STUDYING HEALTH IMPACT OF EXPOSURE TO ORGANIC SOLVENTS ON RENAL FUNCTIONS (A CASE CONTROL STUDY) CAIRO - EGYPT.

Thesis
Submitted for Fulfillment
Of M.D Degree of public Health

BY

Asmaa Mahmoud Mohamed Mohamed
MBBCh, M.Sc of public health
Department of Environmental and Occupational Medicine
National research center

Supervised by

Prof. Dr. Ibrahim S. Hegazy
Professor of public health
Cairo University

Prof. Dr. Hanan A. Al- raghi
Professor of public health
Cairo University

Prof. Dr. Sanaa A. Rizk
Professor of occupational medicine
National research center

Dr. Hend M. Rashad
Assistant professor of environmental medicine
National research center

Faculty of Medicine
Cairo University
2012

بسم الله الرحمن الرحيم

Acknowledgement

Acknowledgement

I would like to express my deepest respect, gratitude and appreciation to Prof. Dr. ***Ibrahim S. Hegazy,*** *professor of public health, Faculty of medicine, Cairo University* for his continuous supervision, guidance, great help during analysis and finalization of the results, support and encouragement.

My deepest thanks, gratitude and appreciation to Prof. Dr***. Hanan A. El-*** raghi, *professor of public health, Faculty of medicine, Cairo University* for her great help, support and continuous supervision.

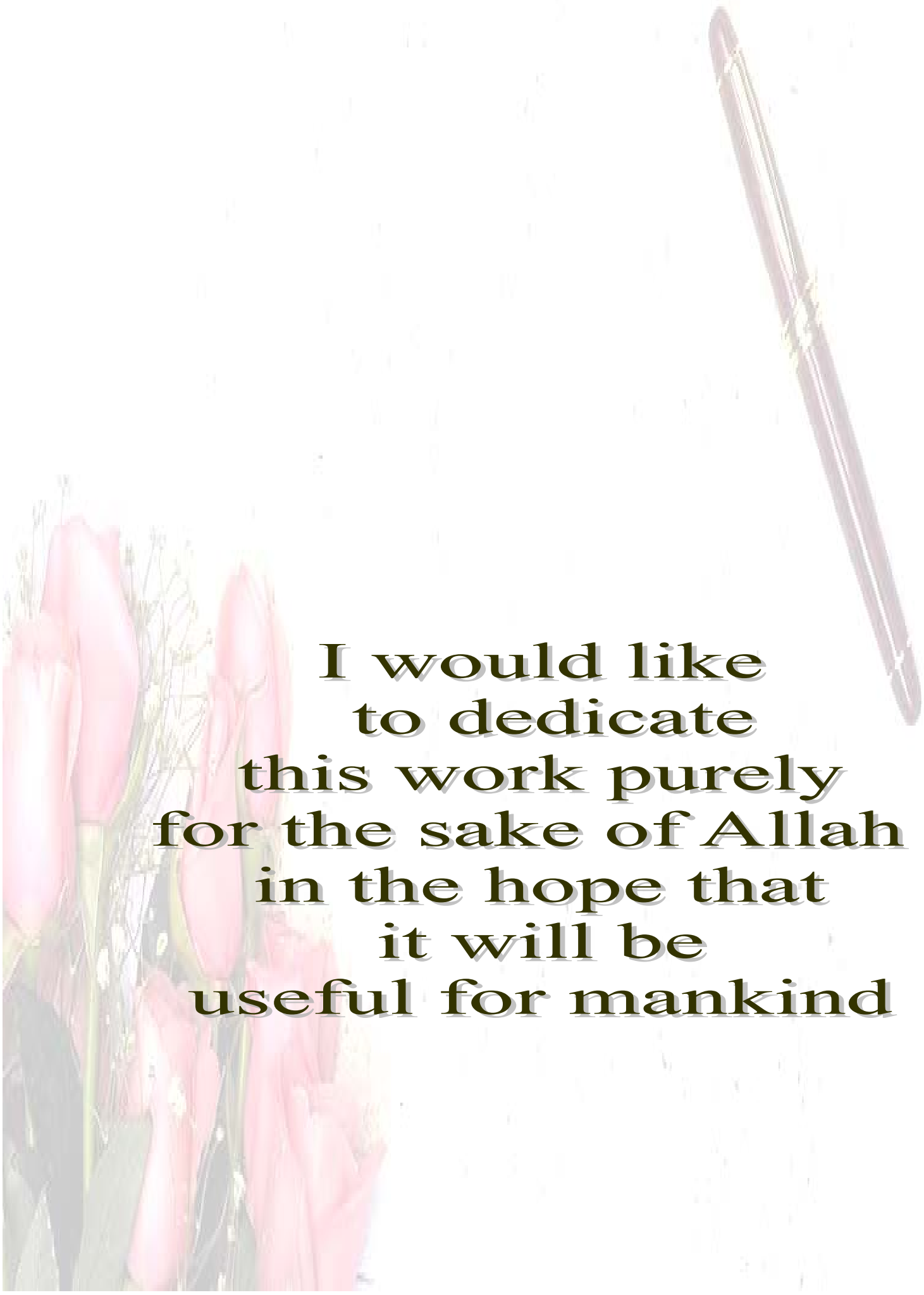
My deepest respect and appreciation to Prof. Dr **Sanaa A.Rizk ,** *professor of occupational medicine, National research center,* for her help, support and continuous encouragement .

I'm thankful to Prof Dr.Hend **M. Rashad,** Assistant professor of environmental medicine, *National research center,* for her support.

I'm thankful to Prof Dr.Nadia Badawy, professor of Occupational Medicine, National Research Centre, for her encouragement and support.

Many thanks to Prof. Dr. Fateheya Mohamed Metwally, professor of Occupational Medicine, National Research Centre, for her support in all stages of this work.

My thanks are extended to all the members and colleagues in my work, environmental and occupational medicine department, national research center, for their support.


I would like
to dedicate
this work purely
for the sake of Allah
in the hope that
it will be
useful for mankind

Abstract:

Introduction: the results of the studies performed to study the effect of exposure to organic solvents on kidney in workers occupationally exposed to organic solvents over the last twenty years are contradictory. **Subjects and methods:** we studied the effect of occupational exposure to organic solvents on renal functions using both routine renal functions namely; serum urea, serum creatinine, estimated glomerular filtration rate and early renal urinary biomarkers namely; N acetyl-B-D glucosaminidase and B2 microglobulin.

This is an analytical case control study conducted on 181 male worker in paint manufacturing factory exposed to organic solvents during their work and 186 control individual never exposed occupationally to organic solvents and engaged in administrative tasks in organization outside the factory. **The results** of the study revealed statistically significant difference between the Urinary –N-Acetyl glucosaminidase activity (NAG index) as well as B2microglobulin (P-value<0.001) in the workers that exposed to organic solvents and their matched controls**.** The proportion of exposed workers that have abnormal NAG activity (53.6%) is higher than that in their matched controls (29.6%) and represent about two fold increase in the activity with high statistically significant difference (p-value=0.000). **Conclusion:** results of this study point to a possibility of early renal effects, but not to a serious to influence on the routine kidney function tests at the current levels of occupational exposure to organic solvents. **Recommendations**: workers exposed to paints, glues, degreasing solvents, and cleaning solvents must be evaluated periodically for renal effects using Urinary NAG excretion and B2microglobulin as reliable markers of the tubulo-toxicity and non-invasive tests.

Key words:

Organic solvents – renal impairment- early renal biomarkers – NAG -B2M.

Contents

Contents

List of tables

List of figures

Abbreviations list

AAP	Alanine amino peptidase
ACGIH	American Conference of Governmental Industrial Hygienists
ALP	Alkaline phosphatase
ANOVA	Analysis Of Variance
ATN	Acute tubular necrosis
BMI	Body Mass Index
B2M	B2-Microglobulin
BUN	Blood urea nitrogen
CCIE	Chamber of Chemical Industries – Egypt
CDC	Centers for Disease Control and Prevention
CNS	Central nervous system
CRF	Chronic renal failure
ESRD	End stage renal disease
EEG	Electroencephalography
GBM	Glomerular basement membrane
GFR	Glomerular filtration rate
GN	Glomerulonephritis
IARC	International Agency for Research on Cancer
IPCS	International program on chemical safety
MDRD	Modification of Diet in Renal Disease
MEK	Methyl ethyl ketone
MN	Membranous nephropathies
MNBK	Methyl-n-butyl ketone
NAG	N-acetyl-B-D-glucosaminidase
NKF	National Kidney Foundation
NIOSH	National Institute of Occupational Safety and Health
OMAL	Ontario Association of Medical Laboratories
OSHA	Occupational Safety Health Administration
PCE	perchloroethylene
PPE	personal protective equipment
TCA	Trichloroethane
TCE	Trichloroethylene
TLV	The Threshold Limit Value

Abbreviations list

TWA	time weighted average

Introduction

Chronic kidney (CKD) disease is a major public health problem throughout the world and the prevalence of CKD is largely sustained by the inclusion of a substantial proportion of the elderly population within stage 3 CKD, according to the Kidney Disease Outcomes Quality Initiative staging system. Adverse outcomes of chronic kidney disease can be prevented through early detection and treatment **(Mangione & Dal Canton , 2011**).

It is clear that an individual's likelihood of developing progressive Chronic kidney disease results from complex interactions between multiple genetic (none modifiable factors) and environmental factors (modifiable factors) (**Satko, et al, 2007).** Identification of the modifiable and controllable risk factors e.g. exposure to nephrotoxic substances such as organic solvents, is an important first step in understanding and hopefully, revering the increasing incidence of such disease **(Thoenen, 2006).**

A solvent is a substance that dissolves another substance forming a solution. Solvents that contain carbon are known as organic solvents and can contain chemicals considered hazardous (**Brautbar, 2008).**

The organic Solvents represent an important group of environmental pollutants to which people are exposed daily in the household settings and workplace They are present as ingredients in paints, varnishes, lacquers, glues, adhesives, degreasers, cleaners and in the production of dyes, polymers, plastics, textiles, printing inks, agricultural products and pharmaceuticals **(Bale, et.al,2011).** Organic solvents are present also in detergents (citrus terpenes), in perfumes (ethanol), home deodorizers, toothpaste (formaldehyde), carpets cleaners, nail polish removers, bathroom cleaners and glue solvents (acetone, methyl acetate, ethyl acetate), in dry cleaning (e.g. tetrachloroethylene), paint thinners (e.g. toluene, turpentine), in spot removers (e.g. hexane, petrol ether), furniture oils, shoe care products **(Andrews, 1989)** .

Exposure can occur through inhalation due to volatilization of the solvent. Primary exposure concerns result from inhalation exposure from occupational work such as metal degreasing operations and/or residential exposures resulting from off gassing from the factories using these agents or from groundwater contamination. Many varied health effects including toxicity to the liver, kidney, lungs, and carcinogenic effects have been reported in the literature**. (Bale, et al, 2011).** Millions of workers are exposed to organic solvents worldwide at different workplaces. Depending on the vapor pressure of the individual solvents, workers may be exposed by inhalation. Exposure concentrations may be very high, at least for some procedures (e.g. cleaning). In addition, dermal exposure may contribute considerably to the overall exposure. Exposure may occur despite the use of protective clothing, because solvents may penetrate gloves or cloth. Solvent mixtures are frequently used. Therefore, effects may also be caused by combined exposures. Threshold limits in the air, established by several national and international institutions, enable control of a large number of solvents in air at the workplace. **(Mangelsdorf, 2009).**

Among the health hazards of exposure to organic solvents, are renal problems. The severity of these effects is largely dependent on the compound and the level of exposure. (**Gunnar et al, 2008)**.

In recent years case reports, case studies and experimental animals studies demonstrated that solvents are causing a variety of kidney disorders including acute and chronic kidney failure. The major routes of absorption of these compounds are through the lungs and the skin. Once in circulation, these compounds are concentrated in the kidney by mechanism remains uncertain but may be related to a solvent-induced disruption of the structural and functional integrity of the limited membranes of the kidney cells. A number of studies have demonstrated a significant association between organic solvents exposure and the development of glomerulonephritis through immune mediated mechanisms. (**Brautbar, 2008).**

Workers with a history of exposure to paints, glues, degreasing solvents, and cleaning solvents must be evaluated for renal impairment. Such patients may not know the risks of their exposure and may actually not understand the relationship between an