

# LONG TERM EFFECTS OF OPIATE ADDICTION ON MALE FERTILITY

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## ABSTRACT

**Objective:** To assess the fertility of chronic opiate addicts by correlating their semen analysis with the healthy controls.

**Material and Methods:** The study was conducted on 25 opiate addicts admitted in Khyber Teaching Hospital Peshawar and Lady Reading Hospital Peshawar. All patients were male and were more than 15 years of age. All patients were studied for hormone analysis including FSH, LH, prolactin and testosterone. Semen analysis of addicts was compared with 25 normal healthy controls.

**Results:** Study included 25 male opiate addicts of mean age of 30.16 years ( $\pm$  8.56) and 25 healthy controls of mean age 31.06 ( $\pm$  9.76). Mean duration of opiate addiction was 27.36 months ( $\pm$  7.64). 36% of patients had urinary metabolites of 200-1000 ng/ml. The rest had levels of more than 2000 ng/ml. Reduced sexual ability was present in 64% of patients. No significant difference among levels of FSH, LH and testosterone before and after treatment except for prolactin level which raised from pretreatment level of mean 3.95 ( $\pm$  3.14) to mean 16.39 ( $\pm$  1.87) ng/ml.

**Conclusion:** Severe abnormalities in opiate addicts may result from hyperprolactinemia.

**Key words:** Opiate, addicts, fertility.

## INTRODUCTION

Weak social and economic conditions of any country have gross impacts on its overall health situation and increased vulnerability of the general population to drug problems. A number of socioeconomic

factors like youth, unemployment, large disparities between income groups, slums, poverty and urbanization are known to be linked to drug abuse and crime.

Heroin was synthesized in the year 1898 and at that time it was believed to be a good cure for morphine addiction but soon it was

realized that it can be more harmful than beneficial. However despite reduction in the poppy production in Pakistan, the Frontier Province of Pakistan and Afghanistan are the major drug producers of the world. Pakistan being the major transit country used by the drug traffickers, its local population has been very badly affected by the drug abuse problem. The national survey on drug abuse in 1993 revealed that there were 3.01 million chronic drug abusers in Pakistan, rising at a rate of nearly 7% annually. About 1.5 million people are addicted to heroin. Nearly 72% of the drug abusers are under 35 years of age and 97.2% of the drug abusers are male<sup>(2)</sup> Chronic Drug Abuse adversely effects the physical, mental and psychological status of the individuals. As majority of drug abusers are young and in the productive age group, concerns have been shown regarding sexual dysfunction in chronic drug abusers. Various studies have been done to study the effects of drug abuse on sex behaviour and fertility of male and female drug addicts<sup>(3-9)</sup>.

As nearly 97% of drug addicts in Pakistan are male<sup>2</sup> and local infertility date shows oligospermia and Azospermia in 4.6% and 2.1% of the infertile patients<sup>(10)</sup>, this study was aimed to assess the fertility of chronic opiate male addicts in comparison with healthy controls.

## MATERIAL AND METHODS

This study was conducted on 25 patients who were opiate addicts, admitted in Khyber Teaching Hospital Peshawar and Lady Reading Hospital Peshawar. All patients were male and were more than 15 years of age. All patients were studied for hormone analysis including FSH, LH, prolactin and testosterone. 25 healthy males were used as controls. Routine semen analysis of these addicts and the normal controls was also performed. The urine samples were stored at -20°C after the addition of preservative sodiumazide. About 50 ul of urine samples

for opiates was processed along with the controls. The routine lab technique was used for the analysis of FSH, LH, prolactin and testosterone. Reagents for flouoroimmuno assay of opiates comprised of Abbot opiates reagent pack containing.

- (W) Opiate was solution buffer with protein stabilizer. Preservative = 0.1% sodium azide.
- (S) Opiates Antiserum (Sheep) in buffer with protein stabilizer.
- (T) Opiates derivatives – Flourescin tracer in buffer with surfactant and protein stabilizer. Preservative = 0.1% sodium azide.

### OPIATE CALLIBRATOR

Six vials with accurately measured amounts of morphine in normal human urine at the following concentrations.

<u>Vial</u>	<u>Morphine Concentration (ng/ml)</u>
A	0.0
B	100.0
C	200.0
D	350.0
E	600.00
F	1000.00

Preservative – 0.1 % sodium azide.

### OPIATES CONTROLS

Two vials of morphine in normal human urine which read within the following ranges:-

<u>Vial</u>	<u>Morphine Concentration (ng/ml)</u>
L (low)	225-275
H (high)	680-920

Preservations = 0.1% sodium azide.

## RESULT

This study comprised of 25 male patients addicted to opiates. Mean age of

**PERCENTAGE OF PATIENTS TAKING OPIATES OVER DIFFERENT PERIODS OF TIME.**

Duration of addiction in months	Number of patients n = 25	% age
1 - 12	2	8
13 - 18	3	12
19 - 24	3	12
25 - 30	8	32
> 30	9	36

TABLE - 1

patients was 30.16 years (SD ± 8.56) and mean age of controls was 31.06 (SD ± 7.64) WITH 68%. Mean duration of opiate addiction was 27.36 months (50 ± 7.64) with 68% of patients having more than 2 years duration of opiate addiction.

Thirty six percent of addicts had urinary metabolites level of 200-1000 ng/ml where as rest of patients had levels of more than 2000 ng/ml. The lowest level of opiate detected to be positive in these patients was 248 ng/ml whereas the highest positive level was 54800 ng/ml.

Most of the opiates showed GIT manifestations presenting with anorexia in 88% of cases followed by CNS manifestation like confusion in 72% of cases. Reduced

**PERCENTAGE OF OPIATE ADDICTS HAVING SYSTEMIC MANIFESTATIONS.**

Systemic manifestations of opiate addiction	No. of opiate addiction n = 25	% age
Anorexia	22	88
Confusion	18	72
Reduced sexual ability	16	64
Dizziness	12	48
Nausea	11	44
Slurring of speech	10	40

TABLE - 2

**MEAN VALUE OF PROLACTIN, FSH, LH AND TESTOSTERONE LEVEL IN OPIATE ADDICTS BEFORE AND AFTER TREATMENT.**

	Before treatment mean value (SD)	After treatment mean value (SD)
Prolactin ng/ml	3.95(±3.14)	16.39(± 1.87)
FSH miu/ml	4.58(± 1.23)	4.56(± 1.09)
LH miu/ml	4.8(±1.10)	4.50(± 2.81)
Testosterone ng/ml	3.9(±1.22)	4.65(± 1.81)

TABLE - 3

sexual ability was present in 64% of patients.

There were no significant differences when before treatment and after treatment samples were compared for serum testosterone, FSH and LH. (Table 3). However a significant difference was observed when serum prolactin before treatment (mean 3.95 ng/ml ± 3.114) was compared with the serum prolactin level after treatment; (Mean = 16.39 ±1.87) Different parameters of semen analysis showed significant difference when semen analysis of opiate addicts was compared with those of healthy individuals. (Table 4).

## DISCUSSION

World wide, drug abuse has been related to various socioeconomic factors and various means and tools have been designed to help the drug addicts to protect themselves from drug abuse and other social and health threats. But in Pakistan, no ongoing surveillance system is available to monitor the trends over the time or to study the outcome measures of drug addiction or to register any drug related overdose or deaths. There is a strong need of continuous medical supervision to the person and an affective screening programme to detect the drug addicts and to screen them for various medical complications. Detection of opiates in stool and urine by florescence polarization

COMPARISON OF SEMEN ANALYSIS OF  
HEALTHY MALES (n=25) AND HEROIN  
ADDICTS (n = 25).

PARAMETERS	Healthy controls median (range)	Patients median (range)
1. FULL ACTIVE		
a. 15 min %	70 (55-85)	27.5 (10-5)
b. 1 h %	47.5 (30-60)	13.8 (5-20)
c. 2 h %	25 (15-35)	6.7 (3-10)
d. 5 h %	8.25 (5-15)	2.3 (1-4)
e. 24 h %	0.37 (0 - 1)	0.62 (0-1)
2. SLIGHTLY ACTIVE		
a. 1 h %	4 (2-7)	5 (2-7)
b. 2 h %	6 (4-9)	8 (7-9)
c. 5 h %	8 (6-11)	10 (9-12)
3. VOLUME		
(ml)	3 (1.0-3.5)	2 (1.0-3.5)
4. SPERM COUNT		
(million)	76 (65-95)	20 (5-35)

TABLE - 4

immunoassay by the TDx analyzer is very reliable. The most commonly abused opiate in our part of the world is heroin, which is rapidly hydrolyzed in the blood stream to 6 - monoacetyl morphine which undergoes further hydrolysis to morphine. Morphine is excreted in the urine or is further metabolized to morphine glucuronides. Detection of urinary metabolites of opiates can be used to label the patient as positive or negative for drug addiction. Methadone is a drug given to patients as a substitute for abused

narcotics. Methadone is a narcotic with an extended duration of action. The patient using methadone should be regularly screened for urine analysis. If urine analysis indicates the presence of methadone in urine, it confirms that the patient is using the drug. Urine analysis also helps in the detection of other abused substances.

Drug abuse adversely affects the health of the patient in different ways. Apart from various biomedical consequences, drug abuse can cause sexual dysfunction and infertility in both men and women. However as men are more involved in drug addiction, the overall impact of drug abuse on male sexual dysfunction is more pronounced.

This study was conducted on male addicts only, the hormones FSH, LH, testosterone and prolactin were assayed in the chronic opiate (heroin) addicts before and after treatment. There was no significant difference between the before and after treatment levels of FSH, LH and testosterone. However the serum level of prolactin was more than the reference range (0.20- 9.40 ng/ml) in the patients after treatment with opium capsules or methadone.

Ragni et al<sup>(11)</sup> (1988) reported that the FSH, LH and testosterone levels were normal in the study conducted by them but the prolactin level was raised to more than 15 ng/ml. Semen analysis of both the heroin addicts and the heroin methadone users were abnormal. Asthenospermia was found in all the cases. 24% showed hypospermia and 17% had oligozoospermia. This is due to the possible toxic effects of heroin to the male reproductive system.

Ragni et al<sup>(11)</sup> (1988) reported the seminal pathology in terms of volume, motility and count in heroin addicts. They observed that the semen abnormalities gave much earlier signs of testicular damage than do abnormalities of hormone levels. Spagnolli et al<sup>(12)</sup> (1987) also reported increased level of prolactin in heroin addicts.

In the present study the prolactin level raised after the treatment. The hyperprolactinaemia observed in heroin addicts may be due to the effects of opium capsules (containing crude opium), which were used as replacement therapy in these patients.

Semen analysis of chronic opiate addicts revealed that the volume, sperm count and activity of sperm was significantly decreased when analyzed against the significantly decreased when analyzed against the healthy controls. Singer et al<sup>(13)</sup> (1986) reported that oligozoospermia and the sperm pathology both resulting from a significant spermatogenesis arrest and abnormally processing spermatogenesis may be caused by the long standing use of heroin.

According to Singer et al<sup>(13)</sup> (1986) the possibility that the prolonged use of narcotics has a deleterious autoimmune influence on sperm production should be considered. They observed that forty years male had a positive history of heroin addiction for the last 12 years. On examining of his semen it was found that the patient had oligozoospermia, asthenozoospermia and morphologically abnormal sperms. Normal sperms were not found. A possible correlation was assumed between the duration of addiction and the semen abnormalities.

## CONCLUSION

Semen abnormalities in opiate addicts may also result because of hyperprolactinaemia. Further research is required to elucidate the exact causative factors especially if normal spermatogenesis is restored, as frequently occurs after withdrawal of spermatogenesis suppressing substances.

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## REFERENCES

1. Lewis DC, Finberg NE. A historical perspective on a difficult medical problem. *N Eng J Med*; 20: 1045.
2. Country Report. UNDP, Pakistan-2002.
3. Ragni G, DeLaurts L, Gambaro V et al. Semen evaluation in heroin and methadone addicts. *Acta Eur Fertil* 1985; 16: (4) 245.
4. Harding C, Ritche J. Contraceptive practice of women with opiate addiction in a rural center. *Aust R Rural Health* 2003; 11(1): 2.
5. Fasolis G, Colombo M, Tarabuzzi R, Fonitana D. Drug, Impotence and fertility. *Arch Ital Urol Netrot Androp* 1991; 63 (4): 397.
6. Wein AJ, Van Arsdalen KN. Drug induced male sexual dysfunction. *Urol Clin North Am* 1988; 15 (1): 23.
7. Buchanan JF, Davis LJ. Drug Induced Infertility. *Drug Intell Clin Pharm* 1984; 18(2): 122.
8. Brock JB, Ine TF. Drug Induced male sexual dysfunction An update. *Drug Safety* 1993.
9. Ozaki S. Psychoactive Substance-induced sexual dysfunction in men. *Nippon Rinsho*, 2002; 60 suppl 6: 421.
10. Mehmood G, Sadia S. Infertility data of maternal and childhealth center, PIMS J Surg 2001; 21-22: 10.
11. Ragni G, De Launete L, Bestelli O et al. Gonadal Function in male heroin and methadone addicts. *J Andrology*, 1988; 11: 93.
12. Spagnolly W, Torboli P, Matterei M. et al. Calcitonin and Prolactin Serum levels in heroin addicts: study on methadone treated group. *Drug and Alcohol dependence*, 1987; 20: 143.
13. Singer R, Bassat B, Malik Z. Oligozoospermia, asthenozoospermia and sperm abnormalities in ex-addicts to heroin, morphine and hashish. *Arch of Andrology*; 1986; 16: 167.