

# Synergetic effect of hookah smoking on varicocele-associated male reproductive impairment in the Saudi community in Al Jouf region, Saudi Arabia

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## Abstract

**Purpose:** The aim of this study is to explore the clinical relationship between the varicocele-associated male infertility with hookah smoking practice in the Saudi community in the al Jouf region.

**Materials and Methods:** A total of 192 patients were categorized into two groups; varicocele with (Varicocele-Associated Hooka (VH) group;  $n = 100$ ) and without smoking (NHV group;  $n = 92$ ). Laboratory investigations such as hormonal (follicle-stimulating hormone, and luteinizing hormone [LH]), semen analysis were performed. Ultrasonography-based varicocele screening was performed. Data were analyzed with SPSS version 21.0.  $P < 0.05$  was considered statistically significant.

**Results:** Increased prevalence of varicocele Grade 2 (57%) and Grade 3 (52.5%) in HV groups. In contrast, Grade 1 was increased in NHV group (55.6%). A significant ( $P = 0.05$ ) decrease in testosterone levels in the HV group ( $2.83 \pm 0.21$ ) as compared to NHV group ( $2.33 \pm 0.07$ ) observed. Decreased levels of sperm count ( $21.96 \pm 6.31$ ) and sperm morphology ( $14.09 \pm 0.45$ ) were observed in HV groups as compared to NHV group ( $22.5 \pm 5.49$ ,  $14.51 \pm 5.02$ , respectively). HV groups showed the increased diameter of the testicular vein ( $3.52 \pm 0.71$ ) as compared to NHV group ( $3.42 \pm 0.72$ ). Chronic smoking revealed a statistically significant effect on testosterone ( $P = 0.015$ ) and LH levels ( $P < 0.041$ ) in the HV group. In addition, hookah smoking sessions per week affect sperm motility ( $P = 0.02$ ) in the HV group. A significant correlation was observed in sperm count ( $r = 0.24$ ,  $P < 0.016$ ) and motility ( $r = 0.25$ ,  $P = 0.010$ ) in HV group.

**Conclusion:** Chronic hookah smoking significantly affects the reproductive hormonal and semen parameters in varicocele patients as compared to people with varicocele without smoking. This implies that hookah has an adverse effect on male reproductive and infertility.

**Keywords:** Hookah smoking, infertility, male reproductive dysfunction, oligozoospermia, varicocele

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## INTRODUCTION

Hookah, or waterpipe smoking, is present concern global public health threat mostly among youth and elders,<sup>[1]</sup> with claims that there are >100 million people worldwide

who smoke hookah daily.<sup>[2]</sup> Hookah smoking has its origins in Africa and the Middle East<sup>[2]</sup> and is prevalent among United States immigrants from those regions.<sup>[3]</sup> For centuries, Hookah smoking limited only to the male

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as a cultural habitual phenomenon endemic only in the Middle-Eastern region. Today, Hookah smoking is a rampant social phenomenon plaguing the Saudi Arabia, and other Western countries.

It has evolved to include both genders, as a nonaddictive and safer practice as a smoking alternative in young adults.<sup>[4]</sup> Despite numerous public health efforts to promote a tobacco-free environment, several epidemiological studies reveal hookah use has the highest prevalence amongst youth as an alternative to tobacco.<sup>[5,6]</sup>

Smoking considered one of the major risk factors for the varicocele as a major causative factor for the 40% male infertility<sup>[7]</sup> as compared to nonsmokers. Varicocele population with smoking showed oligozoospermia is ten-fold significantly higher in the Varicocele population associated with smoking with altered semen parameters such as decreased semen quality, functional integration of semen, elevated sperm oxidative stress, DNA fragmentation, necrosis, apoptosis, and sperm immaturity.<sup>[8]</sup> The pathogenesis of varicocele is still uncertain. Recent studies reported that oxidative stress might play a role in sperm dysfunction in varicocele patient.<sup>[9]</sup> Globally, from the past two decades, the rate of infertility was not significantly elevated.<sup>[10]</sup> The statistical data of fertility in Saudi Arabia between 1970 and 2010 were significantly declined by 4.3%.<sup>[11]</sup> Recent data from this country showed about 20% of infertility were significantly observed in both genders (www.medic8.com). This impels the health administrative sector to educate the community regarding the risk factors such as smoking habits associated with the increased infertility in the Saudi population.

## MATERIALS AND METHODS

This study was conducted in primary health centers in the Aljouf region, Saudi Arabia. Mean age between 20 and 60 years with hookah smoking was included in the study. The sample was selected conveniently according to the available participants in the targeted settings, with a sample size of 129, calculated using G. Power 3.1.9.2 software second version. Using Power of 0.8, Alpha of 0.5, and a medium-size effect 0.25 to overcome the dropout problem 30% was added. To overcome the effect of being a multicenter study such as technical issues, another 15% was added. This yielded a total number of 192 participants.

A well-designed questionnaire with baseline data such as age, gender, patient height, weight, years of hookah smoking, smoking sessions per week, past medical illness (reproductive hormone profile) were

collected. Post to the patient consent, they all forward to laboratory investigations, including hormonal analysis (total testosterone follicle-stimulating hormone [FSH], and luteinizing hormone [LH]) with commercially available radioimmunoassay assays kits (Diagnostic Systems Laboratories Inc., Webster, TX, USA) as per assay protocol. In the laboratory, Hormonal analysis was conducted by collecting a 5 ml blood sample from each of the study participants in the early morning (7.30–10.30 am). The samples were centrifuged to obtain the serum that was analyzed for the hormonal content (Testosterone, FSH, LH).

Semen analysis (sperm count, sperm motility, and sperm morphology) was performed as per standard procedures. A total of 192 semen specimens were obtained from the study participants through masturbation. The samples were collected in sterile plastic containers and allowed to liquefy for 30 min abstinence time was 48–72 h. The samples were analyzed after 120 min after collection.

The hormonal analysis was conducted by collecting a 5 ml blood sample from each of the study participants. The samples were centrifuged to obtain the serum that was analyzed for the hormonal content (Testosterone, FSH, LH).

All the investigations were carried out on the same patient visiting day. The body mass index (BMI) was calculated by dividing weight by height squared ( $\text{kg}/\text{m}^2$ ). Ultrasonography was performed to screen the varicocele in the study population. Ultrasonography was double-checked by different researchers to ensure the highest accuracy of the results. Varicocele grading was defined as per the Sarteschi classification. All grades of varicocele after ultrasonography were included in this study, whereas, participants with any history of inguinoscrotal surgery, undescended testicle, endocrine disorders, azoospermia, and use of any exogenous androgen or aromatase inhibitors were excluded before the study.

Sarteschi classification includes five different classes or grades of varicocele; they are grade one that includes “reflux in the inguinal channel during Valsalva,” Grade 2 that includes “small varicosities extend to superior pole of testis,” Grade 3 that includes “vessels enlarged at the inferior pole of testis only in standing position,” Grade 4 that includes “vessels appear enlarged in the supine position,” and Grade 5 that includes “Venous ectasia even in prone decubitus and supine positions.”

Data were analyzed with SPSS version 21.0 (Chicago, IL, USA). Statistical tests including, Descriptive analysis, Pearson

correlation, independent *t*-test, Chi-square, and Levene's test of equal variance were applied in this study. Data were presented as means  $\pm$  standard deviation. Significance was set at  $P < 0.05$ .

The present study protocol was reviewed and approved by the Local Committee of Bioethics, Jouf University (approval number: 5-15-9/40). Informed consent was obtained by all subjects when they were enrolled.

## RESULTS

Our results showed, increased prevalence of varicocele Grade 2 (57%) and Grade 3 (52%) in HV groups as compared to NHV group (43%, 47.5%). In contrast, Grade 1 was increased in NHV group (55.6%) [Table 1]. There was no significant difference in age ( $P = 0.84$ ) and BMI ( $P = 0.10$ ) among both groups. Our results explored a significant ( $P = 0.05$ ) decrease in testosterone levels in the HV group ( $2.83 \pm 0.21$ ) as compared to NHV group ( $2.33 \pm 0.07$ ) [Table 2]. In contrast, no significant effect of hookah smoking on FSH and LH levels in both groups were observed [Table 2]. Decreased levels of sperm count ( $21.96 \pm 6.31$ ) and sperm morphology ( $14.09 \pm 0.45$ ) was observed in HV groups as compared to NHV group ( $22.5 \pm 5.49$ ,  $14.51 \pm 5.02$ , respectively). Our data showed HV groups patients with an increased diameter of the testicular vein ( $3.52 \pm 0.71$ ) as compared to NHV group ( $3.42 \pm 0.72$ ).

Chronic hookah smoking revealed a statistically significant effect on testosterone ( $P = 0.015$ ) and LH levels ( $P < 0.041$ ) in the HV group patients. In contrast, no significant effect of chronic smoking on FSH levels, sperm count, morphology, and motility. Furthermore, our results explored that hookah smoking sessions per week was significantly affect sperm motility ( $P = 0.02$ ) in the HV group [Table 3]. The levels of testosterone in HV group patients showed a significant correlation with sperm count ( $r = 0.24$ ,  $P < 0.016$ ) and motility ( $r = 0.25$ ,  $P = 0.010$ ) as compared to NHV group [Table 3].

## DISCUSSION

Varicocele is the abnormalities in the spermatic vein that includes tortuousness and dilatation. Varicocele prevalence in the general adult population is approximate 15%–20%.<sup>[12]</sup> Its incidence in secondary infertility male patients is between 75% and 81%.<sup>[13]</sup>

In our study, the significant incidence of Grade 2 and 3 varicocele was observed in patients with hookah smoking. Nonsmoking associated varicocele patients are reported

**Table 1: Frequency and percentage of varicocele grades (1-3) among the study groups**

Variable	HV group (n=100), n (%)	NHV group (n=92), n (%)
Grade 1	51 (51)	51 (55.6)
Grade 2	57 (57)	40 (43)
Grade 3	52 (52)	44 (47.5)

**Table 2: Mean and standard deviation for age, body mass index, testosterone, follicle-stimulating hormone, luteinizing hormone, sperm count and morphology, and diameter of the testicular**

Variable	HV group (n=100)	NHV group (n=92)	P
Age	43.17 $\pm$ 1.17	42.93 $\pm$ 1.03	0.84
BMI	29.05 $\pm$ 1.11	30.21 $\pm$ 0.94	0.10
Testosterone	2.83 $\pm$ 0.21	2.33 $\pm$ 0.07	0.0016
FSH	23.8 $\pm$ 13.6	23.5 $\pm$ 8.9	0.310
LH	9.4 $\pm$ 7.2	8.8 $\pm$ 6.2	0.261
Sperm count	22.5 $\pm$ 5.49	21.96 $\pm$ 6.31	0.002
Sperm morphology	14.51 $\pm$ 5.02	14.09 $\pm$ 0.45	0.214
Diameter of the testicular	3.52 $\pm$ 0.71	3.42 $\pm$ 0.72	0.014

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

**Table 3: Association between Hookah smoking sessions per week, sperm motility, level of testosterone, and sperm count in HV group**

Variable	Sperm motility	Sperm count
Hookah smoking sessions per week		
<i>r</i>	0.02	0.04
<i>P</i>	0.003	0.014
Level of testosterone		
<i>r</i>	0.25	0.24
<i>P</i>	0.010	0.016

high Grade 1 varicocele. This results emphasizes that hookah smoking potentially associated with the development of varicocele induced male infertility by effect the semen parameters. Our observations are in agreement with previous reports stated that, Grade-3 varicocele association with low semen quality.<sup>[14]</sup>

It was reported that Hookah smoking session for 1 h emits approximately four times of volatile aldehydes, carcinogenic polyromantic hydrocarbons in the side stream along with carbon monoxide equal to 30 cigarettes.<sup>[15]</sup> Smoking influences the male reproductive hormones levels and considered risk factor for sub-fertility.<sup>[16]</sup> Till to date, there is no literature evidence on the role of hookah smoking on aggravation of varicocele. In this study, the levels of testosterone in varicocele patients associated with smoking were significantly ( $P < 0.05$ ) low as compared to nonsmoking-associated varicocele. In contrast, some studies reported that the levels of testosterone are increase in smokers by induction of the testicular Leydig cells.<sup>[17]</sup> Meanwhile, some studies revealed no effect of smoking

on testosterone levels;<sup>[18]</sup> hence, the specific effect remains uncertain. Follicle-stimulating hormone and LH hormones are involved in the regulation of Leydig cell and Sertoli cell function. Increased levels of FSH was associated with varicocele.<sup>[19]</sup> Our results revealed there is no significant difference of hookah smoking on the levels of FSH in both study groups. However, the varicocele and FSH associations still unclear.<sup>[20]</sup> No significant differences in serum LH levels among the two groups. Chronic smoking shows a negative effect on the levels of testosterone by enhancing hepatic metabolism. In our study, chronic hookah smoking revealed a statistically significant effect on testosterone ( $P = 0.015$ ) and LH levels ( $P < 0.041$ ) in the HV group patients. Our results supported by Blanco-Muñoz *et al.* study reported that increased levels of LH in smokers who smoke more than five smoking sessions.<sup>[17]</sup>

Abnormal spermatogenesis is associated with the impaired reproductive hormone system and testis dysfunction (Reyes JG 2012). Smoking deteriorates the ultrastructure detriment of testis<sup>[21]</sup> and also induces apoptosis,<sup>[22]</sup> germ cells, Sertoli cells and Leydig cells number reduction.<sup>[23]</sup> In our study, increased diameter of the testicular vein in varicocele associated hookah smokers was observed. Smoking effects the proteins (nuclear factor- $\kappa$ B, Akt, Pkc (s), and ERK1/2) of the cell signal pathway networks responsible for spermatogenesis and DNA methylation of the testis.<sup>[24]</sup> Reproductive pathology also reported in smokers due to epididymal dysfunction.<sup>[25]</sup> Animal studies revealed attenuation of sorbitol dehydrogenase followed by increased lactate dehydrogenase in epididymis resulted as sperm maturation defect.<sup>[26]</sup> Our study showed significantly decreased levels of sperm count, sperm morphology in varicocele associated hookah smokers as compared to nonsmokers with varicocele. Our results comparatively supported by earlier studies reported that population with varicocele associated with tobacco smoking experienced with oligozoospermia ten-fold greater than nonsmokers along with altered sperm functional integrity and semen quality.<sup>[8]</sup>

Conventional semen parameters relationship with smoking is till controversial for the last 30 years.<sup>[27]</sup> It was also reported that smoking-induced oxidative stress negatively affect the spermatozoa.<sup>[28]</sup> Our study showed significantly decreased levels of sperm count, sperm morphology in varicocele associated hookah smokers as compared to nonsmokers with varicocele. This is in agreement with recent studies revealed, sperm dysfunction in varicocele patients associated with oxidative stress.<sup>[9]</sup>

## CONCLUSION

Hookah smoking in varicocele patients shown a significantly negative effect on semen parameters such as semen quality and motility as compared to nonhookah smokers with varicocele. This study mainly highlighted the effect of hookah on decreased levels of testosterone levels in patients with varicocele. In addition, chronic hookah smoking and the number of hookah smoking sessions also potentially affected the reproductive hormonal levels and semen analysis in the varicocele patients as compared to varicocele patients without hookah smoking. The outcomes of this study open a scope for further research regarding the acute as well as chronic effects of hookah smoking associated with male infertility.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Chaouachi K. A critique of the WHO's TobReg's "Advisory Note" report entitled: "Waterpipe tobacco smoking: health effects, research needs and recommended actions by regulators." *J Negat Results Biomed* 2006;5:17.
2. Knishkowsky B, Amitai Y. Water-pipe (narghile) smoking: An emerging health risk behavior. *Pediatrics* 2005;116:e113-9.
3. Aljarrah K, Ababneh Z, Al-Delaimy W. Perceptions of Hookah smokingharmfulness: Predictors and characteristics among current Hookah users. *Tob Induc Dis* 2019. 18;5:16.
4. Sadiq MA, Parekh MA, Zubairi ABS, Khan J, Frossard PM. Cross-sectional study identifying forms of tobacco used by Shisha smokers in Pakistan. *JPMA. The Journal of the Pakistan Medical Association* 2012;62:192-5.
5. Gilreath TD, Leventhal A, Barrington-Trimis JL, Unger JB, Cruz TB, Berhane K, *et al.* Patterns of alternative tobacco product use: Emergence of Hookah and E-cigarettes as preferred products amongst youth. *J Adolesc Health* 2016;58:181-5.
6. Montgomery SB, De Borja-Silva M, Singh P, Dos Santos H, Job J S, Brink TL. Exploring demographic and substance use correlates of hookah use in a sample of southern *California community college students.* *Californian journal of health promotion* 2015;13:26-37.
7. Antonia M, Intasqui P, Camargo M, Zylbersztejn DS, Cedenho AP, Bertolla RP. Harmful effects of smoking to male fertility. *Fertility and Sterility*, 2014;102:194-e195.
8. Fariello RM, Pariz JR, Spaine DM, Gozzo FC, Pilau EJ, Fraietta R, *et al.* Effect of smoking on the functional aspects of sperm and seminal



- plasma protein profiles in patients with varicocele. *Hum Reprod* 2012;27:3140-9.
9. Agarwal A, Sharma RK, Desai NR, Prabakaran S, Tavares A, Sabanegh E. Role of oxidative stress in pathogenesis of varicocele and infertility. *Urology* 2009;73:461-9.
  10. Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: A systematic analysis of 277 health surveys. *PLoS Med* 2012;9:e1001356.
  11. Centers for Disease Control and Prevention. Smoking and Tobacco Use: Hookah 2013. Available from: <[http://www.cdc.gov/tobacco/data\\_statistics/fact\\_sheets/tobacco\\_industry/hookahs/index.htm](http://www.cdc.gov/tobacco/data_statistics/fact_sheets/tobacco_industry/hookahs/index.htm)> [Last accessed on 2020 Mar 25].
  12. Reesink DJ, Huisman PM, Wiltink J, Boeken Kruger AE, Lock TMTW. Sneezing and popping: A ruptured varicocele; analysis of literature, guided by a well-documented case-report. *BMC Urol* 2019;19:14.
  13. Miyaoka R, Esteves SC. A critical appraisal on the role of varicocele in male infertility. *Advances in urology* 2011;2012:1-10.
  14. Naughton CK, Nangia AK, Agarwal A. Varicocele and male infertility. Part II. Pathophysiology of varicoceles in male infertility. *Hum Reprod Update* 2001;7:473-81.
  15. Daher N, Saleh R, Jaroudi E, Sheheitli H, Badr T, Sepetdjian E, *et al*. Comparison of carcinogen, carbon monoxide, and ultrafine particle emissions from narghile waterpipe and cigarette smoking: Sidestream smoke measurements and assessment of second-hand smoke emission factors. *Atmos Environ (1994)* 2010;44:8-14.
  16. Jeng HA, Chen YL, Kantaria KN. Association of cigarette smoking with reproductive hormone levels and semen quality in healthy adult men in Taiwan. *J Environ Sci Health A Tox Hazard Subst Environ Eng* 2014;49:262-8.
  17. Blanco-Muñoz J, Lacasaña M, Aguilar-Garduño C. Effect of current tobacco consumption on the male reproductive hormone profile. *Sci Total Environ* 2012;426:100-5.
  18. Pasqualotto FF, Sobreiro BP, Hallak J, Pasqualotto EB, Lucon AM. Cigarette smoking is related to a decrease in semen volume in a population of fertile men. *BJU Int* 2006;97:324-6.
  19. Pasqualotto FF, Lucon AM, de Góes PM, Sobreiro BP, Hallak J, Pasqualotto EB, *et al*. Semen profile, testicular volume, and hormonal levels in infertile patients with varicoceles compared with fertile men with and without varicoceles. *Fertil Steril* 2005;83:74-7.
  20. Kumanov P, Nandipati K, Tomova A, Agarwal A. Inhibin B is a better marker of spermatogenesis than other hormones in the evaluation of male factor infertility. *Fertil Steril* 2006;86:332-8.
  21. Abdul-Ghani R, Qazzaz M, Dabdoub N, Muhammad R, Abdul-Ghani AS. Studies on cigarette smoke induced oxidative DNA damage and reduced spermatogenesis in rats. *J Environ Biol* 2014;35:943-7.
  22. La Maestra S, De Flora S, Micalé RT. Effect of cigarette smoke on DNA damage, oxidative stress, and morphological alterations in mouse testis and spermatozoa. *Int J Hyg Environ Health* 2015;218:117-22.
  23. Ahmadnia H, Ghanbari M, Moradi MR, Khaje-Dalouee M. Effect of cigarette smoke on spermatogenesis in rats. *Urol J* 2007;4:159-63.
  24. Xu W, Fang P, Zhu Z, Dai J, Nie D, Chen Z, *et al*. Cigarette smoking exposure alters pebp1 DNA methylation and protein profile involved in MAPK signaling pathway in mice testis. *Biol Reprod* 2013;89:142.
  25. González-Jiménez MA, Villanueva-Díaz CA. Epididymal stereocilia in semen of infertile men: Evidence of chronic epididymitis? *Andrologia* 2006;38:26-30.
  26. Zhu Z, Xu W, Dai J, Chen X, Zhao X, Fang P, *et al*. The alteration of protein profile induced by cigarette smoking via oxidative stress in mice epididymis. *Int J Biochem Cell Biol* 2013;45:571-82.
  27. Mak V, Jarvi K, Buckspan M, Freeman M, Hechter S, Zini A. Smoking is associated with the retention of cytoplasm by human spermatozoa. *Urology* 2000;56:463-6.
  28. Yu B, Qi Y, Liu D, Gao X, Chen H, *et al*. Cigarette smoking is associated with abnormal histone-to-protamine transition in human sperm. *Fertil Steril* 2014;101:51-7, e1.