ISSN: 0976-3031

Available Online at http://www.recentscientific.com

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 9, Issue, 6(A), pp. 27219-27224, June, 2018

International Journal of Recent Scientific Research

DOI: 10.24327/IJRSR

Research Article

POLYMORPHISMS OF GSTM1 AND GSTT1 GENES CONTRIBUTE TO THE RISK OF ADVERSE REPRODUCTIVE OUTCOME IN STEEL INDUSTRY WORKERS

Indira Priyadarshini U*[1]., Vanitha Baluka[1]., Prashanth Ch[1]., Pranay Krishna P[2]., Latheef S A A[3] and Reddy P.P[1]

[1]Department of Genetics, Bhagwan Mahavir Medical Research Centre, Hyderabad, Telangana
[2]ACSR Government Hospital, Nellore Andhra Pradesh, India
[3]Department of Genetics, Osmania University Hyderabad, Telangana, India

DOI: http://dx.doi.org/10.24327/ijrsr.2018.0906.2213

ARTICLE INFO

Article History:
Received 17th March, 2018
Received in revised form 12th April, 2018
Accepted 04th May, 2018
Published online 28th June, 2018

Key Words:

Epidemiology, reproductive outcome, occupational exposure, genetic polymorphisms, glutathione-S transferase.

ABSTRACT

Context: The root causes of many adverse pregnancy outcomes are not well understood, but there is growing evidence that both the environmental and genetic factors play an important role. The present study aims to investigate the association of polymorphisms of GSTM1 and GSTT1 genes with adverse reproductive outcome in steel industry workers.

Methods: The study populations consisted of 150 male steel industry workers in the age group of 18-55 years and 146 males in the same age group and socio economic status and not occupationally exposed to any chemical agents were studied for the reproductive outcome in their spouses. The information on reproductive outcome including the number of pregnancies, fertility, infertility, live births, spontaneous abortions, premature births, neonatal deaths, still births etc. was collected. Blood samples were collected, DNA extraction and genotyping was done for GSTM1 and GSTT1 using multiplex PCR.The study was approved by the Institutional Ethics Committee of the Centre and written informed consent was obtained from all the participants of the study. The results were analyzed statistically using the appropriate chi square test and logistic regression analysis to find the significance of the association of GSTM1 and GSTT1 polymorphisms with reproductive outcome in steel industry workers and control subjects.

Results: The results showed an increase in the frequency of abortions, still births, premature births and neonatal deaths in the workers with homozygous deletions of GSTM1 and GSTT1 but the increase was not statistically significant compared to that of active GSTM1 and GSTT1 variants.

Conclusion: The results did not provide any evidence for the influence of polymorphisms of GSTM1 and GSTT1 genes on the reproductive outcome. Neither GSTM1 nor GSTT1 null variants were associated with adverse reproductive outcome.

INTRODUCTION

Recent epidemiological studies indicated involvement of genetic and environmental factors for the risk of adverse reproductive outcome in males (Fisch *et al*., 2000; Oliva *et al*., 2001; Sharpe, 2001; Damgaard *et al*., 2002; Fisher, 2004) and females (Kamrin *et al*., 1994; Sharara *et al*., 1998; Nicolopouloustamati and Pitsos, 2001).

During the last few decades deterioration of male reproductive capacity in industrialized countries as a result of exposure to environmental contaminants (toxic and heavy metals) has been reported (Sengupta *et al*., 2013). A drastic decline in the sperm count associated with sperm quality over the years was shown by Waissmann *et al*., (2002). Exposure to heavy metals showed adverse effects on male reproductive system that include size of testis, semen abnormality, semen quality, sperm motility, seminal vesicle, impotency, altered genetic material of sperm, altered spermatogenesis and genetic diseases in offspring (Astrid Sigel *et al.,* 2011;Sengupta *et al.,* 2013). Elbetieha, *et al;* (1997) observed increased risk of infertility and reduced semen quality among male welders. Xenobiotic compounds are associated with oxidative stress in male reproductive organs which may contribute to adverse reproductive outcome (Aitken and Krausz, 2001; Agarwal and Sushil, 2005; Tremellen, 2008; Turner and Lysiak, 2008). Gerhard *et al.,* (1998) and Kumar.,

Corresponding author:* **Indira Priyadarshini U
Department of Genetics, Bhagwan Mahavir Medical Research Centre, Hyderabad, Telangana

(2011) showed spontaneous abortions and fetal abnormalities in women due to long term exposure to heavy metals.

GSTM and GSTT are the cytosolic enzymes that play a key role in the Phase II detoxification pathways in humans against various physiological and xenobiotic substances and also act as important antioxidants in testis tissues (Listowsky *et al.,* 1998; Strange *et al.,* 2001). They are extensively present in the testis and seminiferous tubule fluid as well as in the sperm (Hemachand *et al*., 2002; Mukherjee *et al.,* 1999) and protect germ cells against the damage caused by oxidative stress. Some studies showed that GSTs might be involved in spermatogenesis impairment (Castellon, 1999). The homozygous deletion (null genotype) of the GSTM1 or GSTT1 gene results in the total absence of the enzyme activity and increases the level of oxidative stress resulting in male infertility (Seidegard *et al.,* 1988). Recently we have studied reproductive outcome in steel industry workers and reported infertility and an increase in the frequency of abortions, premature births, still births and neonatal deaths which might be due to undue exposure of workers to steel dust at work place. (Indira Priyadarshini *et al.,* 2017). Thus in this study, we investigated the influence of polymorphisms of GSTM1 and GSTT1 genes on adverse reproductive outcome in steel industry workers.

MATERIALS AND METHODS

150 male steel industry workers in the age group of 18-55 years and 146 males belonging to the same age group and socio economic status and not occupationally exposed to any chemical agent were studied for the reproductive outcome in their spouses. Subjects for the present study were selected among the male workers of the steel industry situated at Patancheru, Hyderabad, India. The information on reproductive outcome including the number of pregnancies, fertility, infertility, live births, spontaneous abortions, premature births, neonatal deaths, still births, etc. was collected.

Peripheral blood samples were collected from all the participants. DNA was extracted and genotyping of GSTM1 and GSTT1 was carried out using multiplex PCR. The study was approved by the Institutional Ethics Committee of the Centre and written informed consent was obtained from all the participants of the study. The results were analyzed statistically using the appropriate chi square test and odds ratio (OR) and 95% confidence intervals (95%CI) were calculated to assess the relative risk conferred by null genotype. In addition, logistic regression analysis was carried out to find the significance of the association of GSTM1 and GSTT1 polymorphisms with reproductive outcome in steel industry workers and control subjects.

Genetic analysis of GSTM1 and GSTT1 gene polymorphisms by multiplex PCR

GSTM1 and GSTT1 genotyping: 5ml blood samples were collected from the male steel industry workers and control subjects and genomic DNA was extracted by Spin column kit (Bangalore Genei, India). Multiplex PCR assay was used for analyzing the GSTM1 and GSTT1 gene deletions. To detect the GSTM1 deletion, the following primers was used: Forward primer 5′ GAA CTC CCT GAA AAG CTA AAGC 3′ and Reverse primer 5′ GTT GGG CTC AAA TAT ACG GTG G-3′. For GSTT1, Forward primer 5′ TTC CTT ACT GGT CCT CAC ATCTC- 3′ and Reverse primer 5′-TCACCGGATCATGGCCAGCA-3′ were used .The PCR amplified products were electrophoresed on a 2% agarose gel, stained with ethidium bromide, and the results were documented using a gel documentation system. The presence of GSTM1 and that of GSTT1 genes were indicated by the resulting 215 and 480 bp PCR amplicons, respectively. As an internal control, HAB was amplified (350bp) using the primers, HAB F (5′-CAACTTCATCCACGTTCACC-3′) and HAB R (5′-GAAGAGCCAAGGACAGGTAC-3′) for the authentication of multiplex PCR.

Table 1 Distribution of GSTT1, GSTM1 genotypes in steel industry workers and the controls with abortions and still births

Genotype (Case/Control)	Steel industry Workers (n=150) Abortions	Controls Subjects (n=146) Abortions	OR(95% Confidence interval)	p value	Steel industry Workers (n=150) Still births	Controls Subjects (n=146) Still births	OR(95% Confidence interval)	p value
GSTM1 Active(94/95)	3(3.1)	2(2.1)	Reference	0.58^{NS}	1(1.0)	0	Reference	1.0^{NS}
Null(56/51)	6(10.7)	3(5.8)	1.9(0.39-10.3)		2(3.5)	1(1.9)	1.8(0.12-53.3)	
GSTT1 Active(92/91)	4(4.3)	1(1.0)	Reference	1.0^{NS}	1(1.0)	0	Reference	1.0^{NS}
Null(58/55)	5(8.6)	4(7.2)	1.2(0.26-5.72)		2(3.4)	1(1.8)	1.9(0.13-55.4)	

Note: Differences in frequencies between the subjects and control groups were analyzed for statistical significance using logistic regression analysis. Odds ratios (OR) are reported with 95% confidence limits, NS = not statistically significant (P > 0.05).

Table 2 Distribution of GSTT1, GSTM1 genotypes in steel industry workers and the controls with premature births and neonatal deaths

Genotype (Case/Control)	**Steel industry Workers (n=150)**	**Controls Subjects (n=146)**	**OR(95% Confidence interval)**	**p value**	**Steel industry Workers (n=150)**	**Controls Subjects (n=146)**	**OR(95% Confidence interval)**	**p value**
	Premature births	**Premature births**			**Neonatal deaths**	**Neonatal deaths**		
GSTM1 Active (94/95)	1(1.0)	1(1.0)	Reference	0.81^{NS}	2(2.1)	1(1.0)	Reference	1.0^{NS}
Null(56/51)	5(8.9)	3(5.8)	1.5(0.30-8.84)		3(5.3)	2(3.9)	1.4(0.17-12.48)	
GSTT1 Active (92/91)	2(2.1)	2(2.1)	Reference	0.72^{NS}	1(1.0)	0	Reference	1.0^{NS}
Null(58/55)	4(6.8)	2(3.6)	2(0.29-16.2)		4(6.8)	3(5.4)	1.2(0.22-7.67)	

Note: Differences in frequencies between the subjects and control groups were analyzed for statistical significance using logistic regression analysis. Odds ratios(OR) are reported with 95% confidence limits, NS = not statistically significant (P > 0.05).

The PCR protocol included an initial denaturation temperature of 94 °C (5 min) followed by 35 cycles of amplification (denaturation at 94 °C for 1 min, annealing at 59 °C for 1 min and extension at 72 °C for 1 min). A final 10 min extension step (72 °C) terminated the process. The final PCR products were visualized in ethidium bromide stained gel. Individuals with active (+) genotype of GSTM1will have 215 bp band while the individuals with null (-) genotype of GSTM1 will not have this band. Similarly individuals with active (+) genotype of GSTT1will have 480 bp band while the individuals with null (-) genotype of GSTT1 will not have this band.

Statistical Analysis

The results were analyzed statistically using the appropriate chi squared test and odds ratio (OR) and 95% confidence intervals (95%CI) were calculated to assess the relative risk conferred by a null genotype and also to assess the relationship between GSTM1 and GSTT1 gene polymorphisms with adverse reproductive outcome in steel industry workers. In addition, logistic regression analysis was done to find the significance of the association of GSTM1 and GSTT1 polymorphisms with reproductive outcome in steel industry workers and control subjects. The results were considered to be significant at p values of less than 0.05 (indicated by *). Genotype frequencies were checked for deviation from Hardy-Weinberg equilibrium and were not significantly different from those predicted.

RESULTS

The results on the frequency of abortions, premature births, neonatal deaths and still births of steel industry workers with GSTM1 and GSTT1 gene polymorphisms are presented in Tables 1- 2.

The results showed an increase in the frequency of abortions, premature births, neonatal deaths and still births in the spouses of steel industry workers with null genotypes of GSTM1 and GSTT1 when compared to controls .However, the logistic regressions analysis showed no significant increase in all the parameters.

DISCUSSION

The aim and purpose of reproductive epidemiology in the industrial workers is to promote, protect, and restore good health and reduce incidence of reproductive problems by understanding the risk factors in industry workers. In the early 1980s, Levin (1983) and Baird *et al*., (1986) carried out epidemiological research related to adverse reproductive outcomes. Recent epidemiologic studies have shown that both genetic and environmental factors are responsible for adverse reproductive outcome (Edward *et a1.,* 2005; Ramos, 2008; Edwards, 2007).

We have shown an increased frequency of abortions, stillbirths, neonatal deaths and a significant decrease in live births in spouses of steel industrial workers as a result of occupational exposure to steel dust at work place (IndiraPriyadarshini *et al.,* 2017).

The steel dust contains nickel, chromium, iron, manganese, cobalt, tungsten, molybdenum and vanadium which are carcinogenic and mutagenic (Cornelia 2002). Thus the adverse effects might be due to exposure to complex mixtures of these heavy metals whose combined effect may be greater than the sum of their individual effects on reproductive health. Earlier studies carried out in the workers exposed to nickel, chromium, iron, manganese and lead showed adverse effects in both male and female reproductive systems at the workplace (Baranski *et al*., 1993, Bonde *et al*., 1999, Danadevi *et al*., 2003, Kumar *et al.,* 2005, Sengupta, 2012, Agrawal *et al.,* 2012, IndiraPriyadarshini *et al*., 2017). Although pregnancy loss is a common occurrence, its environmental determinants are largely unknown. Heavy metals are considered as environmental teratogens, and exposure could contribute to pregnancy loss (Gardella and Hill, 2000). It has been reported that the both null genotypes of GSTM1 and GSTT1 are associated with a reduced survival rate in women with epithelial ovarian cancer (Howells *et al.,* 1998). Tina *et al.,* (2000) have shown a reduced quantity and quality of semen in man exposed to welding metals. Further, genetic polymorphism in xenobiotic metabolizing genes may influence the effect of environmental contaminants causing adverse reproductive outcomes such as preterm delivery (Mustafa *et al*., 2013). Mustafa *et al*., (2010) showed that GSTM1/GSTT1 (null) genotype may be one of the associated genetic factors for the increased risk of PTL. In this context, the present study was taken up to understand the influence of GSTM1 and GSTT1 gene polymorphisms on the adverse reproductive outcome in male steel industry workers.

The GST system includes one of the most important detoxifying genes in protecting cells from oxidative damage (Chen *et al*., 2002; Quinones *et al*., 2006). Among the GST's, GSTM1 preferentially detoxifies carcinogens derived from tobacco, whereas GSTT1 causes the biotransformation of many toxins. Any alterations due to genetic polymorphisms affect the activities of these genes, thereby increasing the genotoxic risk in humans (Peddireddy *et al*., 2016). It has been demonstrated that GST has a protective role during spermatogenesis in males (Castellon, 1999). Oxidative stress could lead to biological effects in males and females. Studies that have shown the acceleration of spermatozoa apoptosis (Aitken *et al.,* 2012) , abnormality of sperm parameters (Badade *et al*., 2011), decrease of sperm and oocyte fusion capacity (Griveau and Le Lannou, 1997), and damage of DNA integrity in sperm mitochondrial (Aitken *et al*., 1998) due to oxidative stress in males. These detoxifying genes inactivate xenobiotic compounds especially the heavy metals when the males are occupationally exposed and if this gene is inactive, it results in the male infertility (Sharma, *et al*., 2004, Axelsson *et al*., 2010).

In the present study the influence of polymorphisms of GSTM1 and GSTT1 genes on the reproductive outcome was investigated in the steel industry workers. This is first novel study to investigate the association of GSTM1 and GSTT1 gene polymorphisms with reproductive outcome in steel industry workers. The results of the study showed that the differences in the reproductive outcome between null and active genotypes are not statistically significant thus, indicating the absence of an association with polymorphisms of GSTM1 and GSTT1 genes.

Our results are in agreement with that of Suryanarayana *et al*., (2004) who observed no significant association between GSTM1 and GSTT1 and recurrent pregnancy loss in the South Indian population. However they suggested the occurrence of

the CYP1A1*2A allele as a probable risk factor in idiopathic recurrent miscarriages.

Our results are in agreement with that of Renato Polimanti *et al.,* (2012) who observed no significant differences in the frequencies of GSTM1 and GSTT1 variants between recurrent miscarriages in Italian women. Zusterzeel *et al*., (2000) reported no influence of GSTT1 and GSTM1variants with recurrent early pregnancy loss in Caucasian populations. Nonaka *et al.*, (2011) also observed no difference in the distribution of GSTM1 and GSTT1 genotypes in recurrent pregnancy loss in Japanese populations in relation to smoking or consumption of coffee or alcohol.

Sena *et al.,* (2009) and Aydemir *et al*., (2007) have studied GSTM1 and GSTT1 genotypes association with infertility in males. Aydemir *et al*., (2007) observed significant association with GSTT1 with idiopathic infertility in males. They did not find significant association of GSTM1 variant with idiopathic infertility. Sena *et al*., (2009) studied the association of GSTM1 and GSTT1 variants with infertility in Turkish males and observed significant association only with GSTT1 gene. Olshan *et al.,* (2010) from the United States of America reported that reduced sperm concentration and semen count in fertile men were associated with the GSTT1 non-null genotype.

Contrary to our findings, Tang *et al.,* (2012) conducted a study and reported both GSTM1 and GSTT1 null genotypes may predispose sperm to increased oxidative damage in infertile males with varicocele in Northwestern China. Li *et al.,* (2013) carried out meta-analysis of the studies on the association of GSTs with male infertility and showed that GSTM1 null genotype contributed to increased risk of male idiopathic infertility in Caucasians while males with dual null genotype of GSTM1/GSTT1 were particularly susceptible to developing idiopathic infertility. Vani *et al*., (2010) observed an association of GSTM1 null genotype with male infertility in South Indian population whereas Wu *et al.,* (2008) reported the association of GSTT1 null genotypes with infertility in males in both Asian and Caucasian groups. Finotti *et al.,* (2009) indicated significant association of GSTM1 and GSTT1 null genotypes with idiopathic male infertility and suggested that individuals polymorphic for GSTM1 and GSTT1 genes are susceptible to reduction in sperm quality and infertility. GSTM1 null genotypes were found to be associated with RPL in Japanese (Hirvonen *et al.*, 1996) and North Carolina (Sata *et al.*, 2003) populations. Parveen *et al*., (2010) revealed an association between the GSTT1 null genotype and the risk of RPL in North Indian subjects. Rohini *et al*., (2013) studied the association of GSTM1 and GSTT1 with early pregnancy loss (EPL) and showed significant association of GSTT1 null genotype with EPL. Bustamante, *et al.,* (2012) reported increased risk for preterm delivery in Spanish women with GSTM1 deletion.

The overall studies revealed that the associations of detoxification genes vary greatly in different studies. This might be due to region selected, ethnicity, life style, habits and the gene- environment interactions. Further studies in more populations from different regions in larger sample size and different environmental settings are worthwhile.

CONCLUSIONS

The study did not provide any evidence for the influence of polymorphisms of GSTM1 and GSTT1 on the reproductive outcome in steel industry workers. Further studies are warranted to generate more information on the association of genetic variability of detoxification genes on reproductive outcome.

Acknowledgments

The authors wish to thank all the workers who participated in the study. We are also indebted the management of the steel industries. Thanks are also due to Shri Motilal Jain, Chairman, Shri Mahendra Ranka, Vice-chairman, Shri Sushil Kapadia, Managing Trustee and Shri Ashok Kothari, Trustee Treasurer of our Research centre for their support and for providing necessary infrastructure facilities to carry out this project.

Conflict of Interest

None of the authors of this paper had any personal or financial conflicts of interest.

References

Aydemir B, Onaran I, Kiziler AR, Alici B, Akyolcu MC, 2007. Increased oxidative damage of sperm and seminal plasma in men with idiopathic infertility is higher in patients with glutathione S-transferase Mu-1 null genotype. *Asian J Androl*, 9:108-15.

Agarwal A, Sushil P, (2005). Oxidative stress and antioxidant in male infertility: a difficult balance. *Iranian J Reprod Med,* 3(1):1-8.

Aitken R De, Iuliis G, Gibb Z, (2012). The simmet lecture: new horizons on an old landscape-oxidative stress, DNA damage and apoptosis in the male germ line. *Reprod Domest Anim,* 47 (4):7-14.

Aitken RJ, Gordon E, Harkiss D, (1998). Relative impact of oxidative stress on the functional competence and genomic integrity of human spermatozoa. *Biol Reprod,* 59:1037-1046.

Aitken RJ, Krausz C, (2001). Oxidative stress, DNA damage and the Y chromosome. *Reproduction* 122:497-506.

Astrid Sigel, Helmut Sigel, Roland K, Sigel.O, (2011). Metal Ions in Toxicology: Effects, Interactions, Interdependencies. *Royal Society of Chemistry*, 8: 1559-0836.

Axelsson J, Bonde JP, Giwercman YL, (2010). Gene-environment interaction and male reproductive function. *Asian J Androl*, 12: 298-307.

Badade G, More K, Narshetty G, (2011). Human seminal oxidative stress: correlation with antioxidants and sperm quality parameters. *Ann Biol Res,* 2:351-359.

Baird DD, Wilcox AJ and Weinberg CR, (1986).Use of time to pregnancy to study environmental exposures. *Am J Epidemiol,* 124:470-480.

Boguslaw Baranski, (1993). Effects of the Workplace on Fertility and Related Reproductive Outcomes. Environmental Health Perspectives Supplements, 101 (2): 81-90.

BondeJP, ErnstE, (1999). Sex hormones and semen quality in welders exposed to hexavalent chromium. *Hum Exp Toxicol,* 11: 259-263.

Bustamante M, Danileviciute A, Espinosa A, Gonzalez JR, Subirana I, Cordier S, Chevrier C, Chatzi L, Grazuleviciene R, Sunyer J, Ibarluzea J, Ballester F, Villanueva CM, Nieuwenhuijsen M, Estivill X, Kogevinas M,(2012). Influence of fetal glutathione S-transferase copy number variants on adverse reproductive outcomes. *BJOG*, 119:1141-1146.

Castellon EA, (1999). Influence of age, hormones and germ cells on glutathione S-transferase activity in cultured Sertoli cells. *Int J Androl*, 22:49-55.

Chen SS,Chang LS, Chen HW, Wie YH, (2002). Polymorphisms of glutathione S-transferase M1 and male infertility in Taiwanese patients with varicocele. *Hum Reprod*, 17:718-725.

Cornelia Richardson-Boedler, (2002). Metal passivity as mechanism of metal carcinogenesis: Chromium, nickel, iron, copper, cobalt, platinum, molybdenum. *Toxicological & Environmental Chemistry*, 89:15-70.

Damgaard IN, Main KM, Toppari J and Skakkebaek NE, (2002). Impact of exposure to endocrine disrupters in utero and in childhood and adult reproduction. *Best Pract Res Clin Endocrinol Metab* 16:289-309.

Danadevi.K, RoyaRozati, ReddyPP, Paramjit Grover in Reproductive toxicology Elmsford NY,(2003). Semen quality of Indian welders occupationally exposed to nickel and chromium. *reproductive toxicology*, 17(4): 451-456.

Edward V.Younglai1, Alison C.Holloway and Warren G.Foster, (2005). Environmental and occupational factors affecting fertility and IVF success. *Human Reproduction Update*, 11(1): 43-57.

Edwards T.M, Myers J.P, (2007). Environmental exposures and gene regulation in disease etiology. *Environ. Health Perspect,* 115: 1264-1270.

Elbetieha A, Al-Hamood MH, (1997). Long-term exposure of male and female mice to trivalent and hexavalent chromium compounds: effect on fertility. *Toxicol*, 116: 39-47.

Finotti AC, Costa E Silva RC, Bordin BM, Silva CT, Moura KK,(2009). Glutathione S-transferase M1 and T1 polymorphism in men with idiopathic infertility. *Genet Mol Res,* 8: 1093-1098.

Fisch H, Hyun G and Golden R, (2000). The possible effects of environmental estrogen disrupters on reproductive health. *Curr Urol Rep*, 1:253-261.

Fisher JS, (2004).Environmental anti-androgens and male reproductive health: focus on Phthalates and testicular dysgenesis syndrome. *Reproduction*, 127: 305-315.

Gardella, J.R. and Hill, J.A (2000) Environmental toxins associated with recurrent pregnancy loss. *Semin. Reprod. Med* 18: 407- 424.

Gerhard I, Waibel S, Daniel V, Runnebaum B,(1998). Impact of heavy metals on hormonal and immunological factors in women with repeated miscarriages. *Hum Reprod Update*,4(3):301-9.

Griveau GF, Le Lannou D, (1997). Reactive oxygen species and human spermatozoa: physiology and pathology. *Int J Androl,* 20:61-69.

Hemachand T, Gopalakrishnan B, Salunke DM, *et al*. (2002). Sperm plasma membrane associated glutathione S-transfer- ases as gamete recognition molecules. *J Cell* Sci, 115: 2053-2065.

Howells RE, Redman CW, Dhar KK, Sarhanis P, Musgrove C, Jones PW, Alldersea J, Fryer AA, Hirvonen A, Taylor JA, Wilcox A, Berkowitz G, Schachter B, Chaparro C, Bell DA, (1996). Xenobiotic metabolism genes and the risk of recurrent spontaneous abortion. *Epidemiology*, 7: 206-208.

Indira Priyadarshini U, Prashanth Ch., Vanitha Baluka and Reddy P.P, (2017) Reproductive performance in wives of steel industrial workers. *International Journal of Multidisciplinary and Current Research*, 5: 1436-1440.

Kamrin MA, Carney EW, Chou K, Cummings A, Dostal LA, Harris C, Dostal LA, Harris C, Henck JW, Loch-Caruso R *et al*. (1994). Female reproductive and developmental toxicology: overview and current approaches. *Toxicol Lett*, 74:99-119.

Kumar S, Sathwara NG, Gautam AK, (2005). Semen quality of industrial workers occupationally exposed to chromium. *J Occup Health*, 47:424-30.

Levin SM, (1983). Problems and pitfalls in conducting epidemiological research in the area of reproductive toxicology. *Am J Ind Med*, 4:349-364.

Listowsky I, Rowe JD, Patskovsky YV, (1998). Human testicular glutathione S-transferases: insights into tissue-specific expression of the diverse subunit classes. *Chem Biol Interact,* 111-112:103-112.

Li X, Pan J, Liu Q, Xiong E, Chen Z, Zhou Z, Su Y, Lu G,(2013). Glutathione S-transferases gene polymorphisms and risk of male idiopathic infertility: a systematic review and meta-analysis. *Mol Biol Rep*, 40(3):2431-8.

Mukherjee SB, Aravinda S, Gopalakrishnan B, (1999). Secretion of glutathione S-transferase isoforms in the seminifer- ous tubular fluid, tissue distribution and sex steroid binding by rat GSTM1. *Biochem J,* 340:309-320.

Mustafa M, Pathak R, Tripathi AK, Ahmed RS, Guleria K, (2010). Maternal and cord blood levels of aldrin and dieldrin in Delhi population. *Environ Monit Assess*, 171: 633-638.

Mustafa MD, Banerjee BD, Ahmed RS, Tripathi AK, Guleria K, (2013). Gene-environment interaction in preterm delivery with special reference to organochlorine pesticides. *Mol Hum Reprod*, 19: 35-42.

Nicolopoulou-Stamati P and Pitsos MA, (2001). The impact of endocrine disrupters on female reproductive system. *Hum Reprod Update*, 7: 323-330.

Nonaka T, Takakuwa K, Tanaka K, (2011). Analysis of the polymorphisms of genes coding biotransformation enzymes in recurrent miscarriage in the Japanese population. *J Obstet Gynaecol Res*, 37(10):1352-1358.

Oliva A, Spira A and Multigner L, (2001). Contribution of environmental fac- tors to the risk of male infertility. *Hum Reprod*, 16:1768-1776.

Olshan AF, Luben TJ, Hanley NM, Perreault SD, Chan RL, (2010). Preliminary examination of polymorphisms of GSTM1, GSTT1, and GSTZ1 in relation to semen quality. *Mutat Res,* 688: 41-6.

Pallav Sengupta, (2013). Environmental and Occupational Exposure of Metals and their role in Male Reproductive

Functions. *Drug and Chemical Toxicology*, 36(3):353-68.

Parveen F, Faridi RM, Das V, Tripathi G, Agrawal S, (2009). Genetic association of phase I and phase II detoxifi cation genes with recurrent miscarriages among North Indian women. *Mol Hum Reprod*, 16:207-14.

Peddireddy V, Badabagni SP, Gundimeda SD, Mamidipudi V, Penagaluru PR, Mundluru HP,(2016). Association of CYP1A1, GSTM1 and GSTT1 gene polymorphisms with risk of non-small cell lung cancer in Andhra Pradesh region of South India. *Eur J Med Res*, 18:21:17.

Prasher D,(2009). Heavy metals and noise exposure: Health effects. *Noise Health*, 11:141-4.

Quinones LA, Irarrazabal CE, Rojas CR, Orellana CE, Acevedo C, Huidobro C, Varela NE, Caceres DD, (2006). Joint effect among p53, CYP1A1, GSTM1 polymorphism combinations and smoking on prostate cancer risk: an exploratory genotype-environment interaction study. *Asian J Androl*, 8:349-355.

Ramos R.G, Olden K, (2008). Gene-Environment Interactions in the Development of Complex Disease Phenotypes. *Int. J. Environ. Res. Public Health*, 5: 4-11.

Renato Polimanti,Sara Piacentini, Natalia Lazzarin, Elena Vaquero Maria Antonietta Re, Dario Manfellotto, and Maria Fuciarelli, (2012). Glutathione S-transferase genes and the risk of recurrent miscarriage in Italian women. *Fertility and Sterility*, 98(2) : 396-400.

Rohini R Nair , Anuradha Khanna, Kiran Singh, (2013). Association of GSTT1 and GSTM1 polymorphisms with early pregnancy loss in an Indian population and a meta-analysis. *Reproductive Healthcare*, 26: 313-322.

Sena Erdogan Aydos, Mehmet Taspinar, Asuman Sunguroglu, Kaan Aydos, (2009). Association of CYP1A1 and glutathione S-transferase polymorphisms with male factor infertility. *Fertility and Sterility*, 92(2): 541-547.

Sata F, Yamada H, Kondo T, Gong Y, Tozaki S, Kobashi G, Kato E.H, Fujimoto S, Kishi R, (2003). Glutathione S-transferase M1 and T1 polymorphisms and the risk of recurrent pregnancy loss, MHR: Basic science of reproductive medicine, 9 (3): 165-169.

Seidegard J, Vorachek WR, Pero RW Here, (1988). Dietary differences in the expression of the human glutathione S- transferase activity on trans-stilbene oxide are due to a gene deletion. *Proc Natl Acad Sci U SA*, 85:7293-7297.

Sharara FI, Seifer DB and Flaws JA, (1998). Environmental toxicants and female reproduction. *Fertil Steril*, 70:613-622.

Sharma R, Yang Y, Sharma A, Awasthi S, Awasthi YC,(2004). Antioxidant role of glutathione S-transferases: protection against oxidant toxicity and regulation of stress-mediated apoptosis. *Antioxid Redox Signal*, 6: 289-300.

Sharpe RM, (2001). Hormones and testis development and the possible adverse effects of environmental chemicals. *Toxicol Lett*, 120:221-232.

Strange RC, Spiteri MA, Ramachandran S, (2001). Glutathione-S-transferase family of enzymes. *Mutat Res*, 482:21-26.

Sunil Kumar, (2011). Occupational, Environmental and Lifestyle Factors Associated With Spontaneous Abortion. *Reproductive Sciences*, 18(10): 915-930.

Tang K, Xue W, Xing Y, Xu S, Wu Q, (2012). Genetic polymorphisms of glutathione S-transferase M1, T1, and P1, and the assessment of oxidative damage in infertile men with varicoceles from northwestern China. *J Androl,* 33: 257-63.

Suryanarayana V, Deenadayal M, Singh L,(2004). Association of CYP1A1 gene polymorphism with recurrent pregnancy loss in south Indian population. *Hum. Reprod*, 19: 2648-2652.

Tang K, Xue W, Xing Y, Xu S, Wu Q, (2012). Genetic polymorphisms of glutathione S-transferase M1, T1, and P1, and the assessment of oxidative damage in infertile men with varicoceles from northwestern China. *J Androl*, 33: 257-63.

Tina Kold Jensen, Jens Peter Bonde, Michael Joffe, (2006). The influence of occupational exposure on male reproductive function. *Occupational Medicine*, 56(8): 544-553.

Tirumala Vani G, Mukesh N, Siva Prasad B, Rama Devi P, Hema Prasad M, Reddy P.P,(2010). Role of glutathione S-transferase Mu-1 (GSTM1) polymorphism in oligospermic infertile males. *Andrologia*, 42: 213-7

Tremellen K, (2008). Oxidative stress and male infertility-a clinical perspective. *Hum Reprod Update,* 14:243-258.

Turner TT, Lysiak JJ, (2008). Oxidative stress: a common factor in testicular dysfunction. *J Androl*, 29:488-498.

Waissmann, W. (2002). Health surveillance and endocrine disruptors. *Cad Saúde Pública* 18:511-517.

Windham G.C, Hopkins B, Fenster L, Swan S.H, (2000). Prenatal active or passive tobacco smoke exposure and the risk of preterm delivery or low birth weight. *Epidemiology*, 11: 427-433.

Wu QF, Xing JP, Tang KF, Xue W, Liu M, (2008). Genetic polymorphism of glutathione S-transferase T1 gene and susceptibility to idiopathic azoospermia or oligospermia in northwestern China. *Asian J Androl*, 10: 266-70.

Zusterzeel P.L.M, Nelen W.L.D.M, Roelofs H.M.J, Peters W.H.M, Blom H.J, Steegers E.A.P, (2000). Polymorphism in biotransformation enzymes and the risk for recurrent early pregnancy loss. *Mol. Hum. Reprod,* 6: 474-478.

How to cite this article:

Indira Priyadarshini U *et al*.2018, Polymorphisms of Gstm1 and Gstt1 Genes Contribute To the Risk of Adverse Reproductive Outcome in Steel Industry Workers. *Int J Recent Sci Res.* 9(6), pp. 27219-27224.
DOI: http://dx.doi.org/10.24327/ijrsr.2018.0906.2213

****