

Prevalence of Drug abuse among ante partum females, Obstetric Department, Beni Suef University Hospital, Egypt

Dalia Abd Elwhab Hassan¹, Manar .A Ahmad¹, Salwa Mahmoud Ali², Mohamed A Hussien², Doaa M. Khalil³, Inas Abd El Rahim Ali⁴, Mostafa Abdallah Abdel Alim¹

¹Researcher of Forensic Medicine and Clinical Toxicology Department, Faculty of Medicine, Beni-Suef University, Beni-Suef, 62514 Egypt, ²Researcher of Obstetrics and Gynecology department, Faculty of medicine, Beni-Suef University, Beni-Suef, 62514 Egypt, ³Researcher of Public Health And Community Medicine Department, Faculty of Medicine, Beni-Suef University, Beni-Suef, 62514 Egypt, ⁴Researcher of Public health Family And Community Department, Faculty Of Medicine, Misr University for science and Technology MUST, 6th of October, 12566, Egypt

Abstract

The consumption of drugs of abuse among females in the Health Services is a frequent problem, but often it is not diagnosed. *Aims:* We have analyzed the variations in the clinical profile of female patients came to obstetric emergency department in a period of six months and made screening for various drugs to assess the percentage of addicted females in this period of life. Secondly, we have assessed also the accuracy of the presumptive method of detection compared to the confirmatory method. *Method:* Urine samples were taken from pregnant females came to obstetric emergency department, Beni Suef University hospital and was screened to detect the drugs of abuse that taken by these females by immunoassay and GC-mass and clinical assessment of the babies were done. *Results:* from 300 females there were 20 cases Tramadol positive by immunoassay but all of them were false positive when GC-mass was used. There was a questioned cross reactivity between Ranitidine and tramadol by Immunoassay needing for more researches. 62.3% of the female were no educated 42% of the female's husbands were SHISHA smokers. Intra uterine growth retardation was the most common fetal complication

Conclusions: scientific survey which done to detect drug abuse among group of people should never depend on immunoassay methods. The belief that women are more biologically complicated than men and that they were too busy caring for their children to participate in studies should be changed. Women should be included in clinical researches.

Keywords: drug abuse, ante partum female, immunoassay, cross reactivity, GC-mass, Beni Suef

Introduction

The problem of drug abuse is not in the individual alone but its general impact on the family and society. The impact of addiction is catastrophic for the family

as a whole; Relationships suffer, financial sources get depleted, health costs increase. Also, the consequences of addictive devastating sexual relations and the resulting sexual transmitted diseases and epidemics which is difficult and sometimes impossible to cure them.

Addiction is also strongly associated with domestic violence, which increases the physical and emotional distress of the family. Having an addicted woman in the family is a catastrophe as women are the backbone of the family, the mother and the wife, and women are also the most suffering from men as a result of addiction. Therefore alternative strategies to identify women with problems related to drug abuse should be used.¹

Corresponding author:

Manar .A Ahmad

Address: Department of Forensic medicine and clinical, Faculty of Medicine, Beni Suef University, Beni-Suef, 62514 Egypt.

Tel: +2 01142572316

E mail: Manar.kenawy30@gmail.com

Scientists have discovered that the problem of addiction in women has to do with hormonal changes such as menstruation, pregnancy, childbirth, breastfeeding and menopause. Also, women themselves describe unique reasons completely different from men for using drugs, including get rid of excess weight, fighting exhaustion, coping with pain, and attempts to self-treat mental health problems.²

Immunoassays dominate urine drug screens (UDSs) because they are simple to use, easy to automate and provide rapid results. Unfortunately, they are subject to cross-reactivity with structurally related and unrelated compounds potentially yielding false-positive results.³

Because many Technicians have limited knowledge of immunoassay cross-reactivity data, patients with false-positive results may be inappropriately terminated from employment or suffer from medical staff bias because of lack of trust and also contribute in giving false survey on the accurate number of drug abuse and gives a false bad impression about a particular sector of population. As a result, programs are put in place to combat addiction in the wrong unsuitable places.

Opiates belong to a large class of compounds characterized by their ability to interact with endogenous opiate receptors. Synthetic opioids as Tramadol that bind to opiate receptors generally require separate immunoassays for screening purposes.⁴

The aim of this study was to detect the drug abuse among ante partum females In Beni Suef and to evaluate if it is enough to depend on Immunoassays urine drug screens as a method to make a survey on a sector of population concerning drug addiction.

Methodology

Subjects

The current study was done on 300 pregnant female in Beni Suef City. Samples were collected from obstetric emergency department, Beni Suef University hospital in a period of 6 months (January to June) in the year of 2019. Every one filled a complete written consent and a questionnaire before collection of samples. Confidentiality of records was kept. The screened drugs were cannabis, benzodiazepine, morphine, tramadol and Amphetamine.

Samples collection

Urine samples (usually 10-50 ml from each driver) were collected from drivers in plastic containers, transferred to lab in ice boxes and free zed in (-20°C) until analysis. The samples were collected in front of guardian to avoid dilution of the samples. . Each sample took a serial number in view of the females.

Samples analysis

Screening: All samples were screened by dip stick to detect studied types of drugs at forensic lab at Beni Suef University.

Confirmatory: positive samples were confirmed by G.C at forensic lab at Beni Suef University.

(1) Dip stick

Principle of use of dip stick to examine urine sample before extraction:-

It is an immunoassay based on the principle of competitive binding. Drug which present in the urine specimen compete against their respective drug conjugate for binding sites on their specific antibody. During testing, a urine specimen migrates upward by capillary action.

Results

Negative: - A colored line in the control line region(C) and a colored line in the test line region (T) for a specific drug indicate a negative result. This indicates that the drug concentration in the urine specimen is below the designated cut- off level for that specific drug. The shade of color in the test region (T) may vary, but it should be considered negative whenever there is even a faint colored line.

Positive: - A colored line in the control line region (C) but no line in the test line region (T) for a specific drug indicates a positive result. This indicates that the drug concentration in the urine specimen exceeds the designated cut-off for that specific drug.

Invalid: - Control line fails to appear due to insufficient volume or incorrect procedural techniques .These is the most likely reasons for line failure.

(3) Gas chromatography:

Instrument: Thermo scientific Trace1300 Gas chromatography

Type of column: Thermo scientific .TG-SQC. Length: 30 m, I.D:0.25mm.

Carrier gas: Helium

Flow rate: 1 ml/ min

Injection volume: 1 micro

Detector: Thermo scientific Trace, ISQ.QD. Single Quadrupole Mass Detector.

Retention time: time of standard peak start from time of injection to time of appearance of peak.

Method of extraction

2 ml urine + 5 ml dichloromethane then vortex for 10 minutes then centrifuge. Aqueous part is discarded and solvent is evaporated then reconstitution with 50 micro methanol. Reagents used are G.C grade.

Questionnaire were answered by pregnant female including age, Educational level, Medicinal history, Maternal complication, Premature labor, Fetal complication, Drug intake by Husband.

Ethical Considerations: Written consent was taken for all participant pregnant female in line with the Ethics protocol of medical research.

Results

About 62% of the participated females were non-educated. Ranitidine was the most common drug (4.7%) which had taken during pregnancy while about 91% of the participated females were not on any drug during pregnancy. 12 % of the ante-partum females have pre- eclampsia followed by Diabetes Miletus 3.3% as a maternal complication during pregnancy. 42% of their husband were Shisha smoker, 6.7% were cigarette smoker. Fetal complications were variable as IUGR, macrosomia and congenital anomalies. IUGR came as the major fetal complication by 22%. 15.3% of fetus entered in the incubators because of many complications. From 300 females there were 20 cases Tramadol positive by immunoassay but when GC-mass was used all of them were discovered to be false positive. So in our survey there were no cases of drug abuse among 300 ante partum females came to Obstetric Department, Beni Suef University Hospital.

Educational level

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	non-educated	187	62.3	62.3	62.3
	primary education	14	4.7	4.7	67.0
	secondary education	88	29.3	29.3	96.3
	high education	11	3.7	3.7	100.0
	Total	300	100.0	100.0	

Medicinal history

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	no	274	91.3	91.3	91.3
	ranitidine	14	4.7	4.7	96.0
	Acetaminophen Codeine	8	2.7	2.7	98.7
	Insulin	4	1.3	1.3	100.0
	Total	300	100.0	100.0	

Maternal complication

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	no complications	242	80.7	80.7	80.7
	pre-eclampsia	36	12.0	12.0	92.7
	severe pre-eclampsia	2	.7	.7	93.3
	DM	10	3.3	3.3	96.7
	cardiac	4	1.3	1.3	98.0
	DM&HTN	4	1.3	1.3	99.3
	anemia	2	.7	.7	100.0
	Total	300	100.0	100.0	

Drug intake by husband

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	no	150	50.0	50.0	50.0
	Cigarette	20	6.7	6.7	56.7
	SHISHA	126	42.0	42.0	98.7
	SHISHA and tramadol	4	1.3	1.3	100.0
	Total	300	100.0	100.0	

Fetal complication					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	no	223	74.3	74.3	74.3
	IUGR	66	22.0	22.0	96.3
	macrosomia	7	2.3	2.3	98.7
	IUGR with oligo	2	.7	.7	99.3
	Congenital anomalies	2	.7	.7	100.0
	Total	300	100.0	100.0	

Post natal incubator					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	no	254	84.7	84.7	84.7
	RD	39	13	12.3	97.0
	TTN	6	2.0	2.0	99.0
	HYPOGLYCEMIA	1	.3	.3	99.3
	Total	300	100.0	100.0	

Result of screening					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	negative	280	93.3	93.3	93.3
	Tramadol	20	6.7	6.7	100.0
	Total	300	100.0	100.0	

Result by confirmation					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	negative	300	100.0	100.0	100.0

Discussion

Immunoassays were developed for general screening. Urine drug testing is now done for any occupations (i.e., truck drivers and train engineers, any positional governmental employers and also in proposal for many private works). Interpretation of drug test results should be performed by a medical trained and certified technician, who can make result interpretation to understand the pitfalls in interpreting urine drug screen results.⁷

According to the manufacturer reports there are some agents known to cross-react with each class. This list should not be considered the only substances that making the cross react which mean that there are many unlisted substances could make the same cross react. The sensitivity and specificity of the various components of the immunoassays are variable between manufactures.⁷

There are many factors affecting drug detections in urine as UDS' cutoff or detection level of specified urine metabolite above which the test will be positive, substance' dose, elimination half-life, urine pH, urine dilution, frequency of use, and time of last use.⁹ Thus, health care providers should be aware of all these factors during making their research.

GC/MS is both more sensitive and specific than immunoassay but more expensive, slower, and not readily available for acute management.⁸

Most urine drug screens are designed to detect opiates (namely morphine) and drugs metabolized to morphine by the human body (i.e., heroin) and often "miss" the majority of semi-synthetic and synthetic opioids; although, cross-reactivity does occur and is assay dependent. False positive opiate tests have reportedly been caused by dextromethorphan, diphenhydramine, quinine, quinolones, rifampin, verapamil, and poppy seeds. In the hopes of testing for medical adherence, some urine drug screens specifically include methadone. Of note, false positive methadone screens have been reported to be caused by quetiapine, doxylamine, olanzapine, diphenhydramine, and verapamil.¹⁰

Many studies reported that, positive screens should be confirmed by GC/MS and / or quantitative levels of the specific drug of abuse in question should be sent in these types of cases.⁷

Immunoassays give to some extent helpful information, but should be treated as 'presumptive positive' results which should be confirmed by other an independent procedure such as GC-MS or liquid chromatography-tandem mass spectrometry as we done in our study.

In a study that done on youths and young adults, they suggest that gender may play a role in the patterns of drug use, abuse, and dependence. They found that overall rates of substance use were significantly higher for males than for females.⁵ figure 1 highlights country-level variations in the drug use gender gap in Europe.¹² Another data indicate marked differences in the male to female gender ratio in Georgia and Albania.¹³

In our study there was no case of drug abuse among 300 ante partum females while It was estimated that nearly 30 000 pregnant women use opioids in Europe in a survey done in 2009.¹⁴ Also other studies which done in Canada showed that percentage of drug abuse between females and males resemble approximately 1:2.¹⁶

Our explanation for these results is that Pregnancy and motherhood can be a strong motivator in a woman's pathway to stop any drug addiction and also sense of guilt and fear of having abnormal children.

Also ethnic, cultural and religious diversity needs to be considered when working with this group of women.¹⁵

Federal agencies, including the National Institutes of Health (NIH), have been instrumental in pushing for women to be included in clinical research. These efforts have ensured that broader public health issues related to sex and gender are studied.¹¹

Conclusion

Understanding the reasons for differences between males and females In drug abuse and between females themselves in different countries and continuing to evaluate these patterns over time could help in the development of targeted and more effective prevention and treatment interventions. Scientific survey which done to detect drug abuse among group of people should never depend on immunoassay methods. The belief that women are more biologically complicated than men and that they were too busy caring for their children to participate in studies should be changed. Women should

be included in clinical researches.

Recommendations

Because of the poor sensitivity and specificity of immunoassays the clinician usually make definitive confirmation by other methods as GC/MS but it is done in cases with forensic or legal ramifications but this confirmations should be done also in survey studies to give accurate data that can deal correctly through these results. More surveys should be done on bigger sectors of females to detect cases of drug abuse between them.

Conflict of Interest: Nil

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

- 1- United Nations International Drug Control Programme, Regional Office for South Asia (UNDCP -ROSA).women and drug abuse: the problem in India, 2002. In https://www.unodc.org/documents/ungass2016/Contributions/UN/OHCHR/A_HRC_30_65_E.pdf
- 2- ACOG committee opinion. opioid use and opioid use disorders in pregnancy, American Society of Addiction Medicine, The American College of Obstetricians and Gynecologists, 2017. N711. In <https://www.acog.org/-/media/project/acog/acogorg/clinical/files/committee-opinion/articles/2017/08/opioid-use-and-opioid-use-disorder-in-pregnancy.pdf>
- 3- Reisfield, G.M., Goldberger, B.A., Bertholf, R.L. 'False-positive' and 'false-negative' test results in clinical urine drug testing. *Bioanalysis*, 2009, 1, 937-952.
- 4- Alec Saitman, Hyung-Doo Park and Robert L. Fitzgerald. False-Positive Interferences of Common Urine Drug Screen Immunoassays: A Review, *Journal of analytical toxicology*, 2014. 1-10
- 5- Jessica H. Cotto MPH, Elisabeth Davis MPH., Gayathri J. Dowling PhD., Jennifer C.Elcano MA., Anna B. Staton MPA., Susan R.B.Weiss PhD. Gender effects on drug use, abuse, and dependence: A special analysis of results from the national survey on drug use and health, *journal of Gender Medicine*, 2010. 7; 5: 402-413
- 6- Salima Shaikh, Mindy J. Hull, Kenneth A. Bishop, David A. Griggs, William H. Long, Andrea t. Nixon, and James G. Flood 2008. Effect of Tramadol Use on Three Point-of-Care and One Instrument-Based Immunoassays for Urine Buprenorphine. *Journal of Analytical Toxicology*, 2008. 32: 339-343
- 7- D. Adam Algren & Michael R. Christian. Buyer Beware: Pitfalls in Toxicology Laboratory Testing. *Journal of science of Medicine, Emergency Medicine*,2015. 206: 112-113
- 8- Von Mach MA, Weber C, Meyer MR et al. comparison of urinary on-site immunoassay screening and gas chromatography-mass spectrometry results of 111 patients with suspected poisoning presenting to an emergency department. *Ther Drug Monit*, 2007.29:27-39.
- 9- Heit HA, Gourlay DL. Urine drug testing in pain medicine. *J Pain Symptom Manage*, 2004 ;27:260-267.
- 10- Rogers SC, Pruitt CW, Crouch DJ, Caravati EM. Rapid urine drug screens: diphenhydramine and methadone cross-reactivity. *PediatrEmerg Care*, 2010. 26:665-666.
- 11- National institute on drug abuse. Drug facts. Substance Use in Women, 2018 . N 5 .In www.drugabuse.gov.
- 12- EMCDDA (European Monitoring Centre for Drugs and Drug Addiction) (2016b), Statistical bulletin 2016 (data tables), <http://www.emcdda.europa.eu/data/stats2016>
- 13- ESPAD (European School Survey Project on Alcohol Other Drugs) and EMCDDA (European Monitoring Centre for Drugs and Drug Addiction), ESPAD report 2015, 2017.additional tables (available at <http://www.espad.org/report/table-29b-frequency-lifetime-use-illicit-drugs-gender-2015-percentages>;
- 14- Gyarmathy, V. A., Giraudon, I., Hedrich, D., Montanari, L., Guarita, B. and Wiessing, L. Drug use and pregnancy — challenges for public health', *Euro Surveill*, 2009. 14, pp. 33-36.
- 15- United Nations Office on Drugs and Crime (UNODC). Guidelines on drug prevention and treatment for girls and women, UNODC, 2016. Vienna. In https://www.unodc.org/documents/drug-prevention-and-treatment/unodc_2016_drug_prevention_and_treatment_for_girls_and_women_E.pdf

16- National Center on Addiction and Substance Abuse.
The Formative Years: Pathways to Substance

Abuse among Girls and Young Women Ages 8-22,
2003. New York: CASA.