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Gender Differences in Biochemical Examination Among Paint Industry Workers

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Abstract

The global paint production industry uses volatile organic compounds (VOCs) and heavy metals, which can have an impact on health. It is influenced by different toxicokinetics and toxicodynamics based on gender. Variations in sex hormones, xenobiotic-metabolizing enzymes, and distribution volumes influence the body's response to toxins. This study aims to investigate biochemical parameters, including ALP, AST, ALT, Gamma-GT, total cholesterol, creatinine, cholinesterase, total bilirubin, fasting glucose, N Urea, eLFG, and uric acid in paint industry workers in Surabaya, stratified by gender. An analytical observational study with a cross-sectional design was conducted on 89 workers engaged in production, research and development, and logistics within a paint manufacturing facility. Demographic data were obtained via questionnaires, and laboratory test results were analyzed. Statistical evaluation was performed using the chi-square test to determine the association between gender and biochemical abnormalities. The assessment of paint exposure among workers, based on biochemical test results stratified by gender, demonstrated that gender significantly influences these parameters ($p<0.05$). The findings of alkaline phosphatase (ALP) (OR: 7.500, 95% CI: 1.146–49.100), total cholesterol (OR: 3.841, 95% CI: 1.142–12.916), and creatinine (OR: 30.179, 95% CI: 7.706–118.193) suggest that exposure to paint substances impacts liver function (as indicated by ALP), total cholesterol, and srenal function (creatinine). These outcomes could be attributed to physiological, hormonal, enzymatic, and genetic differences between male and female individuals in their toxicological responses, as supported by biochemical examination results.

Introduction

Paint production involves the use of volatile organic compounds (VOCs). These VOCs naturally occur in the environment, but their levels have increased due to human activities, with recent decades witnessing a significant rise attributable to anthropogenic factors (Zhou *et al*., 2023). A study by Ghobakhloo, Khoshakhlagh, Morais & Mazaheri Tehrani (2023) on paint factory workers in Iran involved collecting VOC samples within the workers' respiratory zones under standard working conditions. Fifteen VOCs were identified, namely benzene, toluene, ethylbenzene, xylene, styrene, n-hexane, n-heptane, n-nonane, trichloroethylene, tetrachloroethylene, n-butyl acetate, n-octane, n-decane, dichlorofluoromethane, and acetone. The highest total VOC concentration was observed in the Plastic Color (PC) sector. Non-carcinogenic risks associated with exposure to benzene, n-nonane, trichloroethylene, tetrachloroethylene, xylene, and ethylbenzene were detected across nearly all factory sectors. Concerning carcinogens, the Lifetime Excess Total Cancer Risk (LTCR) values markedly surpassed the negligible risk threshold of 1.0×10^{-6}. Ethylbenzene and benzene emerged as the most significant pollutants contributing to elevated cancer risks (Ghobakhloo *et al*., 2023).

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An additional study by Ifeoma *et al*. (2022), involving 80 male paint workers (PFW) and 60 male non-paint workers (NPFW) as controls, aged between 21 and 40 years, demonstrated that PFW exhibited significantly higher mean serum levels of aspartate aminotransferase (AST), alkaline phosphatase (ALP), sodium, and chloride compared to NPFW ($P<0.05$) (Ifeoma *et al*., 2022).

Beyond organic compounds, the paint industry also utilizes heavy metals (Nair K *et al*., 2021), including manganese (Mn), cobalt (Co), nickel (Ni), zinc (Zn), arsenic (As), cadmium (Cd), lead (Pb), copper (Cu), and chromium (Cr) (M. R. Khan *et al*., 2021; Puthran & Patil, 2023; Wang *et al*., 2023). Human exposure pathways for heavy metals include inhalation of airborne particles or dust, ingestion of contaminated food or beverages, and dermal contact (Damayanty *et al*., 2020; Jomova *et al*., 2025; Musfirah & Rangkuti, 2019; Wang *et al*., 2023). Bioaccumulation of heavy metals can result in various toxic effects, impacting diverse tissues and organ systems. The toxicity profile of heavy metals depends on soil properties, dosage, exposure route, duration (acute or chronic), and accumulation levels. Both VOCs and heavy metals are deleterious due to the induction of oxidative stress within the body (Jomova *et al*., 2025; Mitra *et al*., 2022). Symptoms among affected populations include headaches, congenital disabilities, cancer, organ impairment, and neurological disturbances such as memory loss, confusion, allergies, neuropsychological disorders, respiratory issues, and additional health effects (Awantari & Susilowati, 2023; Balali-Mood *et al*., 2025; James *et al*., 2022; Marianti *et al*., 2015; Suryadi *et al*., 2022; Susilowati *et al*., 2025; Zucco & Doty, 2021).

Gender-specific health outcomes resulting from exposure to environmental chemicals exhibit differences in pathophysiology, development, and severity, owing to fundamental variations in cellular and molecular mechanisms influenced by sexual dimorphism in organs such as the liver, as well as gene-environment interactions. Consequently, men and women may display distinct responses to toxic exposures (Clayton & Tannenbaum, 2016; Migliore *et al*., 2021a; Wahlang, 2023). A study by Sekhar, Lal, Venugopal, R & Johnson (2024), involving 120 small-scale paint manufacturing workers aged 25–60 years, assessed respiratory symptoms through questionnaires and lung function by the Wright Peak Expiratory Flow Meter (PEFR). Results revealed that concentrations of VOCs such as benzene, ethylbenzene, toluene, xylene (BETX), and dichloromethane exceeded the threshold limit values (TLV) established by the American Conference of Governmental Industrial Hygienists (ACGIH). Approximately 52% of the paint workers reported respiratory symptoms, and around 22% demonstrated reduced lung function (PEFR < 400 L/min). A modest yet significant negative correlation was observed between PEFR and occupational duration ($r = -0.2$, $p = 0.03$) (Sekhar *et al*., 2024). Furthermore, Ogbodo & al. (2024), examining 50 car paint workers in Nigeria, observed significant increases in white blood cells, platelets, alanine transaminase (ALT), aspartate transaminase (AST), total bilirubin (TB), albumin (ALB), urea concentration, creatinine, potassium (K^+), uric acid, and nitric oxide, alongside reductions in packed cell volume (PCV), hemoglobin (HB), lymphocytes (LYM), eosinophils (EOS), alkaline phosphatase (ALP), total protein (TP), direct bilirubin (DB), sodium (Na^+), and bicarbonate (HCO_3^-) (Ogbodo *et al*., 2024). Variations attributed to gender significantly influence toxicokinetics and toxicodynamics. Differences in sex hormones, xenobiotic metabolizing enzymes, and distribution volume modulate the organism's response to toxins (Gochfeld, 2017; Y. H. Khan *et al*., 2022). Prior research predominantly reports combined data without gender stratification; however, recent toxicological investigations have demonstrated differential susceptibilities between males and females concerning hepatic injury, nephrotoxicity, and lipid profile alterations following industrial chemical exposure (Rakshith *et al*., 2023; Sciarra *et al*., 2023). Accordingly, this study aims to analyze gender-based differences in biochemical parameters including: alkaline phosphatase (ALP), aspartate transaminase (AST), alanine transaminase (ALT), gamma-glutamyl transferase (Gamma GT), total cholesterol,

creatinine, cholinesterase, total bilirubin, fasting glucose, urea (N-urea), estimated lung function (eLFG), and uric acid among industrial paint workers in Surabaya, thereby reinforcing the necessity for gender-specific considerations in occupational health surveillance and industrial risk management.

Methods

This study constitutes an analytical observational investigation employing a cross-sectional design, involving 89 respondents from the Manufacturing, Supply Chain, and Research & Development divisions of a paint manufacturing facility in Surabaya. Participation was contingent upon the respondents' willingness to undergo blood sampling and their lack of a prior medical history indicating health issues. Ethical clearance for this research was duly obtained, with certification number KEPK/UMP/49/I/2022, issued by the Health Research Ethics Committee of Universitas Muhammadiyah Purwokerto. The instrument for data collection was a closed-ended questionnaire utilizing an interval measurement scale based on the Likert model. Biochemical analyses were performed on blood samples collected in vacuum tubes and subsequently analyzed at the Prodia Jemursari Surabaya Clinical Laboratory and the Prodia Jakarta Clinical Laboratory. Cholinesterase levels were quantified using serum samples read through the Architec C-8000 device, employing the DGKC Butyrylthiocholine 37°C method to measure absorbance or concentration. Liver function tests, specifically SGPT and SGOT, were conducted using the Architect C System. Gamma GT levels were ascertained via the Agilent 7700 X device. Other measurements, including alkaline phosphatase, total bilirubin, total cholesterol, fasting glucose, blood urea nitrogen, and uric acid, were performed utilizing the Cobas C503 instrument.

Secondary data comprised questionnaire responses serving as research controls, as well as personal data related to the participants' activities, which were employed as samples within the study. The data obtained were subjected to statistical analysis using SPSS software. The chi-square test was applied to evaluate differences in mean age, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Gamma GT, Alkaline phosphatase (ALP), Cholinesterase, Total bilirubin, Total cholesterol, Fasting glucose, N-urea, Creatinine, eLFG, and uric acid, with a significance level set at p-value <0.05.

Result and Discussion

The research data were categorized according to the respondents' gender, examining variables such as age, smoking habits, alcohol consumption, exercise routines, and body mass index.

Table 1. Relationship Between Gender, Age, and Health Data

Variables	Male (n = 72) Total (%)	Female (n = 17) Total (%)	OR	95% CI	P-Value
Age					
≤ 40 years old	41(56.9)	8(47.1)	1.488	0.515 – 4.297	0.461
> 40 years old	31(43.1)	9(52.9)			
Aspartate aminotransferase (AST) (U/L)					
Normal	61(84.7)	16(94.1)	0.347	0.042 – 2.887	0.308
Abnormal	11(15.3)	1(5.9)			
Alanine aminotransferase (ALT) (U/L)					
Normal	61(84.7)	16(94.1)	0.347	0.042 – 2.887	0.308

Abnormal	11(15.3)	1(5.9)			
gamma-glutamyl transferase (GGT) (U/L)					
Normal	66(91.7)	16(94.1)	0.688	0.077 – 6.120	0.736
Abnormal	6(8.3)	1(5.9)			
Alkaline phosphatase (ALP) (U/L)					
Normal	70(97.2)	14(82.4)	7.500	1.146 – 49.100	0.017*
Abnormal	2(2.8)	3(17.6)			
Cholinesterase (U/L)					
Normal	58(80.6)	13(76.5)	1.275	0.360 – 4.510	0.706
Abnormal	14(19.4)	4(23.5)			
Bilirubin total (mg/L)					
Normal	71(98.6)	17(100.0)	0.807	0.728 – 0.894	0.625
Abnormal	1(1.4)	0(0.0)			
Kolesterol total (mg/dL)					
Normal	39(54.2)	4(23.5)	3.841	1.142 – 12.916	0.023*
Abnormal	33(45.8)	13(76.5)			
Glukosa puasa (mg/dL)					
Normal	58(80.6)	15(88.2)	0.552	0.113 – 2.700	0.458
Abnormal	14(19.4)	2(11.8)			
N urea (mg/dL)					
Normal	70(97.2)	17(100.0)	0.805	0.725 – 0.892	0.487
Abnormal	2(2.8)	0(0.0)			
Kreatinin (mg/dL)					
Normal	65(90.3)	4(23.5)	30.179	7.706 – 118.193	0.000*
Abnormal	7(9.7)	13(76.5)			
eLFG(CKD-EPI) (mL/menit/1.73m^2)					
Normal	58(80.6)	16(94.1)	0.259	0.032 – 2.121	0.179
Abnormal	14(19.4)	1(5.9)			
Uric acid (mg/dL)					
Normal	47(65.3)	13(76.5)	0.578	0.171 – 1.962	0.376

Table 1 indicates that gender exerts a statistically significant influence (pvalue < 0. 05) on the outcomes of alkaline phosphatase (ALP) tests (Odds Ratio [OR]: 7.500, 95% Confidence Interval [CI]: 1.146–49.100), total cholesterol (OR: 3.841, 95% CI: 1.146–12. 916), and creatinine (OR: 3.179, 95% CI: 7.706–118.193) among painters. Conversely, other evaluated parameters, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (gamma-GT), cholinesterase, total bilirubin, fasting glucose, urea, estimated glomerular filtration rate (eGFR), and uric acid, did not demonstrate statistically significant effects. The findings of this research revealed that

the mean serum level of alkaline phosphatases (ALP) in male participants was elevated (75.67 ± 1.797 U/L) compared to female participants (72.72.94 ± 4.268 U/L). ALP is an isoenzyme localized to the outer cell membrane, with its primary function being the catalysis of the hydrolysis of phosphate ester bonds in the extracellular matrix. In hepatic tissue, ALP is cytosolic and localized within the canalicular membranes of hepatocytes. It is also present in the placenta, ileal mucosa, kidneys, bones, and liver. Notably, over 80% of serum ALP originates from the liver and bones, with smaller fractions deriving from the intestines (Makris, Mousa, & Cavalier, 2022). ALP plays a significant role in processes related to inflammation and metabolic syndrome (Son, Ha, Park, Kim, & Lee, 2022). Given the function of ALP and its association with adverse health outcomes, it is noteworthy that a study conducted by Maruyama *et al.* (2025), involving 241,670 patients undergoing dialysis (mean age: 69±12 years; 65.9% male; average dialysis duration: 68 months), demonstrated that higher serum ALP levels were independently and linearly associated with increased cardiovascular (CV) mortality and the occurrence of new hip fractures in Japanese dialysis patients (Maruyama *et al.*, 2025). Furthermore, Sankhla *et al.* (2025) carried out an analytical cross-sectional study involving textile industry workers residing in industrial regions and age- and gender-matched controls living approximately 15–20 km away from industrial zones in Pali, Rajasthan. The study revealed significant alterations in serum ALP levels among subjects exposed to occupational hazards when compared to non-exposed individuals (Sankhla *et al.*, 2025). Additionally, a significant elevation in serum ALP levels was observed in mice administered green dye (Peti-Peterdi & Harris, 2010).

The mean total cholesterol level among male respondents (198.36 ± 5.767 mg/dL) was lower than that among female respondents (219.00 ± 7.680 mg/dL). Within this study's female cohort, nine individuals (52.9%) were over forty years old. Older female participants demonstrated significantly elevated body fat percentages and compromised lipid metabolism compared to their younger counterparts. The prevalence of metabolic syndrome (MetS) exhibited an increasing trend across age groups: women under 30 years (0.94%), 30–39 years (2.52%), 40–49 years (5.94%), 50–59 years (12.90%), and those aged 60 years or older (21.64%). Notably, there was a marked decline in the accuracy of residual cholesterol in detecting metabolic syndrome among individuals aged 60 years and above. Overall, the heightened risk of metabolic syndrome observed in women within this study may be attributed to a relative deficiency of estrogen (Zou *et al.*, 2023). Exposure to paint chemicals, which generate free radicals, is suspected to contribute to lipid peroxidation and consequently increase cardiovascular disease risk (Gianazza *et al.*, 2021). These chemicals possess endocrine-disrupting potential in vitro, capable of affecting sex hormone levels and/or activating or blocking hormone receptors (Palaniswamy *et al.*, 2021).

The mean creatinine level among male respondents (0.93 ± 0.0167 mg/dL) surpassed that of female respondents (0.65 ± 0.034 mg/dL). Creatinine, a metabolic byproduct, is primarily filtered from the bloodstream and excreted through urine (Sharma *et al.*, 2022). Elevated creatinine levels may indicate exposure to harmful chemicals and suggest impaired renal function. Furthermore, kidney and liver functions are intrinsically linked; increased creatinine levels can lead to elevated albumin via renal mechanisms or decreased albumin synthesis due to hepatic cellular damage (Rad *et al.*, 2024). Numerous studies have demonstrated that chemical pollutants induce oxidative damage, adversely affecting renal health. The kidneys are particularly vulnerable to the toxicity of heavy metals because of their capacity to reabsorb and concentrate divalent metals, ions, and other metals (Liao *et al.*, 2022; Tejchman *et al.*, 2021). This susceptibility is evidenced by the high incidence of nephropathy in urban and industrial populations (Tsai *et al.*, 2021).

The higher average creatinine levels in males are likely attributable to physiological differences, including hormonal variations. Some research suggests these differences are hormonally driven (Chesnaye *et al.*, 2024). Animal studies further support this, indicating males are more frequently affected by renal

disorders than females (Aufhauser *et al*., 2016). Testosterone is associated with tubular damage, whereas estrogen mitigates conditions such as albuminuria, glomerulosclerosis, and tubulointerstitial fibrosis (Conte *et al*., 2023). In vitro studies also indicate that endogenous estrogen exerts a protective effect on renal tissue (Seppi *et al*., 2016). Biological differences related to gender—encompassing exposure, behavior, anatomy, physiology, biochemistry, and genetics—profoundly influence toxicokinetics and toxicodynamics from molecular to organismal level, leading to variations in xenobiotic responses between males and females in humans and other animals (Gochfeld, 2017). Increasingly, sex and gender are recognized as influential factors in the etiology, prevalence, prognosis, and therapeutic response of numerous diseases, with complex interactions involving sex chromosomes, hormones, and epigenetic mechanisms (Szadvári *et al*., 2023). Diseases such as cardiovascular disease, liver disease, osteoporosis, infectious and autoimmune diseases, and cancer show differential susceptibility between genders (Baggio *et al*., 2013; Migliore *et al*., 2021b).

Gender constitutes a significant factor influencing the immune system's response to various antigens. Evidence indicates that, on average, females exhibit more robust innate and adaptive immune responses than males (Shi *et al*., 2021). The incidence of malignancies is comparatively higher among males, particularly cancers such as esophageal, lung, bronchial, hepatocellular carcinoma, and colorectal cancer (Cook *et al*., 2009; Siegel *et al*., 2022). Furthermore, males generally demonstrate increased susceptibility to infections, including bacterial pathogens such as Legionella pneumophila and Campylobacter jejuni, as well as fungal infections like Cryptococcus neoformans (Gay *et al*., 2021; vom Steeg & Klein, 2016).

The immune systems of men and women exhibit differences attributable to genetic mediators such as sex chromosomes (X and Y), hormonal mediators including estradiol, progesterone, and androgens, environmental factors such as the microbiome, social behaviors related to sexuality like smoking and alcohol consumption, as well as age. Mortality rates tend to be higher in men due to factors involving hormonal regulation, immune system disorders, and the etiology of cancer. Women generally possess higher innate and adaptive immune factors and responses compared to men, thereby contributing to a reduction in cancer mortality rates (Rakshith *et al*., 2023). Differences in chemical metabolism are influenced by sex hormones—estrogen, progesterone, and testosterone—which regulate the expression of various enzymes, including CYP450, the primary enzyme responsible for detoxification (Y. H. Khan *et al*., 2022). Notably, CYP3A4 enzyme levels are elevated in females, impacting the metabolism of drugs such as midazolam and other toxic compounds (Yoon *et al*., 2021). Women typically exhibit a more robust immune response, but are also more susceptible to autoimmune reactions and inflammation resulting from toxic exposure

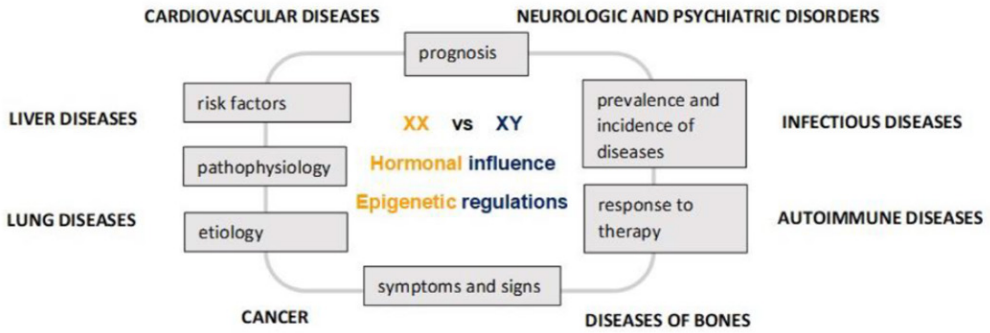

Figure 1. Gender Differences in Disease (Szadvári et al., 2023)

(Sciarra *et al*., 2023). Toxins such as heavy metals (e.g., Pb, Cd) can induce systemic inflammation that varies between genders (Gade *et al*., 2021).

The intestinal mucosa in males appears to be more susceptible than the oral mucosa, with females experiencing fewer digestive side effects from xenobiotics. Most xenobiotics are absorbed predominantly in the jejunum and duodenum, with minimal gastric absorption. The mucosal cells are protected from harmful substances primarily through the functioning of the redox system, wherein glutathione plays a critical role by neutralizing electrophiles and reactive oxygen species using redox buffers. Evidence indicates that glutathione S-transferase is significantly less abundant but more active in the intestines of males, rendering male mucosal tissue less resistant to oral toxins (Rakshith *et al*., 2023). These differences are influenced not solely by gender but also by factors such as dietary habits, including the consumption of vegetables and fruits to enhance enzyme production, suggesting lifestyle-related effects on glutathione S-transferase activity.

Xenobiotic concentrations in the bloodstream are dependent on the volume of distribution and clearance rate (Cl). Men generally have a higher blood volume even after body weight correction, whereas women typically possess a higher body fat percentage (Meyer & Maurer, 2022). Women exhibit slightly lower average renal clearance, reflected in a lower glomerular filtration rate (GFR) (Melsom *et al*., 2022). Xenobiotics are eliminated from the body through excretion or stored in organs; the elimination or clearance curves for various substances display specific half-lives (T1/2) within the entire body and across different compartments (Melsom *et al*., 2022). Post-absorption, xenobiotics distribute within the blood; lipophilic compounds rapidly partition into adipose tissue, increasing the distribution volume (Ben Seghir *et al*., 2023). Consequently, women exhibit a 28% larger volume of distribution (Vd) for lipophilic drugs, whereas the Vd for water-soluble medications is 36% lower in women (Gochfeld, 2017).

The findings from this study indicate gender-related differences in parameters such as liver function (ALP), total cholesterol, and renal function (creatinine). These disparities likely stem from physiological, hormonal, enzymatic, and genetic expression differences between males and females in their toxicological responses, as evidenced by biochemical assessments. However, the study bears limitations due to the absence of direct investigation into these physiological, hormonal, enzymatic, and genetic factors. Therefore, caution should be exercised when interpreting gender differences; it is also essential to consider the influence of social environment and other unexamined factors. Gaining an improved understanding of biologically driven variability between men and women holds significant potential for future applications.

Conclusion

The assessment of paint exposure among workers, as determined through biochemical examination results stratified by gender, indicates that gender exerts a significant influence (p-value < 0.05) on the outcomes of various laboratory tests. Specifically, there is a notable impact on alkaline phosphatase (ALP) levels (odds ratio [OR]: 7,500; 95% confidence interval [CI]: 1,146–49,100), total cholesterol (OR: 3,841; 95% CI: 1,142–12,916), and creatinine (OR: 30,179; 95% CI: 7,706–118,193). Conversely, other laboratory parameters, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (gamma-GT), cholinesterase, total bilirubin, fasting glucose, N-urea, estimated glomerular filtration rate (eGFR), and uric acid, did not demonstrate any statistically significant effects.

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