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Original Research Article

Effect of malignancy on semen quality in men undergoing fertility preservation prior to cancer treatment

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ABSTRACT

Background: Advances in cancer therapy have significantly improved survival rates, making fertility preservation an essential component of cancer care in young men. While gonadotoxic effects of chemotherapy and radiotherapy are well established, the impact of malignancy itself on semen parameters prior to treatment remains controversial. To evaluate semen parameters in men with various malignancies prior to chemotherapy or radiotherapy and to compare semen quality between testicular and non-testicular cancers.
Methods: This single-center retrospective study included 130 male cancer patients referred for sperm cryopreservation between January 2015 and December 2024. Patients who had received prior chemotherapy or radiotherapy were excluded. Semen samples obtained before initiation of cancer treatment were analyzed for sperm concentration, total motility and progressive motility according to World Health Organization (WHO) criteria, 6th edition 2021. Semen parameters were compared across different malignancy types, including testicular and non-testicular cancers.
Results: The mean age was 25.25 years. Out of 130 patients, 104 patients (80%) had abnormal morphology. Normozoospermia was observed in 13.07% of patients, while 86.9% had at least one semen abnormality. Testicular malignancies were associated with a significantly higher proportion of subnormal sperm concentration (<16 million/ml) compared to non-testicular cancers (58.1% vs. 35.6%, p=0.015). Total sperm motility showed a significant association with cancer type (p=0.034), with hematological and musculoskeletal malignancies demonstrating higher rates of reduced motility. Progressive motility did not differ significantly between testicular and non-testicular cancers.
Conclusions: A substantial proportion of men with cancer exhibit impaired semen parameters even before initiation of gonadotoxic therapy. Testicular malignancy is significantly associated with reduced sperm concentration, while systemic malignancies may adversely affect sperm motility. Early referral for fertility preservation should be strongly recommended for all reproductive-age men diagnosed with cancer.

Keywords: Cancer, Male fertility, Sperm cryopreservation, Semen analysis, Testicular malignancy

INTRODUCTION

Cancer and its treatment pose a significant threat to male reproductive potential. The gonadotoxic effects of chemotherapy and radiotherapy on spermatogenesis are well documented, often resulting in temporary or permanent infertility.[1,2] As survival rates improve, fertility preservation has become an integral component of comprehensive oncological care in reproductive-age men.[3,4] However, whether malignancy itself adversely affects testicular function before initiation of cancer therapy remains a subject of debate. Several studies have reported compromised semen quality in men diagnosed with cancer, particularly those with testicular malignancies, suggesting that the disease process itself may impair spermatogenesis.[5-7] Proposed mechanisms include disruption of testicular architecture, hormonal imbalance, systemic inflammation and paraneoplastic effects.[8,9] In contrast, other studies have demonstrated

semen parameters comparable to those of the general population, especially in non-testicular cancers.[10,11]

This study aimed to assess semen parameters in men with different malignancies before chemotherapy or radiotherapy and to compare semen quality between testicular and non-testicular cancers in a cohort of patients undergoing sperm cryopreservation.

METHODS

This was a single-center retrospective observational study conducted at the Institute of Reproductive Medicine, The Madras Medical Mission, Chennai, over a 10 years period from January 2015 to December 2024. Male patients with a confirmed diagnosis of malignancy who were referred for sperm cryopreservation prior to initiation of chemotherapy or radiotherapy were included in the study. Patients with a prior history of chemotherapy or radiotherapy, recurrent malignancy, inability to produce a semen sample or azoospermia were excluded from the study. A total of 186 patients were referred during the study period. Fifty-six patients were excluded (50 unable to produce a semen sample or were azoospermic and 6 with recurrent cancer). The final analysis included 130 patients. All patients produced at least one semen sample for cryopreservation. Semen analysis was performed at the time of cryopreservation, prior to initiation of cancer treatment. Parameters assessed included sperm concentration, total motility and progressive motility, interpreted according to WHO reference values, 6th edition, 2021.

Statistical analysis

Data were entered in Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 30.0. Continuous variables were expressed as mean±standard deviation and categorical variables were presented as frequencies and percentages. Semen parameters were categorized according to the WHO reference values. The association between semen parameters and type of malignancy was analyzed using the Chi-square test. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 130 male cancer patients were included in the analysis. The mean age was 25.25 years. The mean sperm concentration was 26.28 million/ml, mean total motility was 42.1%, mean progressive motility was 27.9% and mean morphology was 2.13%. Overall, only 13.07% of patients demonstrated normozoospermia, while 86.9% had at least one semen abnormality. The baseline demographic and clinical characteristics of the study population are summarized in Table 1. Hematological malignancies (33.8%) and testicular malignancies (33.1%) constituted the majority of cases, followed by musculoskeletal (15.4%), thyroid (10%), gastrointestinal (3.8%) and other malignancies (3.8%) (Figure 1). Sperm concentration below the WHO reference value of 16 million/ml was observed in 43.1% of patients. When analyzed across individual malignancy groups, sperm concentration did not show a statistically significant difference (p=0.072). However, when malignancies were grouped as testicular versus non-testicular cancers, testicular malignancies demonstrated significantly lower sperm concentration (58.1% vs. 35.6%, p=0.015) (Table 2, Figure 2).

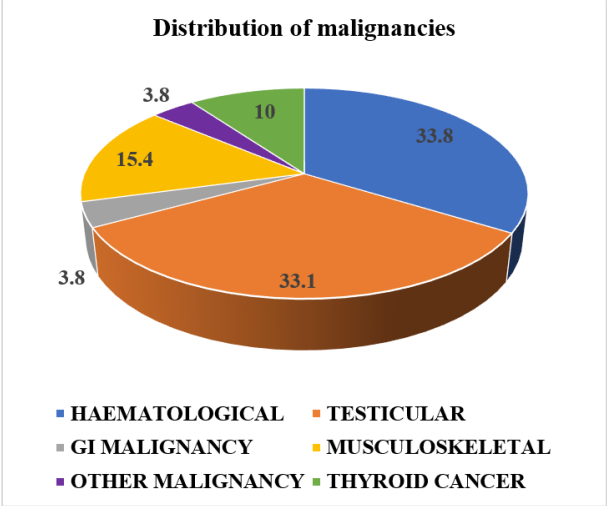

Figure 1: Distribution of various malignancies.

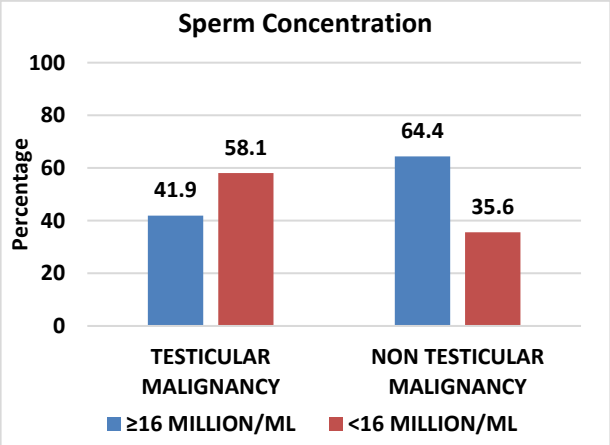

Figure 2: Distribution of sperm concentration in testicular and non-testicular malignancy.

With respect to sperm motility, total motility below the WHO cut-off of 42% was observed in 46.9% of patients. A significant association was noted between type of malignancy and total sperm motility (p=0.034), with higher rates of reduced motility observed in patients with hematological and musculoskeletal malignancies (Table 3). Progressive sperm motility below the WHO reference value of 30% was observed in approximately half of the study population; however, no statistically significant association was found between malignancy type and progressive motility (p=0.062).

Table 1: Distribution of baseline characteristics.

Factors		Distribution N (%)
Age (in years)	<30	106 (81.5)
	≥30	24 (18.5)
Marital status	Married	25 (19.2)
	Unmarried	105 (80.8)
Children	Yes	7 (5.4)
	No	123 (94.6)
Total		130

Table 2: Distribution of various malignancies according to sperm concentration.

Malignancy	WHO-sperm concentration		P value
	≥16 million	<16 million	
	N (%)	N (%)	
GI malignancy	3 (60.0)	2 (40.0)	0.072
Hematological	29 (65.9)	15 (34.1)	
Musculoskeletal	11 (55.0)	9 (45.0)	
Others	2 (40.0)	3 (60.0)	
Testicular	18 (41.9)	25 (58.1)	
Thyroid cancer	11 (84.6)	2 (15.4)	
Total	74 (56.9)	56 (43.1)	

Table 3: Distribution of various malignancies according to total sperm motility.

Malignancy	WHO- Total motility (%)		P value
	≥42%	<42%	
	N (%)	N (%)	
GI malignancy	4 (80.0)	1 (20.0)	0.034*
Hematological	20 (45.5)	24 (54.5)	
Musculoskeletal	8 (40.0)	12 (60.0)	
Others	3 (60.0)	2 (40.0)	
Testicular	22 (51.2)	21 (48.8)	
Thyroid cancer	12 (92.3)	1 (7.7)	
Total	69 (53.1)	61 (46.9)	

*p value<0.05 significant.

Table 4: Distribution of baseline characteristics according to the type of semen abnormality.

Factors		Normal count and motility	Abnormal motility	Abnormal count	Abnormal count and motility	P value
		N (%)	N (%)	N (%)	N (%)	
Age (in years)	<30	32 (30.2)	28 (26.4)	15 (14.2)	31 (29.2)	0.369
	≥30	9 (37.5)	5 (20.8)	6 (25.0)	4 (16.7)	
Marital status	Married	9 (36.0)	3 (12.0)	6 (24.0)	7 (28.0)	0.311
	Unmarried	32 (30.5)	30 (28.6)	15 (14.3)	28 (26.7)	
Children	No	37 (30.1)	33 (26.8)	20 (16.3)	33 (26.8)	0.329
	Yes	4 (57.1)	0 (0.0)	1 (14.3)	2 (28.6)	
Malignancy	GI malignancy	3 (60.0)	0 (0.0)	1 (20.0)	1 (20.0)	0.033*
	Haematological	13 (29.5)	16 (36.4)	4 (9.1)	11 (25.0)	
	Musculoskeletal	4 (20.0)	7 (35.0)	4 (20.0)	5 (25.0)	
	Others	2 (40.0)	0 (0.0)	1 (20.0)	2 (40.0)	
	Testicular	9 (20.9)	9 (20.9)	10 (23.3)	15 (34.9)	
	Thyroid	10 (76.9)	1 (7.7)	1 (7.7)	1 (7.7)	

*p value<0.05 significant.

The distribution of semen abnormalities according to baseline demographic factors and malignancy type is shown in table 4. While 31.5% of patients had normal sperm concentration and motility, only 13.07% fulfilled WHO criteria for normozoospermia after inclusion of morphology. Although sperm morphology was assessed in all patients, the comparative analysis of semen abnormalities was based on sperm concentration and motility, as abnormal morphology was highly prevalent across all malignancy groups. No significant differences in semen abnormality patterns were observed with respect to age, marital status or parenthood status ($p>0.05$). A significant association was observed between malignancy type and semen abnormality pattern ($p=0.033$), with higher proportions of abnormal semen parameters observed in musculoskeletal and testicular malignancies.

DISCUSSION

This study demonstrates that a substantial proportion of men with cancer exhibit impaired semen parameters even before initiation of chemotherapy or radiotherapy. The distribution of malignancies in the study population was relatively balanced between hematological (33.8%) and testicular malignancies (33.1%), followed by musculoskeletal malignancies (15.4%) and thyroid cancer (10%). This distribution allowed a comprehensive evaluation across diverse cancer types, emphasizing the broad impact of malignancy on male fertility. Only 31.5% of patients had normal sperm concentration and motility at baseline, highlighting the importance of early fertility assessment and preservation in this population.[5,10,11] Abnormal sperm morphology (<4% normal forms) was observed in 80% of patients as per the WHO reference values, 6th edition 2021.[16]

The most striking finding was the significantly reduced sperm concentration in patients with testicular malignancies compared to those with non-testicular malignancies. This observation is consistent with previous studies reporting compromised spermatogenesis in men with testicular cancer prior to treatment. Williams et al, and Ku et al, similarly observed lower sperm counts and higher rates of patients with low sperm count in testicular cancer patients, suggesting a direct detrimental effect of the tumor on testicular function.[5,6]

Several mechanisms may explain this phenomenon. Testicular tumors can disrupt the normal architecture of seminiferous tubules, impair local blood supply and alter intratesticular hormonal regulation. Additionally, inflammatory cytokines and paracrine factors released by the tumor may adversely affect spermatogenesis.[8,13] Interestingly, while sperm concentration was significantly reduced in testicular cancer, total and progressive motility did not differ significantly between testicular and non-testicular malignancies. However, when analyzed by individual cancer types, hematological and musculoskeletal malignancies were significantly associated with reduced total motility. This suggests that systemic malignancies may impair sperm motility through indirect mechanisms such as systemic inflammation, oxidative stress, metabolic alterations or endocrine disruption.[9,14,15] The findings align with reports by Gandini et al and Song et al who demonstrated altered semen quality and increased sperm DNA damage in cancer patients even before treatment.[12,15] These results underscore that malignancy itself not only its treatment can compromise male reproductive potential. From a clinical perspective, these findings reinforce the need for prompt fertility counselling and sperm cryopreservation at the time of cancer diagnosis.[3,4] Delays in referral may result in further deterioration of semen quality, reducing future reproductive options.

Limitations

This study is limited by its cross-sectional design and relatively small sample size within some malignancy subgroups. Longitudinal studies assessing semen quality pre- and post-treatment could provide deeper insights into the temporal effects of malignancies and their therapies.

CONCLUSION

A significant proportion of men with cancer demonstrate impaired semen parameters prior to initiation of chemotherapy or radiotherapy. Testicular malignancies are significantly associated with reduced sperm concentration, while systemic cancers may adversely affect sperm motility. These findings highlight the importance of early fertility evaluation and timely sperm cryopreservation in all reproductive-age men diagnosed with cancer, regardless of malignancy type.

Future directions

Further research is warranted to explore molecular mechanisms underlying semen abnormalities in different cancer types and to evaluate the effectiveness of fertility preservation interventions.

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