GMR
The Original

EFFECT OF BETEL NUT / GUTKA CONSUMPTION ON SEMEN ANALYSIS

Dr. Baby Safiya, MBBS, FCPS[1], Dr. Fiza Ali Khan, MBBS, MRCOG, FCPS[2], Dr. Wasim Hassan, MBBS, FCPS[3], Dr. Jea, MBBS, FCPS[4], Dr. Mizna Memon, MBBS, CHPE, FCPS[5], Dr. Rozeena, MBBS, FCPS[6], Dr. Maria Rasool, MBBS, FCPS[7], Dr. Sidra Sardar, MBBS, FCPS[8]

[1] Postgraduate Resident, Department of Obstetrics and Gynaecology, Dr. Ruth K. M. Pfau Civil Hospital, Karachi, Pakistan.
[2] Consultant, Department of Obstetrics and Gynaecology, Dr. Ruth K. M. Pfau Civil Hospital, Karachi, Pakistan.
Qualifications: MBBS, MRCOG, FCPS.
[3] Postgraduate Resident, Department of Urology, Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan.
[4] Postgraduate Resident, Department of Obstetrics and Gynaecology, Dr. Ruth K. M. Pfau Civil Hospital, Karachi, Pakistan.
[5] Postgraduate Resident, Department of Obstetrics and Gynaecology, Dr. Ruth K. M. Pfau Civil Hospital, Karachi, Pakistan.
Qualifications: MBBS, CHPE, FCPS.
[6] Postgraduate Resident, Department of Obstetrics and Gynaecology, Dr. Ruth K. M. Pfau Civil Hospital, Karachi, Pakistan.
[7] Postgraduate Resident, Department of Obstetrics and Gynaecology, Dr. Ruth K. M. Pfau Civil Hospital, Karachi, Pakistan.
[8] Postgraduate Resident, Department of Obstetrics and Gynaecology, Dr. Ruth K. M. Pfau Civil Hospital, Karachi, Pakistan.

ABSTRACT

Background: The consumption of betel nut or gutka is very popular in South Asia, including Pakistan, and has been associated with different negative health effects. The active substances they contain can cause oxidative stress and negatively influence the process of spermatogenesis, which may impact the quality of semen and male fertility. Yet, evidence in the local context on their effects on semen parameters among infertile men is scarce.

Objective: To determine the frequency of abnormal semen parameters among habitual betel nut/gutka users presenting to the infertility clinic of a tertiary care hospital in Karachi.

Methodology: This Cross-sectional research was conducted on the sample of 133 patients at the Department of OBG, Civil Hospital Karachi from **09th February 2026 to 10th May 2026**. A total of 133 males aged 22–49 years with ≥4-year daily betel nut/gutka use and infertility were enrolled via non-probability consecutive sampling. Semen parameters (volume, concentration, motility, morphology) were assessed. Data were analysed using SPSS-26, applying descriptive statistics and Chi-square test at 5% significance.

Result: The mean age was 37.24 ± 8.08 years. There were frequent abnormal semen parameters with teratozoospermia (36.8%) and oligoasthenoteratozoospermia (23.3%). Mean sperm count was 15.68 ± 6.34 million/ml and motility 39.59 ± 10.80%. No statistically significant association was observed between age or duration of gutka use and semen abnormalities (p=0.804; p=0.905).

Conclusion: Habitual betel nut/gutka use among infertile males was associated with a high frequency of abnormal semen parameters, with morphological and combined defects predominating. However, no statistically significant relationship was observed between semen abnormalities and age or duration of consumption. These findings highlight the burden of poor semen quality in this population and underscore the need for substance use counselling as part of routine male infertility assessment.

KEYWORDS: Areca catechu, Smokeless Tobacco, Male Infertility, Azoospermia, Sperm Motility

INTRODUCTION

Areca catechu (areca nut) is the seed of the areca palm (Areca catechu), cultivated widely in tropical Asia, the Pacific islands, and sub-Saharan Africa. Widely consumed as betel quid within betel leaf, often combined with slaked lime and tobacco, or in commercially prepared forms such as gutka, it ranks among the most widely misused psychoactive substances worldwide [1,2]. Areca nut is consumed by an estimated 600 million people globally, constituting approximately 10–20% of the world population, with India and South-east Asia accounting for the largest consumer base [3]. Consumption has no age, gender, socioeconomic barriers and is firmly rooted within the sociocultural aspects of South Asian countries, such as Pakistan, where betel nut and gutka chewing is common amongst urban and rural populations [4,5,6]. Worryingly, the onset of betel nut consumption is reported to be observed even in adolescent and even younger preschool children, which implies that there are serious reproductive and systemic health consequences of the practice at the population level in the long-term [7]. Male infertility is an important and escalating societal health issue. It is estimated that 15 to 20% of couples trying conception cannot become pregnant and in more than a half of them, a male factor is specified as the main or contributory aetiology [8,9]. A range of spermatogenic and functional defects, including impaired sperm concentration, motility and morphology are included within the umbrella

term of male infertility, and are categorised under the standardised nomenclature of oligozoospermia, asthenozoospermia, teratozoospermia, and oligoasthenoteratozoospermia. The impact is especially high in Pakistan; infertility is estimated to affect almost 22% of couples, with male factor causes representing more than a third of infertility cases [11]. Several causative factors have been attributed to the observed progressive reduction in semen quality over the last few decades, among them being aging, exposure to environmental toxins, work-related risks and lifestyle behaviour that are modifiable, like tobacco use and recreational drugs [10,15]. The chemical compounds of areca nut and gutka, arecoline, arecaidine, guvacoline and tobacco-derived nitrosamines, are well documented cytotoxic and genotoxic and have direct effects on the male reproductive physiology [15,18]. These bioactive alkaloids are found to cause oxidative stress, disrupt the hypothalamic-pituitary-gonadal axis, disrupt spermatogenesis, and cause direct cytotoxic effects on spermatozoa. Clinically significant changes in various semen parameters have been linked to habitual gutka use. A study by Kumari et al. (2022) carried out among the infertile males with a documented history of gutka use revealed that teratozoospermia was the most common type of semen abnormality, which was observed in about one-third of the subjects, with other proportions having azoospermia, combined oligoasthenoteratozoospermia, and morphological and volume defects [12]. These results indicate the reproductive toxicity of gutka and the necessity to conduct systematic research in the population where the use of gutka is prevalent. The main and essential investigation in the clinical examination of the male partner of an infertile couple is semen analysis which is performed in accordance with the standardised reference values as defined by the World Health Organisation (WHO) [13,14]. It offers measurable, repeatable information on those important fertility parameters as semen volume, sperm concentration, total and progressive motility and normal morphology and allows categorizing semen profiling as either normal or abnormal by utilizing pre-established lower reference limits. Although the systematic evaluation of semen parameters with special reference to the situation of betel nut and gutka exposure is widely used clinically, it has not been adequately examined in the tertiary care setting in Pakistan. The lack of locally derived, standardised data restricts the ability of clinicians to advise patients on reproductive risk associated with lifestyle, and evidence-based public health advocacy in resource constrained environments. Although betel nut and gutka use is highly prevalent among men of reproductive age in Karachi and Pakistan, in general, there is limited evidence of the effect of such exposure on semen quality that is locally derived [4,12]. Most of the existing literature is based on the Indian population and other South Asian settings and may not necessarily be directly applicable to the sociodemographic, dietary, and environmental context of Pakistani men. Moreover, the current literature does not sufficiently take into consideration significant confounding factors like diabetes mellitus, HTN, and concomitant use of recreational substances, which have independent effects on spermatogenesis and semen quality. This forms a serious gap in local evidence base, especially since the prevalence of gutka use is high, male infertility is a significant burden, and there is a paucity of sophisticated reproductive studies in government tertiary hospitals. This study was therefore designed to determine the frequency of abnormal semen parameters among habitual betel nut/gutka users attending an infertility clinic at a tertiary care hospital in Karachi. The results are expected to present evidence-based, locally relevant data to aid specific clinical counselling, health education programs, and policy-level interventions to alleviate lifestyle-related male reproductive morbidity in resource-constrained environments.

METHODOLOGY

This study was conducted following approval of the synopsis from CPSP. This was a Three-month study, started after approval of the **Dow University of Health Science Institutional Review Board (IRB) Ref: IRB-4326/DUHS/Approval/2025/61,** from **09th February 2026 to 10th May 2026**. Written informed consent was obtained from all participants after explaining the study purpose, potential risks, and expected benefits. Participants were enrolled through non-probability consecutive sampling from the Gynaecology Infertility Outpatient Department. Eligible participants were male partners of infertile couples aged between 22 and 49 years who reported a self-documented history of daily betel nut and/or gutka chewing for more than four years and were presenting for evaluation of primary or secondary infertility, the inability of a couple to achieve pregnancy after 12 months of regular unprotected sexual intercourse, irrespective of any prior conception. Males with known thyroid disorders (hypothyroidism or hyperthyroidism), those taking other recreational drugs like alcohol, cocaine, morphine, or marijuana in addition to betel nut or gutka, and couples whose infertility could be explained by known female-factor causes such as polycystic ovarian syndrome, uterine fibroids, tubal blockage, or uterine anomalies were not included in the study. Betel nut and/or gutka use was operationally defined as a self-reported history of chewing betel nut and/or gutka at least once per day and longer than four years of this practice by the male partner who was being assessed in regard to infertility. Abnormal semen parameters were defined and classified in accordance with WHO reference values as aspermia (absence of any ejaculate), azoospermia (total absence of spermatozoa in the ejaculate), oligozoospermia (sperm concentration below the lower reference limit), asthenozoospermia (percentage of progressively motile spermatozoa below the lower reference limit), teratozoospermia (percentage of morphologically normal spermatozoa below the lower reference limit), or oligoasthenoteratozoospermia (combined deficiency in sperm concentration, progressive motility, and normal morphology). The required sample size was calculated using the formula $n = Z^2\alpha/2 \times P(1–P) / d^2$ for estimation of proportion, where the expected prevalence of teratozoospermia was 33%[12], the precision was 8%, and the C.I was 95%, resulting in a sample size of 133 participants. Demographic data including age, educational status, occupational status, residential status, height, weight, body mass index (BMI), duration of marriage, duration of infertility, and duration of betel nut and/or gutka consumption and comorbid

conditions such as HTN and DM were collected using a predesigned structured proforma. Semen examination was conducted following three days of sexual abstinence, in strict compliance with the WHO 6th edition laboratory manual criteria and all samples were evaluated on the basis of semen volume, sperm concentration, total motility, progressive motility and morphology with classifications as either normal or abnormal. All the data collected were recorded in hard-copy proformas and kept in a locked cabinet that only the principal investigator had access; data in electronic form were kept in a password-secured file and no personal information such as name, address, or contact details were recorded therefore, maintaining the confidentiality of the participants throughout the study. Frequencies with percentages and mean with SD were calculated through SPSS-26. Chi-square test was applied at a 5% level of significance.

RESULTS

Table I shows the demographic and clinical characteristics of the participants. The study included a total of 133 participants with a mean age of 37.24 ± 8.08 years. The mean body mass index was 26.59 ± 4.01 kg/m². Participants reported a mean duration of betel nut/gutka consumption of 8.26 ± 2.71 years, while the mean duration of marriage and infertility was 8.48 ± 3.98 years and 5.94 ± 2.92 years, respectively. Semen analysis revealed a mean total volume of 1.31 ± 0.29 ml, sperm count of 15.68 ± 6.34 million/ml, motility of 39.59 ± 10.80%, and morphology of 4.38 ± 1.73%. In terms of sociodemographic characteristics, 36.8% of participants were illiterate, 24.1% had primary education, 21.1% had secondary education, and 18.0% had intermediate education. The majority of participants resided in urban areas (75.2%), while 24.8% were from rural settings. Primary infertility was observed in 66.9% of cases, whereas 33.1% had secondary infertility. In terms of abnormal semen parameters, the most frequent were teratozoospermia (36.8%), oligoasthenoteratozoospermia (23.3%), asthenozoospermia (15.0%), oligozoospermia (11.3%), azoospermia (9.8%), and aspermia (3.8%). Additionally, 42.9% of participants were hypertensive and 12.8% had diabetes mellitus.

Table II presents the comparison of abnormal semen parameters across age groups and duration of betel nut/gutka consumption among the study participants. When stratified by age, participants aged 22–35 years showed frequencies of aspermia (5.5%), asthenozoospermia (14.5%), azoospermia (10.9%), oligoasthenoteratozoospermia (20.0%), oligozoospermia (14.5%), and teratozoospermia (34.5%). Among participants aged >35 years, the corresponding frequencies were 2.6%, 15.4%, 9.0%, 25.6%, 9.0%, and 38.5%, respectively. The difference across age groups was not statistically significant ($p = 0.804$). Similarly, when analysed according to the duration of betel nut/gutka consumption, participants with 4–9 years of use exhibited aspermia in 2.3%, asthenozoospermia in 15.1%, azoospermia in 9.3%, oligoasthenoteratozoospermia in 23.3%, oligozoospermia in 11.6%, and teratozoospermia in 38.4% of cases. In those with more than 9 years of consumption, the frequencies were 6.4%, 14.9%, 10.6%, 23.4%, 10.6%, and 34.0%, respectively. No statistically significant association was observed between duration of betel nut/gutka consumption and abnormal semen parameters ($p=0.905$).

Table I: Baseline Demographic and Clinical Characteristics of Study (n=133)		
Mean ± Standard Deviation		**95% Confidence Interval**
Age in years = **37.24 ± 8.08**		35.85----38.63
Body Mass Index in kg/m^2 = **26.59 ± 4.01**		25.90----27.28
Duration of Betel nut/gutka consumption in years = **8.26 ± 2.71**		7.79----8.72
Duration of Marriage in years = **8.48 ± 3.98**		7.80----9.16
Duration of Infertility in years = **5.94 ± 2.92**		5.44----6.44
Total Volume in ml = **1.31 ± 0.29**		1.26----1.36
Count in million/ml = **15.68 ± 6.34**		14.60----16.77
Motility in % = **39.59 ± 10.80**		37.73----41.44
Morphology in % = **4.38 ± 1.73**		4.09----4.68
Frequency (%)		
Educational Status	Illiterate	49 (36.8)
	Primary	32 (24.1)
	Secondary	28 (21.1)
	Inter	24 (18.0)
Residential Status	Urban	100 (75.2)
	Rural	33 (24.8)
Infertility Type	Primary	89 (66.9)
	Secondary	44 (33.1)
Abnormal Semen Parameters	Aspermia	5 (3.8)
	Asthenozoospermia	20 (15.0)
	Azoospermia	13 (9.8)
	Oligoasthenoteratozoospermia	31 (23.3)
	Oligozoospermia	15 (11.3)
	Teratozoospermia	49 (36.8)
HTN		57 (42.9)
Diabetes Mellitus		17 (12.8)

Table II: Comparison of Abnormal Semen Parameters with Age group and Duration of Betel nut/gutka consumption (n=133)			
Abnormal Semen Parameters	**Age group**		**P-Value**
	22---35	**>35**	
Aspermia	3 (5.5)	2 (2.6)	0.804
Asthenozoospermia	8 (14.5)	12 (15.4)	
Azoospermia	6 (10.9)	7 (9.0)	
Oligoasthenoteratozoospermia	11 (20.0)	20 (25.6)	
Oligozoospermia	8 (14.5)	7 (9.0)	
Teratozoospermia	19 (34.5)	30 (38.5)	
Abnormal Semen Parameters	**Duration of Betel Nut/gutka**		**P-Value**
	4---9	**>9**	
Aspermia	2 (2.3)	3 (6.4)	0.905
Asthenozoospermia	13 (15.1)	7 (14.9)	
Azoospermia	8 (9.3)	5 (10.6)	
Oligoasthenoteratozoospermia	20 (23.3)	11 (23.4)	
Oligozoospermia	10 (11.6)	5 (10.6)	
Teratozoospermia	33 (38.4)	16 (34.0)	

DISCUSSION

Male infertility is a complicated diagnostic issue because of the multifactorial aetiology and the changes of semen parameters within one person with time. Since semen analysis is still the mainstay of male fertility testing, abnormalities in sperm concentration, motility, and morphology are a major source of information regarding underlying reproductive dysfunction [13]. The discovery of modifiable risk factors assumes clinical significance in high-exposure populations with the environmental and lifestyle toxins including smokeless tobacco.

In the current study, a substantial burden of abnormal semen parameters was observed among gutka users presenting with infertility. The average sperm concentration (15.68 ± 6.34 million/ml) and motility (39.59 ± 10.80) were near or under lower reference limits, which showed impaired spermatogenic activity. Morphology was particularly affected, with a mean of 4.38 ± 1.73%, reflecting borderline or abnormal values. The most common abnormalities were teratozoospermia (36.8%), oligoasthenoteratozoospermia (23.3%), asthenozoospermia (15.0%), and oligozoospermia (11.3%). Other less common but clinically important results were azoospermia (9.8%) and aspermia (3.8%). These findings underscore the significance of morphological and mixed defects in this cohort, as an indication of diffuse disruption of spermatogenesis and no single-function abnormalities.

The results of the current study show consistency and diversity when compared with the literature. Kumari et al. [12] reported teratozoospermia in approximately one-third of gutka users, which is comparable to the 36.8% observed in the present study. Similarly, the proportion of oligoasthenoteratozoospermia (23.3%) aligns with previously reported ranges of 20–30% in populations exposed to smokeless tobacco. The incidence of azoospermia, however, in the given study (9.8%) is a little more than some of the regional reports (5-8%), which can be attributed to variations in exposure period, environmental confounding factors, or referral bias in tertiary care centres. Studies among infertile males without documented smokeless tobacco exposure have reported lower rates of teratozoospermia and combined semen defects, suggesting an additive deleterious effect of gutka constituents on sperm morphology [16].

The patterns observed can be explained in a plausible manner based on the established pathophysiological processes. Betel nut alkaloids such as arecoline and tobacco-specific nitrosamines are well-established inducers of reactive oxygen species (ROS), causing lipid peroxidation of sperm membranes and DNA strand breaks, both of which disproportionately impair sperm morphology and motility [18]. This oxidative stress has a disproportionate impact on sperm morphology and motility as they are very sensitive to reactive oxygen species. Additionally, chronic exposure

may disrupt the hypothalamic–pituitary–gonadal axis, resulting in impaired testosterone synthesis and defective spermatogenesis. These processes offer biological plausibility to the preponderance of teratozoospermia and combined deformities in this study in line with the findings which have shown that environmental, occupational, and other modifiable lifestyle exposures are associated with impaired semen quality and male infertility outcomes [17,20].

Importantly, the study did not demonstrate a statistically significant association between semen abnormalities and either age (p=0.804) or duration of gutka use (p=0.905). The absence of a statistically significant association between semen abnormalities and duration of gutka use suggests a lack of clear dose–response relationship within the observed range. This may reflect threshold effects, individual susceptibility, or unmeasured confounders. Clinically, it indicates that even shorter durations of use may impair semen quality, highlighting the need for early cessation counselling in infertile men. This result indicates that although the quality of semen is impaired with the use of gutka, the effect may not be dose- or duration-dependent in the observed range. Other cross-sectional studies have made similar observations with individual susceptibility, genetic predisposition, and parallel metabolic factors modulating the effect of toxic exposures on fertility outcomes [19]. High disease rates of HTN (42.9%), and DM(12.8%) in the cohort can also be confounding factors since both diseases are independently related with poor semen quality.

Clinically, these results highlight the importance of specific counselling on lifestyle change in infertile men, especially in areas where gutka is endemic. The finding of a high prevalence of abnormal semen parameters demonstrates the importance of substance use history as a part of the routine infertility assessment and the possible value of cessation interventions.

The strengths of the study are that it addresses a locally relevant exposure, standardised protocols of WHO-based semen analysis, and a relatively homogeneous cohort of habitual users. Nevertheless, a number of limitations must be considered. The cross-sectional design does not allow a causal inference and the lack of non-exposed control group restricts the comparative interpretation. The use of non-probability sampling and the single-centre setting may introduce selection bias and restrict generalisability.

CONCLUSION

Habitual betel nut/gutka use among infertile males was associated with a high frequency of abnormal semen parameters, with morphological and combined defects predominating. However, no statistically significant relationship was observed between semen abnormalities and age or duration of consumption. These findings highlight the burden of poor semen quality in this population and underscore the need for substance use counselling as part of routine male infertility assessment.

REFERENCES

1. Salehi B, Konovalov DA, Fru P, Kapewangolo P, Peron G, Ksenija MS, et al. Areca catechu from farm to food and biomedical applications. *Phytother Res.* 2020;34(9):2140-58.
2. Priyadarshini SR, Das R, Panigrahi R, Pati AR, Choudhury BK. Betel nut chewing: a brief review. *Indian J Public Health Res Dev.* 2019;10(11).
3. Dangore-Khasbage S, Bhowate RR, Khubchandani M, Bhowate R. Chemical composition of areca nut and its adverse effects on human health. *Cureus.* 2023;15(8).
4. Farah D, Salman A, Bari K. Smokeless tobacco consumption: evidence-based case study from Karachi, Pakistan. In: *Beyond the pandemic: leaving no one behind.* 2023:153.
5. Luong JH, Kozlakidis Z, Cheong IH, Wang H. Betel nuts, health policies, and adolescent health. *Innov Digit Health Diagn Biomarkers.* 2023;3:46-53.
6. More CB, Patil DJ. Epidemiology of oral submucous fibrosis: prevalence and trends. In: Oral submucous fibrosis: a guide to diagnosis and management. Cham: Springer International Publishing; 2023. p. 17-29.
7. Chatterjee N, Gupte HA, Mandal G. A qualitative study of perceptions and practices related to areca nut use among adolescents in Mumbai, India. *Nicotine Tob Res.* 2021;23(10):1793-800.
8. Mansour HA. Infertility diagnosis and management. *Beni-Suef Univ J Basic Appl Sci.* 2023;12(1):81.
9. Agarwal A, Farkouh AA, Saleh R, Hamoda TA, Harraz AM, Kavoussi P, et al. Controversy and consensus on indications for sperm DNA fragmentation testing in male infertility: a global survey, current guidelines, and expert recommendations. *World J Mens Health.* 2023;41(3):575.
10. Eisenberg ML, Esteves SC, Lamb DJ, Hotaling JM, Giwercman A, Hwang K, et al. Male infertility. *Nat Rev Dis Primers.* 2023;9(1):49.
11. Ahmed FK, Khan TA, Yahya U. Prevalence, causes, and contributing factors of male infertility in Pakistan. *Front Health Inform.* 2024;13(3):10707-12.
12. Kumari K, Dhomeja NL, Gul M, Hashim N, Zain S, Bakhtawar F, et al. Effects of ghutka on semen analysis: observe the effects of ghutka on semen analysis in male patients presenting with infertility. *Pak J Med Health Sci.* 2022;16(12):895.
13. Nieschlag E, Behre HM, Kliesch S, Nieschlag S, editors. Andrology: male reproductive health and dysfunction. Springer Nature; 2023.
14. World Health Organization. WHO laboratory manual for the examination and processing of human semen. Geneva: World Health Organization; 2021. ISBN: 978-92-4-003078-7. Available from: https://www.who.int/publications/i/item/9789240030787.

15. Skakkebæk NE, Lindahl-Jacobsen R, Levine H, Andersson AM, Jørgensen N, Main KM, et al. Environmental factors in declining human fertility. *Nat Rev Endocrinol.* 2022;18(3):139-57.
16. Fan S, Zhang Z, Wang H, Luo L, Xu B. Associations between tobacco inhalation and semen parameters in men with primary and secondary infertility: a cross-sectional study. Front Endocrinol (Lausanne). 2024;15:1396793.
17. Bocu K, Boeri L, Mahmutolu AM, Vogiatzi P. Can lifestyle changes significantly improve male fertility: a narrative review? Arab J Urol. 2025;23(3):190-200.
18. Agarwal A, Baskaran S, Parekh N, Cho CL, Henkel R, Vij S, et al. Male infertility. Lancet. 2021;397(10271):319-33.
19. Rotimi DE, Singh SK. Implications of lifestyle factors on male reproductive health. JBRA Assist Reprod. 2024;28(2):320-330.
20. Chao HH, Zhang Y, Dong PY, Gurunathan S, Zhang XF. Comprehensive review on the positive and negative effects of various important regulators on male spermatogenesis and fertility. Front Nutr. 2023;9:1063510.