

Reproductive Outcome in the Wives of Traffic Policemen Exposed to Automobile Exhaust

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ABSTRACT Adverse health effects and reproductive hazards at the workplace are an issue of increasing health concern and more than 1000 chemicals at workplace have been demonstrated to have adverse effects in animals. However such studies are limited in humans. Since data on reproductive epidemiology in traffic policemen exposed to automobile exhaust is limited, a study on the reproductive endpoints of traffic policemen exposed to vehicular exhaust was undertaken. Information on age, sex, medical history, occupational health problems, reproductive outcome, possible exposure to mutagens, etc was collected and clinical investigations were undertaken. A significant increase in neonatal deaths and abortions in the wives of traffic police and a decrease in live births was observed. The findings suggest that exposure to vehicular exhaust induce adverse reproductive outcome in the traffic police.

INTRODUCTION

The twin cities of Hyderabad and Secunderabad, located in the central Deccan plateau of India covering an area of 217 sq Km has witnessed an explosive growth in the last decade, both in the human and vehicular population. The cities with a human population of 3.1 million and a vehicle count of 9 lakhs present a vast and varied picture of transport for any one involved in managing the traffic. The vehicles have different kinds of combustion engines and use petrol or diesel as the fuel. Thus with the ever-increasing vehicular traffic density, there is an increase in the emission of combustion products into the environment which is posing a continued threat to ambient air quality. Petrol driven vehicles are causing more pollution than diesel driven vehicles particularly in respect of carbon monoxide. Diesel vehicles are responsible for smoke (sulphur dioxide and soot). As per the State's estimate trucks constitute almost 19 per cent of total vehicular density in the city and emission from these automobiles add to the total black carbon concentration of the ambient air. The tiny carbon particles absorb sunlight and contribute to a great extent in polluting the environment. The cumulative effect of unburnt hydrocarbons from both fuel sources makes the air quality stressful. Further, increased use of adulterated petrol and diesel products and the

absence of an integrated and co-ordinated policy for urban air quality management compound this problem. In the third world countries, monitoring of the air pollution has not caught up with the standards setup by the developed countries.

Andhra Pradesh Pollution Control Board (APPCB) has reported that the total vehicular pollution load for the years 1998 - 1999 during the period of study, was 691 Tonnes/day at various centers in the twin cities. The data indicated that the pollution load had increased from 357.13 T/day in the year 1991 to 691 T/day in the year 1999. The total vehicular pollution load in twin cities was contributed by various pollutants like CO (392.2 T/day), HC (239.7 T/day), NO_x (43.6 T/day), SO₂ (6.0 T/day), SPM (9.5 T/day) and lead oxide particles (PbO) (0.162 T/day). Vehicular exhaust is also a source of aldehydes, esters, ethers, peroxides and ketones, which are chemically active.

People including the residents of the shops, houses, offices on the way side, the motorists, the pedestrians, the traffic police are exposed to vehicular pollution in varied degrees. Among all of them the traffic police are unduly and chronically exposed to vehicular exhaust pollutants as they remain on duties for longer periods.

Rebecca et al. (1996) reported that automobile exhaust remains a major source of pollution and the pollutants cause local changes in the air

quality, which affect the human health adversely. Settle and Patterson (1982) showed the toxicity of lead and carbon monoxide, which are the important components of vehicular exhaust. Kumar and Krishnaswami (1995) reported lead nephrotoxicity in automobile mechanics. Leaded petrol is the main source of lead emitted during incomplete combustion of vehicle fuel along with other pollutants. Potula et al. (1998), Onolaja and Claudio (2000) also reported lead induced hematopoietic suppression, anemia, encephalopathy, kidney damage, toxicity to the reproductive system and hypertension at higher concentrations and neurobehavioral disorders and alterations in cognitive development in children at lower exposure levels.

Automobile engine exhaust causes local accumulation of CO adjacent to automotive traffic (Wallace, 1983). CO has a high affinity for hemoglobin and is able to displace oxygen in the blood forming carboxy-hemoglobin and exerts its effects on tissues by interfering with oxygen transport. Atimtay et al. (2000) reported CO induced chronic poisoning which shows its first symptoms as headache, blurry vision, difficulty in concentration and confusion and lower levels of hemoglobin.

The organic compounds of diesel exhaust particles (DEP) were reported to be strong mutagens and carcinogens (Ishinishi et al., 1986). Polycyclic aromatic hydrocarbons in DEP cause cardiovascular and respiratory diseases and cancers in man (Hoffman and Hecht, 1985). OPSMI (1998) also reported particulate matter (PM) in air has been associated with morbidity and mortality from ischemic heart disease in humans. It has also been hypothesized that alveolar inflammation resulting from exposure to PM may induce a state of hyper coagulability, triggering of cardiovascular events in susceptible individuals. Vehicular exhaust pollutants are causative compounds for chronic obstructive pulmonary diseases such as asthma, allergic rhinitis and chronic bronchitis etc.

Environmental pollutants and workplace exposures to lead (Huang et al., 1988), lead and zinc (Bilban, 1998), phenols (Kalina et al., 1998), rubber factory chemicals (Hema Prasad and Reddy, 1993) benzene (Xu et al., 1998) have been shown to adversely affect the reproductive health of males (Michele et al., 2003). Sallmen et al. (2000) reported that exposure to lead in polluted air resulted in decreased fertility rates in men and

delay in the pregnancy rate among their wives. Dejmek et al. (2000) reported reduced birth rates in women and sperm abnormalities in men exposed to higher levels of SO₂. Smrcka and Leznarova (1998) and Hemminki and Niemi (1982) demonstrated adverse reproductive outcome in women occupationally exposed in different workplaces. Studies carried out by Bobak and Leon (1992) reported weak positive associations between neonatal mortality and total suspended particulate matter (TSPM, SO₂ and NO_x).

Data on traffic police exposed to vehicular pollution is limited to adverse effects on health and sperm parameters. Figa-Talamanca et al. (1996) and Tielemans et al. (1999a) reported reduced semen quality in policemen occupationally exposed to vehicular exhaust. Michele et al. (2003) demonstrated adverse affects in sperm parameters in tollgate workers exposed to traffic pollution. Studies from various other countries demonstrated significant increase in the frequency of micronuclei, chromosomal aberrations and sister chromatid exchanges, benzopyrene levels and DNA adducts, endpoints of genetic damage in traffic policemen (Anwar and Kamal, 1988; Carrans and Natarajan, 1988; De Ferrarin et al., 1991; Anwar, 1994; Merlo et al., 1995; Chandrasekaran et al., 1996; Zhao et al., 1998). Since studies on Indian traffic policemen are limited, genetic studies were undertaken in traffic policemen of Hyderabad exposed to vehicular exhaust.

MATERIALS AND METHODS

Based on the information from Pollution Control Board (PCB) of Andhra Pradesh, on vehicular pollution load at various centers in the twin cities of Hyderabad and Secunderabad, traffic policemen who were on duties at the most polluted centers (such as Punjagutta, Ameerpet, Abids and Paradise) with high vehicular traffic density (where more than 2 lakh vehicles cross) were included in the study.

All the subjects were interviewed using the standard questionnaire for information on age, sex, occupation, type of work, hours of work per day, number of years of employment, place and shift of duty, medical history and present health problems, previous exposure to radiation, chemicals, etc. personal habits like smoking, alcohol consumption, chewing of betel leaves, etc.

marital status, type of marriage (consanguineous or not), exposure of spouse to X-rays, drugs, chemicals on the work/home front, personal habits, previous / present medical history of the spouse-regarding contraction of infectious disease like measles, chickenpox, urinary tract infections, gynecological problems before and during pregnancy, etc. The smoking policemen were excluded from the study. The subjects also underwent clinical examination and spirometric evaluation / lung function tests.

The study population consisted of 259 traffic policemen and 200 healthy subjects who belonged to the same age group and socio-economic status were studied for the reproductive performance. Hence, information on the reproductive outcome of 259 traffic policemen was recorded. Details on the reproductive history including the number of pregnancies, live births, abortions, still births, neonatal deaths and congenital malformations in their offspring etc were noted following the criteria set by Danforth (1977).

259 non-smokers in the age group of 22-57 years and their service ranged from 1-32 years. The duties of the traffic police include control of traffic on the roads and check the smooth flow of vehicles, check the documents of the vehicles and drivers, to see the condition of the vehicles by verifying the documents, to monitor vehicular pollution, monitor parking on roads, etc.

Traffic police worked 8 hours a day for 6 days in a week. The traffic policemen were literate (matriculates and under graduates). The wives of the policemen were matriculates or under-graduates and most of them were housewives.

Two hundred non-smoking healthy males including household registered policemen and individuals working in administrative, accounting, secretarial, maintenance and clerical cadres, socially and economically matched with the study population. Working indoors not exposed to vehicular exhaust pollution or any physical or chemical agents at the work place and living in the same geographical area, without any known disease served as the controls. Since, they belonged to the lower socio economic group except for television and refrigerator they hardly used sophisticated electronic gadgets and hence, indoor exposure was minimum. The control subjects living in highly polluted areas were not included in the study.

All the subjects in both the groups of the present study were either non-alcoholics or consumed alcohol occasionally.

Categorical data (married subjects in the control and study groups) were expressed as percentages and compared by the Yate's corrected chi square (χ^2) test.

RESULTS

The data on the reproductive outcome of 259 traffic policemen and 200 controls were evaluated and presented in table 1.

Table 1: Reproductive histories of non-smoking traffic policemen

Particulars	Control group	Exposed group
Number of Males	200	259
Number of fertile males	198 (99)	250 (96.52)
Number of pregnancies	728	873
Number of live births	693 (95.19)	775 (88.77)*
Number of abortions	20 (2.74)	48 (5.49)*
Number of still births	4 (0.54)	11 (1.26)
Number of neonatal deaths	8 (1.09)	31 (3.55)*
Number of congenital defects	3 (0.41)	6 (0.68)
Number of premature births	0 (0.00)	2 (0.22)

Values given in the parentheses are percentages
P<0.05.

Comparison of the reproductive outcome of 259 non-smoking policemen exposed to automobile exhaust with that of 200 non-smoking controls. Results indicated a significant increase in the frequency of abortions in the wives of policemen, neonatal deaths in their offspring and significant decrease in the frequency of live births in the off spring of traffic police when compared to the control group (P<0.05). However, the increase in the frequency of still births, congenital defects and premature births in the exposed group when compared to the controls was not statistically significant. The percentage of fertile males in the exposed group was decreased (96.52%) when compared to the control group (99%). However the decrease was statistically insignificant (P>0.05).

DISCUSSION

The study presents evidence for impaired reproductive outcome in non-smoking traffic policemen. Clinical and cytogenetic investigations were also carried out in traffic policemen enrolled in this study. The increased incidence of respiratory problems (38.43%) diabetes (5.58%), hypertension (12.55%) and increased cytogenetic damage in the peripheral blood lymphocytes of

traffic policemen present evidence for vehicular exhaust induced adverse health effects and genetic damage in traffic police (unpublished data).

This study was conducted on a homogenous population of young to middle aged policemen. In fact, as more than 2 lakh vehicles cross the busy centers during the 8 hours of duty, for 6 days a week, without adequate protection, policemen were equally and constantly exposed to environmental and vehicle discharged pollutants. On site measurements showed that pollution load was very high, 691 tonnes per day with very high levels of carbon monoxide and hydrocarbons followed by NO_x, SO₂, SPM and lead oxide particles (PbO). The traffic police were more exposed to vehicular exhaust pollutants than age matched controls. The apparent decrease in fertility and other reproductive outcome in the traffic police may be attributed to occupational exposure to vehicular pollutants.

The results of adverse health effects, cytogenetic damage to DNA and impaired reproductive outcome in traffic police present evidence for toxicity of the pollutants, induced as a result of the circulation of pollutants in blood and semen of traffic police. Increased circulating levels of methemoglobin (MHb), sulfhemoglobin (SHb), Pb and zinc protoporphyrin (Znpp) had been demonstrated in tollgate workers exposed to vehicular exhaust having higher concentrations of nitrogen oxides, sulphur dioxide, carbon monoxide, and lead (Michele et al., 2003). Monitoring the biomarkers of absorption of environmental pollutants such as MHb, carbonium oxide (COHb), SHb, (indicators of absorption of environmental pollutants such as NO_x, CO, SO₂), and levels of PAH, lead in blood and seminal plasma, is warranted in the test population for measure of exposure. Considering the increased pollution levels of carbon monoxide and hydrocarbons in the congested areas of Hyderabad, it can be speculated that traffic police in the study group occupationally exposed to increased load of vehicular pollutants may have increased levels of circulating carbonium oxide, PAH and lead (low exposure) that needs to be confirmed. However, studies carried out by us, on amount of free radicals super oxide anion, hydrogen peroxide generated, nitric oxide levels and end products of oxidative stress indicated mild oxidative stress in the same test group of traffic police with nitrite levels being more than physiological levels. Increased plasma nitric

oxide levels can affect the semen quality (unpublished data). Another study demonstrated high circulating levels of heavy metals (lead and cadmium), low levels of zinc and selenium and increased levels of xenoestrogens, (polychlorinated biphenyls and phthalate esters) in seminal plasma of infertile males with deterioration in semen quality when compared to fertile males belonging to healthy, occupationally non exposed, urban population of the same geographical area as the study group (Rozati et al., 2000). An other study demonstrated cytogenetic damage with impairment of antioxidant enzymes and increased oxidative stress in seminal plasma of infertile males from the same geographical area (unpublished data).

A large body of evidence demonstrated the toxic effects of several aromatic hydrocarbons, polychlorinated biphenyls, polybrominated biphenyls, lead, organic solvents, etc on the male reproductive function. They act on the male reproductive system either by affecting the neuro endocrine function or process of spermatogenesis resulting in poor semen quality. Exposure to the toxicants resulted in reduced sperm motility, which is attributed to the presence of toxic hydrocarbons/ metabolites in the seminal plasma which can induce changes in the physicochemical characteristics of the semen resulting in increased viscosity and / or incapacity for liquefaction and inhibiting the rapid forward progression of the sperm (Celis et al., 2000).

The presence of heavy metals such as lead and cadmium in the semen of men from the normal human population has been associated with the emissions of exhaust from motor vehicles as well as consumption of tobacco and industrial operations. (Kumar et al., 2000a). Lead progressively accumulates in the body, is stored in the soft tissues, and becomes a continuous source of lead exposure as it is released slowly and poses a greater threat to health as it affects all the systems of the body. Pb accumulates in male reproductive organs. Human testes and sperm contain numerous potassium channels through which metallic toxicants can enter into mature sperm (Benoff et al., 2000).

Several studies on occupational exposure to lead in different workplaces demonstrated adverse effects of increased lead levels in plasma/ blood on sperm parameters (Alexander et al., 1996; Alexander et al., 1998; Weyandt et al., 1996; Robins et al., 1997; Dawson et al., 1998).

The genotoxic effects among the traffic police might be due to exposure to some of the components of vehicular exhaust individually or in different combinations and this is very difficult to confirm. The observed reproductive endpoints may be a consequence of impaired spermatogenesis or spermiogenesis as a result of oxidative stress and possible damage to lipids (sperm membrane damage) and DNA induced by increase levels of toxic pollutants, carbonium oxide, MHb, SHb, PAH and lead in blood and seminal plasma in traffic police on chronic occupational exposure. Exhaust pollutants may collect in the epididymis, seminal vesicles, or prostate. These chemicals may kill the sperm, change the way in which they swim, or attach to the sperm and be carried to the egg or the unborn child.

To conclude, the present study and various other reports present evidence for vehicular exhaust induced impaired reproductive outcome in traffic policemen.

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REFERENCES

- Alexander, B.H., Checkoway, H., Faustman, E.M., van Netten, C., Muller, C.H. and Ewers, T.G.: Contrasting associations of blood and semen lead concentrations with semen quality among lead smelter workers. *Am. J. Ind. Med.*, **34**: 464-469 (1998).
- Alexander, B.H., Checkoway, H., van Netten, C. et al.: Semen quality of men employed at a lead smelter. *Occup. Environ. Med.*, **53**(6): 411-416 (1996).
- Anwar, W.A.: Assessment of cytogenetic changes in human population at risk in Egypt. *Mutat. Res.*, **313**: 183-191 (1994).
- Anwar, W.A. and Kamal A.A.M.: Cytogenetic effects in a group of traffic policemen in Cairo. *Mutat. Res.*, **208**: 225-231 (1988).
- Atimtay, A.T., Emiri, S., Bagei, T. and Demir, A.U.: Urban CO exposure and its health effects on traffic policemen in Ankara. *Environ. Res.*, **82**(3): 222-230 (2000).
- Benoff, S., Jacob, A. and Hurley, I.R.: Male infertility and environmental exposure to lead and cadmium. *Hum. Rep. Update.*, **2**: 107-121 (2000).
- Bilban, M.: Influence of the work environment in a Pb-Zn mine on the incidence of cytogenetic damage in miners. *Am. J. Ind. Med.*, **34**: 455-463 (1998).
- Bobak, M. and Leon, D.A.: Air pollution and infant mortality in the Czech Republic 1986-88. *Lancet*, **340** (8826): 1010-1014 (1992).
- Carrans, A.V. and Natarajan, A.: Consideration for population monitoring using cytogenetic techniques. *Mutat. Res.*, **204**: 379-406 (1988).
- Chandrasekaran, R., Samy, P.L. and Murthy, P.B.: Increased sister chromatid exchange (SCE) frequencies in lymphocytes from traffic policemen exposed to automobile exhaust pollution. *Hum. Exp. Toxicol.*, **15**: 301-304 (1996).
- Danforth, D.N.: *Obstetrics and Gynecology*. Hyper and Row Publishers, New York (1977).
- Dawson, E.B., Ritter, S., Harris, W.A., Evans, D.R. and Powell, L.C.: Comparison of sperm viability with seminal plasma metal levels. *Biol. Trace. Elem. Res.*, **64**(1-3): 215-219 (1998).
- De Celis, R., Fera-Velasco, A., Gonzalez-Unzaga, M., Torres-Calleja, J. and Podron-Nuevo, N.: Semen quality of workers occupationally exposed to hydrocarbons. *Fertility and Sterility*, **73**(2): 221-228 (2000).
- De Ferrarin, Astaso, M., Honassi, S., Bonatli, S. et al.: Cytogenetic biomonitoring of an Italian analysis in peripheral blood lymphocytes. *Mutat. Res.*, **260**: 103-113 (1991).
- Dejmek, J., Jelinsek, R., Solansky, I.: Fecundability and parental exposure to ambient sulfur dioxide. *Environ. Health Perspect.*, **108** (7): 647-654 (2000).
- Dinesh kumar, B., Kamala Krishna swamy.: Detection of occupational lead nephropathy using early renal markers. *Clinical Toxicology*, **33**(4): 331-335 (1995).
- Figa-Talamanca, I., Cini, C., Varricchio, G.C. et al.: Effects of prolonged auto vehicle driving on male reproduction function: a study among taxi drivers. *Am. J. Ind. Med.*, **30**(6): 750-758 (1996).
- Hema Prasad, M. and Reddy, P.P.: Rubber Industry toxicity of work environment. In: *Hand-book of Hazardous Materials*. Academic Press, Inc. U.S.A., pp. 639-648 (1993).
- Hemminki, K. and Niemi, M.L.: Community study of spontaneous abortions relation to occupation and air pollution by sulfur dioxide, hydrogen sulfide and corban disulfides. *Int. Arch. Occ. Env. Health.*, **51**(1): 55-63 (1982).
- Hoffman, D. and Hecht, S.S.: Nicotine derived N-nitrosamines and tobacco related cancer: current status and future directions. *Cancer Res.*, **45**: 935-995 (1985).
- Huang, X.P., Feurg, Z.Y., Zhai, W.L. and Xu, J.H.: Chromosomal aberrations and sister chromatid exchanges in workers exposed to lead. *Biomed. Environ. Sci.*, **4**: 362-367 (1988).
- Ishinishi, N., Kuwabara, N., Nagase, S., Suzuki, T., Ishiwafa, S. and Kohno, T.: *Carcinogenic And Mutagenic Effects of Diesel Engine Exhaust*. Elsevier Amsterdam., p.29 (1986).
- Kalina, I., Brezani, P., Gajdosova, D. et al.: Cytogenetic monitoring in coke oven workers. *Mut. Res.*, **417**(1): 9-17 (1998).
- Kumar, R., Pant, N. and Srivastava, S.P.: Chlorinated pesticides and heavy metals in human semen. *Int. J. Androl.*, **23**(3): 145-149 (2000a).
- Merlo, F., Bologensi, C., Peluso, M., Valerio, F.,

- Abbondandolo, A. and Punteni, R.: Genotoxic damage in subjects exposed to automobile exhaust: Preliminary results. *Epidemiol. Prev.*, **19**: 120-123 (1995).
- Michele, D.R., Stefano, Z., Luigi, P. et al.: Traffic pollutants affect fertility in men. *Human Reproduction*, **18**(5): 1055-1061 (2003).
- Onalaja, A. and Claudio, C.: Genetic influence in lead poisoning. *Environ. Health. Perspect.*, **108**: 23-28 (2000).
- Osaka Physicians Society for Medical Insurance (OPSMI) 1998.
- Potula, V. and Hu, H.: Occupational and lifestyle determinations of blood lead levels among men in Madras, India. *Int. J. Occup. Environ. Health.*, **2**: 1-4 (1996).
- Ramesh Babu, S.: *Cytogenetic, Biochemical and Molecular Aspects of Human Male Infertility*. Thesis, Osmania University (2001).
- Rebecca, B., Philip, A.B., Daniel, L.C. et al.: Health effects of outdoor Air Pollution Part-I, Part-II. *American Journal of Respiratory and Critical Care Medicine*, **153**: 1 and 2 (1996).
- Robins, T.G., Bornman, M.S., Ehrlich, R.I., Cantrell, A.C., Pienaar, E., Vallabh, J. and Miller, S.: Semen quality and fertility of men employed in a South African lead acid battery manufacturing plant. *Am. J. Ind. Med.*, **32**(4): 369-376 (1997).
- Rozati, R., Reddy, P.P. and Rubina, M.: The impact of sedentary occupation and long distance travel on semen quality. *J. Obstetrics and Gynecology.*, **50**(4): 75-78 (2000).
- Sallmen, M., Lindbohm, M.L. and Nurminen, M.: Paternal exposure to lead and infertility. *Epidemiology*, **11**: 148-152 (2000).
- Settle, D.M. and Patterson, C.C.: Magnitude and sources of precipitation and dry deposition fluxes of industrial and natural leads to the North Pacific at Eniwetok. *J. Geophys. Res.*, **87**: 8857-8869 (1982).
- Smrcka, V. and Leznarova, D.: Environmental pollution and the occurrence of congenital defects in a 1-15 year period in a South Moravian district. *Acta Chir. Plast.*, **40** (4): 112-114 (1998).
- Sree Devi, V.: *Genetic, Cytogenetic and Biochemical Studies in Traffic Police*. Thesis, Osmania University (2002).
- Tielemans, E., Burdorf, A., te Velde, E.R., Weber, R.F. et al.: Occupationally related exposures and reduced semen quality: a case control study. *Fertil. Steril.*, **71**(4): 690-696 (1999a).
- Wallace, L.: Carbon monoxide in air and breath of employees in an underground office. *Journal of the Air Pollution Control Association*, **33**: 678-682 (1983).
- Weyandt, T.B., Schrader, S.M., Turner, T.W. and Simon, S.D.: Semen analysis of military personnel associated with military duty assignments. *Reprod. Toxicol.*, **10**(6): 521-528 (1996).
- Xu, X., Wiencke, J.K., Niu, T. et al.: Benzene exposure, glutathione S-transferase theta homozygous deletion and sister chromatid exchanges. *Am. J. Ind. Med.*, **33**(2): 157-163 (1998).
- Zhao, X., Niu, J., Wang, Y., Yan, C., Wang, J.: Genotoxicity and chronic health effects of automobile exhaust: a study on the traffic policemen in the city of Lanzhou. *Mutat. Res.*, **15** (37): 185-190 (1998).