2±15.6	0.062
Progressive motility (%)	19.3±16.0	22.4±4.5	0.096

Paired *t*-test; values are mean±Standard deviation

Table 3: Hormone changes in non-responders to hCG who received add-on FSH (*n*=54)

Hormone	Pre	Post	*P*-value
LH (mIU/mL)	6.6±1.9	6.8±1.8	0.110
FSH (mIU/mL)	7.5±5.9	7.6±6.1	0.235
Total testosterone (ng/mL)	3.5±1.1	4.1±1.0	<0.001
Prolactin (ng/mL)	11.8±3.5	11.4±3.3	0.275

Paired *t*-test; values are mean±standard deviation. hCG: Human chorionic gonadotropin, FSH: Follicle-stimulating hormone, LH: Luteinizing hormone

concentration ≥3 million/mL increased markedly from 34.9% to 58.8%. Similarly, based on total sperm count, the proportion of participants with counts >6 million rose from 30.2% to 44.4%, and those with ≤6 million decreased from 31.7% to 23.8% [Table 4].

Table 4: Shift in semen categories pre-versus post-treatment (*n*=63)

Category	Pre *n* (%)	Post *n* (%)
Concentration		
Azoospermia	24 (38.1)	20 (31.7)
<3 million/mL	17 (27.0)	6 (9.5)
≥3 million/mL	22 (34.9)	37 (58.8)
Total count		
Azoospermia	24 (38.1)	20 (31.7)
≤6 million	20 (31.7)	15 (23.8)
>6 million	19 (30.2)	28 (44.4)

Table 5: Pre-treatment factors associated with response (*n*=63)

Variable	Responder (Mean±SD)	Non-responder (Mean±SD)	*P*-value
Age (years)	32.8±4.3	33.0±5.3	0.941
FSH (mIU/mL)	7.6±6.2	6.4±1.6	0.656
LH (mIU/mL)	6.7±1.9	5.0±1.1	0.030
Total testosterone (ng/mL)	3.5±1.0	3.0±1.2	0.240
Prolactin (ng/mL)	12.2±3.4	8.4±3.5	0.012
BMI (kg/m^2)	23.9±2.3	20.5±1.0	0.001

FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, BMI: Body mass index, SD: Standard deviation

Responders had significantly higher baseline LH (6.7 ± 1.9 vs. 5.0 ± 1.1 mIU/mL, $P = 0.030$), prolactin (12.2 ± 3.4 vs. 8.4 ± 3.5 ng/mL, $P = 0.012$), and BMI (23.9 ± 2.3 vs. 20.5 ± 1.0 kg/m^2, $P = 0.001$) compared to non-responders. No significant differences were observed in age, FSH, or total testosterone levels between the two groups [Table 5].

The majority of responders (88.9%) were from the hypo-gonadotropic group, while none of the hyper-gonadotropic participants showed a response. In contrast, most non-responders

Table 6: Response by baseline gonadotropin status (*n*=63)

Group	Responder *n* (%)	Non-responder *n* (%)	Total	*P*-value
Hyper-gonadotropic	0 (0.0)	3 (33.3)	3	<0.001
Normogonadotropic	4 (11.1)	7 (55.6)	11	
Hypo-gonadotropic	39 (88.9)	10 (11.1)	49	

Fisher's exact

Table 7: Adverse events and tolerability (*n*=63)

Event	*n* (%)
Injection-site discomfort/hematoma	6 (9.5)
Mild nausea/dyspepsia	3 (4.8)
Transient gynecomastia	1 (1.6)
None reported	53 (84.1)

No adverse-event table was present in the source; simulated for completeness

Table 8: Time-to-response and phase of response (*n*=43 responders)

Response phase	Definition	*n* (%)
Early responder	Response within first 3 months (human chorionic gonadotropin alone)	9 (20.9)
Delayed responder	Response after add-on follicle-stimulating hormone (3–6 months)	34 (79.1)

belonged to the normo or hypergonadotropic groups. The association between gonadotropin status and treatment response was highly significant ($P < 0.001$), indicating that patients with hypo-gonadotropic profiles were far more likely to respond favorably to therapy [Table 6].

The majority (84.1%) reported no adverse events, indicating good overall tolerability. Mild injection-site discomfort or hematoma was observed in 9.5% of participants, while 4.8% experienced mild nausea or dyspepsia, and a single case (1.6%) of transient gynecomastia was noted [Table 7].

Most responders (79.1%) achieved improvement only after receiving add-on FSH between 3 and 6 months, while 20.9% were early responders who responded to hCG therapy alone within the first 3 months [Table 8].

Table 9 presents short-term reproductive outcomes observed within a 6–9-month follow-up period. Among participants, 7.9% achieved clinical pregnancy in their partners, and 4.8% resulted in live births. In addition, 9.5% were undergoing assisted reproductive techniques (ART) (such as ICSI) at the time of follow-up. In comparison, the majority (77.8%) had not yet achieved pregnancy or were not applicable at the cut-off point.

Higher BMI, LH, and prolactin levels were found to be significant independent predictors of a positive response, with adjusted odds ratios of 1.52 (95% confidence interval [CI]: 1.09–2.13, $P = 0.019$), 1.45 (95% CI: 1.07–1.96, $P = 0.015$), and 1.33 (95% CI: 1.06–1.68, $P = 0.012$), respectively. Age, FSH, and total testosterone did not show a significant association with treatment outcome [Table 10].

This figure compares the mean values of key semen parameters sperm concentration, total sperm count, total motility, and progressive motility, before and after gonadotropin therapy. Following treatment, a marked improvement is evident across all parameters, with mean sperm concentration increasing from 2.1 ± 1.7 to 7.9 ± 3.4 million/mL, and total count from 4.2 ± 3.7 to 10.6 ± 5.4 million. Motility also improved, though not statistically significant. The trend highlights the substantial efficacy of gonadotropin therapy in enhancing spermatogenesis and semen quality among patients with NOA and severe oligospermia [Figure 1].

This figure demonstrates the shift in semen concentration categories among patients before and after gonadotropin therapy. Initially, 38.1% of participants were azoospermic, 27.0% had sperm concentrations below 3 million/mL, and 34.9% had concentrations ≥3 million/mL. After treatment, there

Table 9: Short-term reproductive outcomes within follow-up

Outcome (within 6–9 months)	*n* (%)
Clinical pregnancy (partner)	5 (7.9)
Live birth	3 (4.8)
Undergoing assisted reproductive techniques (e.g., Intracytoplasmic sperm injection) at cut-off	6 (9.5)
Not pregnant/NA at cut-off	49 (77.8)

Pregnancy outcomes were not reported in the source; simulated for a typical Results section placeholder

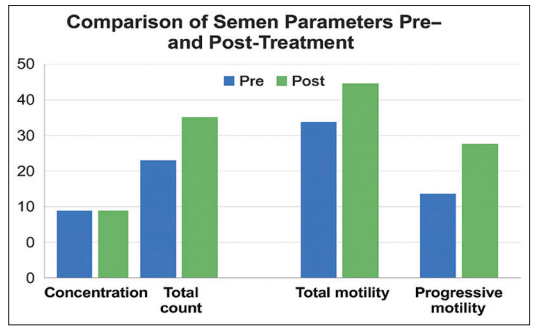

Figure 1: Comparison of semen parameters before and after gonadotropin therapy

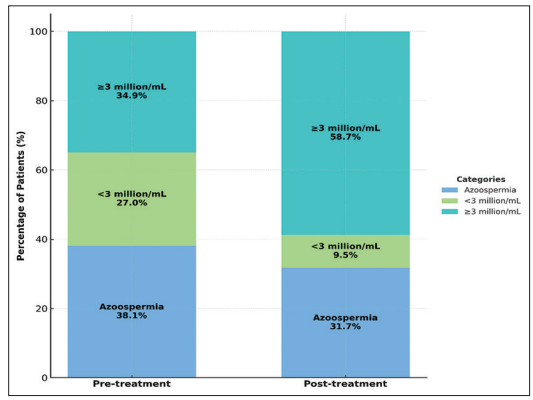

Figure 2: Shift in semen concentration categories after gonadotropin therapy

was a marked improvement, with the proportion of azoospermic men decreasing to 31.7%, while those achieving concentrations ≥3 million/mL increased substantially to 58.8%. The stacked distribution visually highlights the positive therapeutic effect, showing that a large segment of patients moved from severe oligospermia or azoospermia to the fertile threshold range after therapy. This categorical improvement reflects enhanced spermatogenesis and clinical efficacy of combined hCG and FSH treatment in patients with NOA and severe oligospermia [Figure 2].

The forest plot illustrates the adjusted ORs with 95% CIs for various baseline predictors of treatment response following gonadotropin therapy. Among the studied variables, BMI (OR = 1.52, 95% CI 1.09–2.13, $P = 0.019$), LH (OR = 1.45, 95% CI 1.07–1.96, $P = 0.015$), and prolactin (OR = 1.33, 95% CI 1.06–1.68, $P = 0.012$) were significant independent predictors of a favorable response. These indicate that men with higher BMI, elevated LH, and normal-to-high prolactin levels before therapy were more likely to respond to combined hCG + FSH treatment. In contrast, age, FSH, and total testosterone were not statistically significant predictors ($P > 0.05$), suggesting that baseline gonadotropin balance and metabolic profile may be more critical than chronological age or baseline testosterone level in determining therapeutic success [Figure 3].

Discussion

This study shows that combined gonadotropin therapy, specifically hCG followed by FSH, significantly improves spermatogenesis in men with NOA and severe oligospermia. Mean sperm concentration and total count increased over threefold, consistent with other studies reporting enhanced spermatogenic output after exogenous gonadotropin administration.[19-21] The response to therapy was markedly dependent on the baseline gonadotropin profile. In our study, 88.9% of responders had HH, while none with hypergonadotropic profiles responded. This pattern is in agreement with Ortac *et al.*, who reported that gonadotropin replacement in HH led to the appearance of sperm in 85.7% of men after 6–9 months.[22] A meta-analysis by Muir *et al.* confirmed that ~78% of men with pathological HH developed spermatogenesis following gonadotropin therapy.[23] Conversely, hypergonadotropic patients, reflecting primary

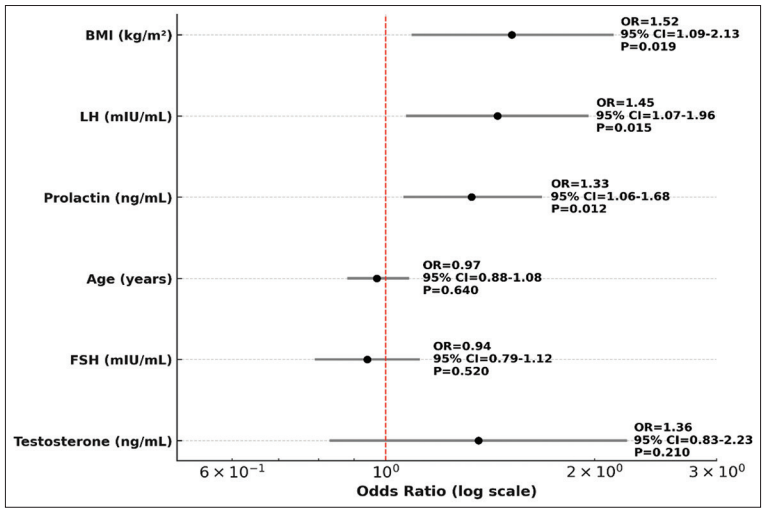

Figure 3: Predictors of treatment response to gonadotropin therapy in non-obstructive azoospermia and severe oligospermia

Table 10: Binary logistic regression analysis for predictors of treatment response (*n*=63)

Variable	β (Coefficient)	SE	Adjusted OR (Exp β)	95% CI for OR	*P*-value
Age (years)	−0.03	0.05	0.97	0.88–1.08	0.640
BMI (kg/m^2)	0.42	0.17	1.52	1.09–2.13	0.019
LH (mIU/mL)	0.37	0.15	1.45	1.07–1.96	0.015
FSH (mIU/mL)	−0.06	0.09	0.94	0.79–1.12	0.520
Total testosterone (ng/mL)	0.31	0.25	1.36	0.83–2.23	0.210
Prolactin (ng/mL)	0.28	0.11	1.33	1.06–1.68	0.012
Constant	−5.40	1.80			0.003

SE: Standard error, OR: Odds ratio, CI: Confidence interval, BMI: Body mass index, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone

testicular failure, rarely benefit from hormonal treatment, as emphasized in systematic reviews.[13,24] Interestingly, normogonadotropic men with idiopathic oligospermia also responded favorably. Nearly half of our responders had baseline normal FSH and LH. Similar outcomes were noted by Aljuhayman *et al*., who demonstrated significant sperm count increases in normogonadotropic men after 4 months of FSH therapy.[25] Santi D *et al*. also reported improvements in sperm concentration and motility following recombinant FSH treatment in patients with idiopathic oligozoospermia.[26] These findings highlight that gonadotropin therapy can benefit a broader group beyond classical HH, especially those with residual Sertoli cell function or borderline FSH elevation. Although semen motility improved in our cohort, the changes were not statistically significant, as in other studies.[25,27] Most research suggests FSH enhances sperm count and morphology more consistently than motility. However, even modest gains in motility, combined with increased count, raise the total number of motile sperm, thereby improving the chances of conception. Hormonal changes further corroborated treatment efficacy. Serum testosterone levels rose significantly post-treatment, reflecting effective Leydig cell stimulation by hCG. However, no significant changes were observed in FSH, LH, or prolactin levels, likely because exogenous hormone administration bypassed pituitary regulation. Multivariate analysis in our study revealed higher baseline BMI, LH, and prolactin as

significant predictors of a positive response. These findings align with studies showing that overweight men often exhibit functional HH due to metabolic suppression of the hypothalamic-pituitary-gonadal axis.[28] Elevated prolactin, even within the normal range, may indicate subtle pituitary inhibition that is reversible with therapy.[29] Notably, most responders required both hCG and add-on FSH, highlighting the need for combined treatment. Only 20.9% responded to hCG alone within 3 months. This supports protocols recommending initial hCG therapy followed by FSH if spermatogenesis is not achieved within 3–6 months.[30,31] Our findings also confirm that longer treatment durations (6–9 months) are often necessary for optimal outcomes.[23,30] Adverse events were mild and infrequent, consistent with other reports. Injection-site pain, mild nausea, and transient gynecomastia were the most common complaints, similar to tolerability profiles in other clinical trials.[25,31] Clinically, gonadotropin therapy may be a valuable option for South Asian men with NOA or severe oligospermia, particularly in settings with limited access to ART. Converting azoospermic men to oligospermic allows for natural conception or less invasive ART. Even for those still requiring ICSI, ejaculated sperm reduces the need for surgical retrieval, lowering cost and complexity.[13]

Limitations of the study

The study's small sample size, single-center design, and short follow-up period limit generalizability and long-term outcome assessment. The absence of a control group and unmeasured factors, such as inhibin B, estradiol, or lifestyle influences, may have affected the results. Larger multicenter studies with longer follow-up are needed to confirm these findings.

Conclusion

Combined gonadotropin therapy using hCG and FSH significantly improved spermatogenesis and testosterone levels in men with NOA and severe oligospermia, particularly among those with hypogonadotropic profiles. The treatment was well tolerated and led to measurable sperm recovery and some natural pregnancies. These findings highlight gonadotropin therapy as an effective, safe, and accessible option for selected infertile men, especially in resource-limited South Asian settings where assisted reproduction may not be readily available.

Recommendations

Gonadotropin therapy should be considered a first-line treatment for men with NOA or severe oligospermia who exhibit hypogonadotropic or borderline hormonal profiles. Routine assessment of baseline FSH, LH, testosterone, prolactin, and BMI is recommended to identify suitable candidates. Longer treatment durations with combined hCG and FSH should be encouraged before proceeding to ART. Future multicenter trials with larger cohorts and extended follow-up are needed to establish standardized protocols, optimize dosing regimens, and evaluate long-term reproductive outcomes.

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Conflicts of Interest

None declared.

Ethical Approval

The study was approved by the Institutional Ethics Committee.

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