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Occupational Exposure to N,N-Dimethylformamide and Hepatotoxicity among Synthetic Leather Workers in Bangladesh: Implications for Workplace Health and Labour Law Compliance

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A B S T R A C T

Purpose:N,N-dimethylformamide (DMF) is a polar aprotic solvent that is extensively used in the production of synthetic leather, polyurethane products, resins, adhesives and surface coatings. Potential sources of occupational exposures are mixing, formulation, coating, solvent transfer, cleaning, maintenance, and spill-response. DMF may be inhaled and absorbed through intact skin, which means that total internal dose for a particular worker may be underestimated by only measuring DMF in the air. Liver is a known target organ of DMF toxicity, and reports of increased liver enzymes and, less frequently, clinically significant liver injury have been reported in workers occupationally exposed to DMF. Increases in liver-function tests, however, are non-specific and can occur in people who drink too much alcohol and/or are obese, and/or may be caused by metabolic disease associated with steatotic liver disease, viral hepatitis, certain medicines (prescribed or not) or other exposures that may occur at work. Therefore, a comprehensive evaluation of possible liver damage from DMF should include exposure history, workplace monitoring, biological monitoring, repeated clinical evaluations, and the careful consideration of other causes of liver damage.

Objective: The aim of this study is to find the relationship between DMF exposure and liver injury in the workers working in the synthetic leather, polyurethane, resin and surface-coating industries. It will consider exposure by inhalation and skin contact, estimate internal exposure as measured by urinary markers, review liver-function patterns as they change over time, determine if another source of liver injury or exposure may have occurred, and determine if a failure of workplace controls or medical surveillance could have led to exposure. The results will help to inform evidence-based occupational-health and medico-legal decisions about the possibility and level of occupational contribution to liver disease.

Methods: An occupational-health study using a mixed-methods approach will be conducted with workers who may be at risk for DMF, such as mixers, formulators, coating operators, solvent-transfer workers, cleaners, maintenance workers, and waste-handling workers. A standardised occupational history will document job titles, length of employment, work patterns, frequency of tasks, use of DMF containing products, past chemical exposures, spillages, symptoms, hygiene practices and use and suitability of personal protective equipment (PPE).

Task specific workplace exposure assessments will be carried out and personal air sampling will be used, wherever possible, especially during transfer, mixing, coating, cleaning and maintenance activities. The results of the air-monitoring will be evaluated against relevant occupational exposure concentrations with an understanding that an exposure below the airborne concentration limit does not mean there is no significant dermal absorption. The dermal exposure potential will be evaluated by conducting facility observations and interviews with workers, which will include direct hands-on contact with the material, use of contaminated gloves and clothing, gloves used, gloves replaced, local exhaust ventilation, housekeeping, spill control, washing facility, training, and working practices.

The urinary concentrations of N-methylformamide (NMF) and N-acetyl-S-(N-methylcarbamoyl)cysteine (AMCC) will be measured for internal DMF exposure. These are markers of systemic exposure from all routes of exposure including inhalation and skin contact. Ideally, urine samples will be collected at the end of shift and end of work week, or at other suitable times depending on the toxicokinetic properties of the biomarker. Urine dilutions, e.g. creatinine, specific gravity etc., will be corrected and results interpreted taking into account the timing of the sample, the analytical procedure and available biological guidance values.

Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP) levels, bilirubin, albumin and international normalised ratio (INR) will be measured at regular intervals. These tests will assist in the identification of hepatocellular, cholestatic or mixed liver injury patterns and be useful in identifying transient, persistent or progressive liver injuries. Symptoms such as fatigue, nausea, abdominal discomfort, jaundice, pruritus and constitutional symptoms will also be recorded.

Systematic assessment of potential confounding factors and alternative diagnosis. Alcohol intake, BMI, presence of diabetes, metabolic disease, pre-existing liver disease, other hepatotoxic chemicals and drug or supplement use will be recorded. Investigations may consist of a hepatology specialist review, abdominal ultrasound and hepatitis B and C testing, where clinically appropriate and consented to.

There will be a structured medico-legal review, combining evidence from 4 domains – exposure, biological plausibility, individual clinical disease and duty of care. Occupational history and occupational monitoring will support the results of urinary biomarkers as evidence of internal exposure. The adequacy of engineering controls, local exhaust ventilation, training, spill management, hazard communication and medical surveillance will be taken into account in the duty of care assessment. Challenging with the drug after a possible hepatotoxic reaction will not take place.

Expected Results: The study will not pre-judge causation as there is currently no data. It is anticipated to see if the workers with high overall or task specific exposure would have higher levels of urinary NMF and AMCC, and if these workers would have more frequent and persistent liver-test abnormalities. It will also be evaluated if liver enzymes improve if DMF exposure is reduced or eliminated, if follow up is available. Importantly, the analysis will differentiate isolated elevations of enzymes from a pattern of occupationally related disease.

Conclusions:Concurring inhalational and dermal exposure to DMF is an occupational-health hazard that can be prevented. Task-based exposure assessment, urinary biomarkers, serial liver tests, clinical differential diagnosis and structured medico-legal analysis is a better approach for assessing possible occupational hepatotoxicity than liver enzymes alone. Decisions regarding the possibility, probability and highly probable occupational contribution will be based on the overall evidence and distinct from legal liability.PPE, training, spillage or medical surveillance had a significant impact on the workers.

Introduction

N,N-Dimethylformamide (DMF) is a polar aprotic organic solvent that is used extensively in the production of synthetic leather, polyurethane, resins, adhesives, pharmaceuticals and textiles. The leather goods, synthetic leather, plastics, resin, and chemical-processing industries are also growing in Bangladesh and workers could be exposed to DMF and other hazardous solvents. Inhalation of solvent vapours and direct skin contact with solvent can be a source of exposure for workers involved in solvent mixing, coating, printing, cleaning, transfer, maintenance of equipment or waste disposal.

DMF is a significant occupational health issue – it can be easily inhaled or absorbed through intact skin. Thus, the measurement of airborne DMF concentrations may not completely reflect exposure of workers. These factors can increase exposure via dermal and inhalation routes, such as inadequate local exhaust ventilation, chemical splashes, contaminated work surfaces, long working hours, poor personal hygiene, and inappropriate and inconsistent use of personal protective equipment (PPE) (Occupational Safety and Health Administration [OSHA], n.d.). In workplaces where the solvent is handled, skin protection is especially important, due to the high potential for dermal absorption of DMF (American Conference of Governmental Industrial Hygienists [ACGIH], 2024).

Biological monitoring can provide a more comprehensive assessment of total DMF exposure. The urinary metabolites of DMF, N-methylformamide(NMF) and N-acetyl-S-(N-methylcarbamoyl)cysteine (AMCC) can serve as markers of work-related exposure. The biomarkers are indicative of both inhalation and dermal exposure, as dermal exposure may not be fully represented by workplace air monitoring (Kawai et al., 1992; Sakai et al., 1995). Thus, biological monitoring can be used in conjunction with environmental monitoring to obtain a more precise estimate of the total individual exposure.

One of the key organs of DMF toxicity is the liver. Liver enzymes elevated such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) have been reported as effects of occupational exposure to DMF. Exposed workers can experience mild liver-function abnormalities, liver dysfunction or, in severe exposures, toxic hepatitis (Choi et al., 2001; Wang et al., 2009). DMF undergoes main hepatic metabolism, and the metabolites could cause hepatocellular injury.

The abnormal liver-function test can however, not prove liver damage is directly due to DMF. Other liver dysfunction can be caused by viral hepatitis, metabolic dysfunction-associated steatotic liver disease, alcohol, obesity, diabetes mellitus, medication, herbal medicine, and other chemicals in the workplace. Thus, the history of occupational exposure, clinical symptoms, medical history, and any other factors that could affect liver function should be taken into account in interpreting liver-function abnormalities.

A comprehensive assessment should be made to determine if there is possible hepatotoxic effects caused by DMF due to occupational exposures. This should involve detailed occupational history, observations of job tasks, frequency and duration of solvent handling, working hours, use of PPE, dermal contact incidents, splashes, environmental monitoring of airborne DMF concentrations (if possible) and biological monitoring by measuring urinary DMF metabolites. The history, physical exam, liver-related symptoms, and liver-function tests (including ALT, AST, bilirubin, alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT)) should all be part of the clinical evaluation.

Additionally, other possible causes of liver damage should be looked into such as a history of hepatitis, alcohol use, obesity, diabetes, hepatotoxic medications, other chemical exposures, and herbals. High occupational exposures, biological sampling evidence, abnormal liver-function findings, compatible clinical symptoms, and negative for non-occupational important exposures would provide more evidence of possible occupational DMF-related hepatotoxicity.

In studies in which there is not any air monitoring or urinary biomarkers, there should be no description of the finding as confirmed DMF-induced hepatotoxicity. Rather, the study can evaluate potential DMF exposure in occupations and self-reported symptoms that might be associated with hepatotoxicity.

Materials and methods

Patient Enrollment and Data Collection

This cross-sectional descriptive study was conducted among workers employed in selected synthetic leather manufacturing factories in Bangladesh from June 2026 to October 2026. Workers were enrolled based on their potential occupational exposure to N,N-dimethylformamide (DMF) and other solvent-containing materials used during synthetic leather production.

Eligible participants were workers aged 18 years or above who had been employed in the selected factory for at least six months. Workers involved in coating, mixing, lamination, cleaning, printing, finishing, and solvent-handling activities were considered potentially DMF-exposed. Workers from administrative, packaging, security, and other departments without direct solvent handling were included as the non-exposed comparison group.

A total of 100 workers were included using convenience sampling. Data were collected through face-to-face interviews using a structured and pretested questionnaire, along with direct workplace observation using a checklist. Demographic and occupational variables, including age, sex, educational status, marital status, monthly income, smoking status, duration of employment, job designation, working hours, department, type of work, frequency of chemical handling, and use of personal protective equipment, were collected.

All participants provided written informed consent before participation. Ethical permission was obtained from the Department of Pharmacy and the Department of Law, Daffodil International University, Bangladesh.

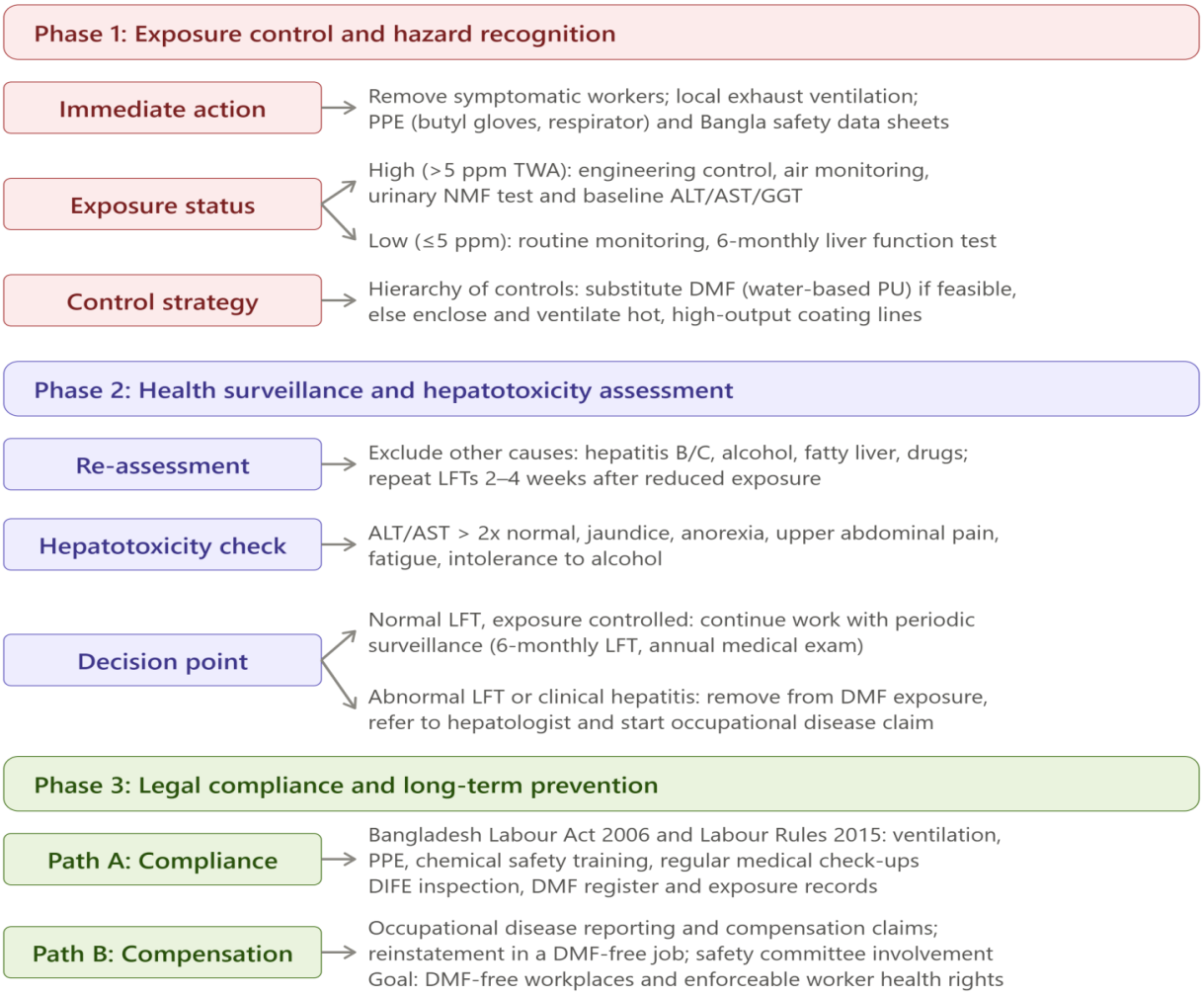


Fig. 1. Integrated framework for DMF exposure control, hepatotoxicity surveillance, and labour law compliance in synthetic leather factories

Case demonstration

Case 1. A 29-year-old man employed in synthetic-leather coatings for 4 years had been using DMF in the application of polyurethane coatings. He was responsible for running an open coating line, cleaning rollers and using solvent soaked cloths. He mentioned that his gloved hands would get wet very often and solvent would splash at times to his forearms. HEV was not used consistently. Urinary NMF and AMCC concentrations at the end of the shifts were higher, suggesting significant amounts of internal absorption of DMF. Routine liver function tests repeated over time revealed elevated AST and ALT levels and slightly elevated GGT, suggesting hepatocellular pattern of liver damage. Viral hepatitis screening was negative, there was minimal alcohol consumption, and ultrasonography showed no significant liver abnormality. When exposed to DMF for 8 weeks, ALT was found to be decreased upon removal from DMF. The occupational contribution was considered to be probable.

Case 2. A 42-year-old man who was the mixer in a polyurethane-resin manufacturing plant had been employed for 11 years in an enclosed mixing area. He had to add DMF to open tanks by hand, and talked about frequent spills on gloves and work clothes. No local exhaust or other effective ventilation was provided in the workplace and gloves worn were thin latex disposable gloves which were not chosen to be DMF resistant. Increased urinary NMF and AMCC levels were obtained at the end of the work week. Liver tests have shown persistent elevated ALT, elevated AST and mildly elevated bilirubin. He was obese and had Type 2 Diabetes; his ultrasound showed fatty liver. Ventilation was improved and protective gloves replaced with chemically compatible gloves; after moving him away from open handling of solvents, the liver enzymes have improved but not fully normalized. The possible to probable occupational contribution was classified and there was also a contribution from metabolic liver disease.

Case 3. A 35-year-old woman was the quality-control technician in a synthetic-leather factory who routinely inspected, cleaned samples and manually wiped coated materials with DMF. Despite a measured

airborne DMF concentration that was less than the relevant occupational exposure limit, she worked regularly with wet samples without wearing gloves as this prevented detailed inspection. Significant increases in NMF were noted with end-of-shift urine testing, and AMCC was elevated at the end of the work week. She developed fatigue, nausea, and right upper quadrant discomfort, with ALT and AST levels ~4-5 times the upper reference limit. She denied alcohol use, regular medications, and had negative hepatitis B and C serologies. Enzymes were brought back to near baseline when the employees were restricted from working and gloves were used and safe cleaning practices were introduced. The occupational contribution was deemed to be highly probable.

Case 4. A 51 year old maintenance worker at a resin manufacturing plant was responsible for regular cleaning and maintenance of a DMF transfer pipe, pump and storage tank. When a pump seal failed, he got a good solvent drench on his hands, arms and clothes. It was not reported as an incident and no immediate medical assessment was made. One week later he became anorexic, developed dark urine and jaundice. The results of blood tests were significant for elevated ALT and AST levels, elevated bilirubin, and elevated INR, which all suggested acute hepatocellular liver injury. DMF urinary biomarkers from immediately after exposure confirmed significant recent systemic exposure. Other causes were ruled out such as viral hepatitis, obstruction of the bile duct and toxicity from acetaminophen. He was admitted to the hospital, but did better after being taken out of the exposure and receiving supportive care. The occupational contribution was considered to be very likely.

Case 5. This 31-year-old man was a solvent transfer operator for a two-year period in a polyurethane-coating plant. His duties were to join hoses together, fill drums and move formulations containing DMF. He noted the existence of frequent minor leaks, wet gloves, poor washing facilities and messy eating habits in the work site. High exposures were detected by personal air monitoring during drum filling activities. The level of urinary NMF and AMCC was found to be higher following transfer shifts than following non-transfer duties. Mild ALT and GGT elevations were repeated in the liver tests over a 12 month period. He was consuming alcohol in a social setting, he had a normal BMI, negative viral serology and no relevant medication exposure. Urinary biomarker levels and liver enzymes were reduced after closed transfer equipment and hygiene controls were installed. The occupational contribution was deemed probable.

Case 6. This was a 46-year-old female janitor in a surface coating factory who was cleaning floors, mixing solvents and equipment containing DMF. She wore reusable gloves that were obviously worn out and she indicated that she worked in areas with inadequate ventilation. She had higher NMF and AMCC results at the end of the shift and at the end of the week, although the results of the full-shift air-monitoring were relatively low. Elevated AST, ALT and GGT were found on serial testing. In her case, however, she had a BMI which was consistent with obesity, hyperlipidaemia and ultrasound evidence of hepatic steatosis. Following re-assignment to non-solvent cleaning, liver enzymes showed some improvement. Results confirmed metabolic dysfunction-associated steatotic liver disease, with a potential additional contribution of occupational DMF. The possible occupational contribution was determined in the case of the occupational contribution.

Case 7. A 38-year-old male printing-line operator used inks that contained DMF when cleaning screens and performing equipment maintenance. He said that he suffered from headaches, eye irritation, and nausea after long hours, especially when working the presses by hand. Ventilation was in place but it was not maintained or performance tested. High production weeks led to an increase in urinary NMF and AMCC. Liver tests revealed a variable hepatocellular pattern, with elevations of ALT that paralleled the time spent on intensive cleaning activities. Liver enzymes were reduced in the 3 weeks when the factory was shut down and raised when the factory re-opened. Low alcohol consumption, normal body weight, negative hepatitis markers, and unremarkable ultrasound. The contribution of the occupation was considered probable.

Case 8. The 54-year-old male formulation supervisor had 18 years' experience in the resin manufacturing process. While he didn't work as many hours with DMF as the production people did, he was in mixing areas every day, investigating spills and helping with equipment failures. Although he had been exposed for many years, he did not have any baseline liver tests or routine biological monitoring. Medical screening revealed elevated ALT, AST, ALP and GGT levels in the hepatocellular-cholestatic pattern. Urinary AMCC collected after a workweek was increased. He was also known to be a hypertensive and an alcoholic, but had negative hepatitis tests and biliary imaging. Liver enzymes showed improvement following a reduction in alcohol intake and strengthening of work exposure controls, but an individual specific cause could not be identified. Possible was assigned to the occupational contribution.

Case 9. The temporary worker was a 27-year-old man, who worked there for 6 months, mainly cleaning coating equipment and stripping away leftover material from trays. He was only briefly introduced to his work and didn't know that DMF could be absorbed through the skin. He often handled materials that were contaminated with solvents without suitable gloves or his bare hands. After many weeks of intensive cleaning, he became tired, anorexic, nauseated and had stomach discomfort. The serum ALT level was found to be elevated, as was end-of-shift urinary NMF level, and the serum AST level was elevated. He had no family or personal history of any liver disease, alcohol abuse, obesity, diabetes, medication or viral hepatitis. He was taken off DMF exposure and liver tests returned to normal during follow-up. Highly probable was used for the occupational contribution.

Case 10. A 59-year-old male waste-handling worker in a factory that manufactured polyurethanes, handled used containers, contaminated rags, and waste from products containing DMF. His job was to break and organize containers that were partially closed in a limited waste storage area. Chemical waste was not well segregated, no extraction ventilation was found, PPE was not always available and there was no biological monitoring programme. Several consecutive shifts led to increased urinary NMF and AMCC. He had continued elevated ALT and GGT, however, he was also diabetic, obese and was found to have a fatty liver on ultrasound. Since introducing the controls at the workplace—such as closed disposal system for working with waste, suitable gloves, respiratory protection as needed, better ventilation, and medical surveillance—the biomarker levels were reduced and liver enzymes were improved slightly. Along with significant metabolic risk factors was a classification of the occupational contribution as possible.

Case No	Exposure history	NMF/MF	AMCC	Liver findings	Differential diagnosis	Dechallenge	Final status
01	Repeated manual handling; possible dermal contact	Elevated, end-shift	Elevated, end-week	ALT/AST/GGT increased	Viral, alcohol, medication to be documented	Expected improvement after removal	Highly probable, pending records
02	Mixing/coating; moderate	Incomplete	Incomplete	Mild ALT/GGT elevation	Obesity, diabetes, MASLD prominent	Not sufficient	Possible

	exposure Incomplete						
03	High repeated production exposure	Elevated, end-shift	Elevated, end-week	Moderate-to-severe hepatocellular injury	Major alternatives expected negative	Improvement expected/ observed after removal	Highly probable
04	Spill, wet gloves or poor ventilation	Positive	Positive or pending	Marked ALT/ AST; bilirubin may rise	Viral, autoimmune and DILI must be excluded	Urgent removal and follow-up	Highly probable, pending exclusion
05	Routine intermittent DMF task	Partial	Positive or partial	Mild-to-moderate mixed pattern	Alcohol, medication, MASLD	Improvement supports causality	Probable
06	Cleaning or transfer task	Uncertain	Elevated	Moderate GGT/ ALT elevation	Alcohol, medication, biliary disease	Task restriction indicated	Probable
07	Repeated production exposure	Partial	Partial	Mild-to-moderate elevation	Mild metabolic risk	Serial testing required	Probable
08	Poorly documented exposure	Not available	Not available	Mild nonspecific abnormality	Multiple alternative causes	No reliable dechallenge	Uncertain
09	Open handling and repeated exposure	Elevated, end-shift	Elevated, end-week	Moderate hepatocellular pattern	Alternatives largely excluded	Biochemical improvement after removal	Highly probable
10	Moderate production exposure	Negative /inconclusive	Negative/inconclusive	Persistent mild ALT/ GGT elevation	Obesity, diabetes, fatty liver	No clear dechallenge	Possible

Data-Collection Checklist and Illustrative Case Data for Dimethylformamide Exposure Assessment

Imaginary training outputs – not actual patient outcomes. This appendix is included as an example of how to report occupational exposure to dimethylformamide (DMF). Any clinical interpretation and work decisions should be based on accurate patient information, regulations applicable within the workplace and on evaluation by qualified occupational-health professionals.

1. Participant and Employment Information

Variable	Recorded information
Case identification number	DMF-2026-001
Date of assessment	15 October 2026
Age	34 Years
Sex	Male
Department	Chemical Process Operator, Synthetic Leather Coating Unit
Main DMF-related tasks	Mixing, transfer, coating-machine operation, and cleaning of DMF-containing solutions
Duration in current role	4 years
Typical shift	8-hour day shift, 08:00–16:00, 6 days/week
DMF-related work duration	Approximately 5–6 hours per shift, 5–6 days/week

2. Medical and Lifestyle Information

Variable	Recorded information
Previous liver disease or abnormal liver tests	No
Relevant medical conditions	No known chronic medical condition
Prescribed medications	None
Non-prescription medicines	Occasional paracetamol use; no herbal products reported
Alcohol intake	Approximately 1–2 drinks/week
Smoking/vaping status	Non-smoker; no vaping history
Recent illness or other hepatotoxic exposures	None reported

3. Workplace Exposure Characterization

Variable	Recorded information
Assessment date and shift	14 October 2026, day shift, 08:00–16:00
Work activity	Routine mixing, transfer, coating operation, and equipment cleaning
Estimated DMF handling duration	Approximately 5 hours
Potential exposure routes	Inhalation and dermal contact
Exposure event	Minor splash during manual transfer of DMF-containing coating solution
Event description	A small volume contacted the left glove and forearm area at approximately 13:30; glove replacement occurred approximately 20 minutes later
Engineering controls	General ventilation and local exhaust ventilation near the mixing area
Respiratory protection	Half-face respirator with organic-vapor cartridges
Gloves	Nitrile gloves; changed once per shift and after visible contamination
Other PPE	Chemical-resistant apron, safety goggles, and long-sleeved workwear
Glove breakthrough	Possible glove contamination; no visible skin irritation
Coworkers with similar symptoms	No

4. Clinical Assessment

Variable	Recorded information
Symptom onset	14 October 2026, approximately 17:30
Reported symptoms	Mild headache, fatigue, nausea, and reduced appetite
Severity and duration	Mild; symptoms persisted for approximately 24 hours
Physical examination	No jaundice; mild upper abdominal discomfort; vital signs within normal limits
Occupational-health assessment	Suspected low-to-moderate occupational DMF exposure; biological monitoring and liver-function testing requested

Emergency referral	No
Initial management	Temporary removal from DMF-related duties, hydration advice, symptom monitoring, and follow-up testing

5. Biological Monitoring and Clinical Laboratory Results

Collection date/time	Relative timing	Specimen/test	Result	Unit	Laboratory reference interval	Comment
15 Oct 2026, 07:40	Pre-shift	Urinary NMF	8.2	mg/g	Laboratory-specific	Collected before shift
15 Oct 2026, 16:20	Post-shift	Urinary NMF	24.6	mg/g creatinine	Laboratory-specific	Collected shortly after shift
16 Oct 2026, 08:00	Follow-up	Urinary AMCC	32.1	mg/g creatinine	Laboratory-specific	Approximately 16 hours after shift
22 Oct 2026, 08:10	Follow-up	Urinary NMF	4.1	mg/g creatinine	Laboratory-specific	After 7 days without DMF duties
22 Oct 2026, 08:10	Follow-up	Urinary AMCC	7.8	mg/g creatinine	Laboratory-specific	Declining concentration after cessation
15 Oct 2026	Baseline	ALT	58	U/L	7–56 U/L	Mild elevation
15 Oct 2026	Baseline	AST	42	U/L	10–40 U/L	Mild elevation
15 Oct 2026	Baseline	GGT	71	U/L	9–48 U/L	Elevated
15 Oct 2026	Baseline	ALP	96	U/L	44–147 U/L	Within reference interval
15 Oct 2026	Baseline	Total bilirubin	0.8	mg/dL	0.2–1.2 mg/dL	Within reference interval
15 Oct 2026	Baseline	Direct bilirubin	0.2	mg/dL	0.0–0.3 mg/dL	Within reference interval
15 Oct 2026	Baseline	INR	1.0	Ratio	0.8–1.2	Within reference interval
15 Oct 2026	Baseline	Serum creatinine	0.9	mg/dL	0.7–1.3 mg/dL	Within reference interval
22 Oct 2026	Follow-up	ALT	34	U/L	7–56 U/L	Returned to reference interval
22 Oct 2026	Follow-up	AST	28	U/L	10–40 U/L	Returned to reference interval
22 Oct 2026	Follow-up	GGT	49	U/L	9–48 U/L	Near reference interval

The activity specifications for collecting and submitting of specimens: Spot urine samples collected. Urine creatinine concentration was 112 mg/dL, and urinary biomarker results were creatinine corrected. Post-shift NMF sample taken was taken about 20 minutes after the last observed DMF exposure. The worker was switched from DMF to other work following post-shift sampling.

Interpretation note: Urinary NMF & AMCC are frequently used biomarkers of occupational DMF exposure. The general rule is that NMF tends to be representative of more recent exposures, whereas AMCC can take a longer time to detect and could be useful for assessing exposure over a longer time frame. Biomarkers should be considered together with the sampling time, work-shift pattern, dermal exposure potential, laboratory analytical method, creatinine correction, and the national biological exposure guidance values for that exposure. In this fictional case, mild elevations of ALT, AST, and GGT were found and temporally linked to suspected DMF exposure and resolved with withdrawal from exposure, but this does not prove causation. Clinically, other causes of liver injury should be sought.

6. Assessment of Alternative Causes of Liver Injury

Assessment domain	Finding
Viral hepatitis evaluation	Hepatitis B surface antigen and hepatitis C antibody negative
Alcohol-related liver disease	No evidence of heavy alcohol consumption
Medication & supplement-related hepatotoxicity	No regular hepatotoxic medicine, supplement, or herbal-product use reported
Metabolic liver-disease risk	Body mass index: 24.8 kg/m^2; no diabetes or known dyslipidemia
Autoimmune liver-disease assessment	Not performed; not clinically indicated after laboratory improvement
Specialist assessment	Not required at initial evaluation
Other occupational or non-occupational hepatotoxic exposures	None identified

B7. Exposure-Control and Follow-up Measures

Variable	Recorded information
Immediate response	Contaminated glove removed; forearm washed with soap and water; incident reported to supervisor
Work restriction	Temporary reassignment to packaging and documentation tasks for 7 days
Incident investigation	Completed
Corrective actions	Local exhaust ventilation review, strengthened closed-transfer procedure, glove-compatibility review, mandatory glove replacement after contamination, and PPE refresher training
Follow-up appointment	22 October 2026
Follow-up biomonitoring	22 October 2026
Follow-up liver-function testing	22 October 2026
Clinical outcome	Symptoms resolved; liver enzyme concentrations improved after removal from DMF-related work
Return-to-work decision	Returned to DMF-related work with enhanced exposure-control measures
Reviewer	Occupational Health Physician, MD

8. Abbreviations

Abbreviation	Full term
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
AMCC	N-acetyl-S-(N-methylcarbamoyl)cysteine
AST	Aspartate aminotransferase
DMF	Dimethylformamide

GGT	Gamma-glutamyl transferase
INR	International normalized ratio
NMF	N-methylformamide
PPE	Personal protective equipment

9. References

1. International Agency for Research on Cancer. N,N-Dimethylformamide. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Lyon: International Agency for Research on Cancer; 1999.

2. National Institute for Occupational Safety and Health. NIOSH pocket guide to chemical hazards: Dimethylformamide. Atlanta (GA): Centers for Disease Control and Prevention; 2024. Available from: https://www.cdc.gov/niosh/npg/

3. Occupational Safety and Health Administration. Dimethylformamide: safety and health topics. Washington (DC): United States Department of Labor; 2024. Available from: https://www.osha.gov/

4. European Chemicals Agency. N,N-Dimethylformamide: substance information. Helsinki: European Chemicals Agency; 2024. Available from: https://echa.europa.eu/substance-information

5. American Conference of Governmental Industrial Hygienists. 2024 TLVs and BEIs: threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati (OH): ACGIH; 2024.

6. International Labour Organization. International chemical safety card: N,N-dimethylformamide (ICSC 0457). Geneva: International Labour Organization; 2024. Available from: https://chemicalsafety.ilo.org/dyn/icsc/

7. World Health Organization. Environmental health criteria 114: Dimethylformamide. Geneva: World Health Organization; 1991.

Bangladesh Labour Law and Occupational Safety Compliance

This study is conducted to evaluate the occupational safety compliance of a synthetic-leather manufacturing factory outside of an Export Processing Zone (EPZ) in Savar District of industrial area, Bangladesh. The general labor law and occupational-safety framework of non-EPZ industrial establishments such as Bangladesh Labour Act, 2006 (amended), Bangladesh Labour Rules, 2015 (amended) and relevant government inspectors and occupational health provisions were taken into account.

Data collecting and clinical or biological evaluation was conducted only with ten workers at the factory, which hired many workers for similar or related manufacturing processes. This group of participants was not the entire workforce, but a sample. Thus the results should not be considered as representative of the level of exposure or health effects among all workers in a factory but rather as a site-specific indicator of occupational-health and safety related problems for the workers being assessed.

Data gathered from the ten participants on demographics, work tasks, length of exposure, hours worked, reported symptoms, personal protective equipment (PPE), workplace ventilation, chemical handling, and documentation of workplace records, as well as clinical or biological findings, were utilized in the assessment. It was more specific to the potential for exposure to N,N-dimethylformamide (DMF), a solvent used in the manufacture of some synthetic leathers and which can be inhaled or absorbed through the skin.

The general labour-law regime in Bangladesh requires the employer to take reasonable steps to ensure the health and safety of the employees. Where solvents are used, these measures could involve identifying hazardous chemicals, setting up safe handling procedures, controlling skin exposure and vapours, ensuring that adequate ventilation is provided, ensuring that suitable PPE is provided, training staff, keeping relevant records and reacting appropriately to any reported symptoms and/or suspected chemical exposure.

Chemical identification and hazard communication were evaluated in the ten participants' account and workplace information. Prevention of DMF exposure involves identification of DMF containing products, keeping a current chemical inventory, providing product labels and Safety Data Sheets, and communicating the chemical risks to workers in an understandable format. The knowledge participants have of the chemicals they were dealing with, the health risks, and safety information available is thus pertinent to the assessment. These responses, however, do not give an idea of the degree of awareness among workers not part of the study.

Exposure controls for the various tasks including solvent mixing, coating, transfer, cleaning, drying, and handling synthetic-leather materials were also taken into account. The inhalation exposure reduction measures of importance include general ventilation, local exhaust ventilation, process enclosure and maintenance practice, as well as safe handling practice and appropriate protective equipment in order to reduce skin exposure. If any of the 10 participants report strong solvent odours, problems with air movement, sight of solvent vapours, enclosed work area or ongoing problems with symptoms, there may be a concern for control that needs to be investigated. Such observations would be a statement about the assessed workers, not a statement about the condition of all employees or work areas.

PPE provision is not sufficient evidence of effective protection. Chemical protective clothing, gloves and masks or respirators, where applicable, must be suitable for the chemicals being used, be properly fitted, be maintained and replaced, and be supplemented by appropriate practical training. The assessment should therefore include what the 10 participants said or what was observed by the researchers, and differentiate it from information that the researcher did not gather with the rest of the workforce.

The clinical and biological results (such as alanine aminotransferase (ALT), aspartate aminotransferase (AST) and urinary N-methylformamide (NMF) if measured) should be taken with caution. Ten workers are not enough to determine the frequency of abnormal findings in the factory and to prove that DMF produced the liver abnormality for an individual worker. Each worker's task and exposure history, employment time, and other relevant medical factors should be taken into consideration when interpreting. These findings could, however, signal the need for further medical or exposure evaluation or occupational-health surveillance.

Many other workers reportedly have been engaged in this type of work, so results obtained from the 10 participants may warrant a broader investigation of chemical controls, ventilation, PPE, training, medical surveillance, and recordkeeping. The identified concerns would need to be reviewed to ascertain if other workers or departments are facing similar concerns.

Compliance Findings Matrix

Compliance area	**Evidence collected from the 10 participants**	**Significance and limitation**
Factory location and legal framework	Factory location and non-EPZ status	dentifies the general framework considered; legal applicability should be verified against current law

Chemical identification	Participant awareness, product labels, chemical inventory, and Safety Data Sheets, where assessed	Indicates hazard-communication issues among assessed workers; does not establish workforce-wide awareness
Exposure profile	Tasks, working hours, employment duration, solvent handling, symptoms, and observations	Helps characterize potential exposure among the sample
Training	Training records, language, worker knowledge, and reporting procedures, where assessed	Indicates whether participants received and understood safety information
Medical surveillance	ALT, AST, urinary NMF, referrals, repeat testing, and health-record access, where available	Supports assessment of the participants' health findings; does not estimate prevalence among all workers
Symptoms and incident response	Participants' reports of symptoms, spills, complaints, and management response	May identify issues for follow-up; reports are limited to the sample
Recordkeeping	Chemical, ventilation, PPE, training, exposure, and medical records, where reviewed	Helps assess available documentation and identify gaps
Engineering controls	Ventilation, local exhaust, enclosure, and maintenance information, where available	May identify control concerns requiring a broader workplace assessment
PPE	Reported or observed equipment, condition, availability, and use	Assesses protection among participants; provision alone does not prove suitability or effectiveness

The results are preliminary and site specific, and based on a sample of ten workers. They can facilitate further investigation into the occupational health or regulatory aspects but results on the entire workforce will only be found after wider sampling and examination of factory records, work areas, and exposure control. Medical findings alone cannot be used as evidence for illness due to DMF unless there is a good clinical and occupational-exposure assessment.

Prevention, Medical Surveillance and Corrective Remedies for Occupational DMF Exposure.

Dimethylformamide (DMF) is a commonly used organic solvent in the manufacturing of synthetic-leather in mixing, transferring, coating, cleaning and maintenance processes. Occupational exposures can come from the inhalation of vapour and dermal absorption, particularly when handling items open, during spillages, from contaminated gloves, manual transfer and poor ventilation. Thus, the guides for prevention should be to eliminate or reduce the exposure at its source, then to implement engineering controls, then administrative controls, then personal protective equipment, then biological monitoring, and then medical follow-up.

There are several potential concerns that could be related to exposure in the present case set of 10 workers, including repeated manual handling, open processing, mixing and coating, cleaning and transferring, spills, wet gloves, potential for dermal contact, and poor ventilation. In several cases, urinary N-methylformamide (NMF) and/or N-acetyl-S-(N-methylcarbamoyl)cysteine (AMCC) levels were also elevated, in addition to liver-enzyme abnormalities. The findings are indicative and should not be considered as a diagnosis of liver disease related to DMF if laboratory results or sampling history are incomplete, or if differential diagnosis or follow-up data are unavailable.

Exposure to DMF is prevented.DMF Exposure is prevented.
The primary prevention strategy should be implemented in order of the hierarchy of controls. However, using PPE alone is not enough since DMF can be absorbed through skin and the gloves can be contaminated or can break down depending on the type of material, thickness, duration of contact and handling conditions.

First, the employer should keep an up-to-date list of all products containing DMF and have Safety Data Sheets (SDS) for every product. Labels, SOP, training materials and warning signs should be provided in a language that workers understand, including Bengali where applicable. Workers should be provided with information regarding DMF hazards, modes of absorption, signs of possible exposure, safe work practices, spill response, hygiene needs, and procedure for reporting incident/illness.

Engineering controls should be the main control measure. Where technically possible, mixing, transfer, coating and cleaning should be enclosed and/or closed transfer and pumping facility. Local exhaust ventilation should be provided at emission sources such as mixing vessels, coating machinery, transfer stations and cleaning areas. The ventilation system must be regularly inspected, maintained and performance-tested. Vapours produced during handling of equipment with an open area or during a spill may be controlled only by general ventilation.

Administrative controls should minimize the handling of the product and the length of time that it is handled. Written procedures should include safe procedures for transferring chemicals, cleaning up equipment, chemical spills, chemical waste disposal, and contaminated PPE removal. The use of manual pouring and decanting should be kept to a minimum. Work schedules can be changed to minimize the amount of time that individual workers are exposed to a high-risk task, but job rotation should never be a substitute for good engineering controls. Every spill incident, glove contamination incident, ventilation failure and worker symptoms should be recorded and investigated.

PPE needs to be provided, maintained and worn properly. Chemical-resistant gloves should be used for workers handling DMF; gloves should be of a suitable type and should be indicated by a record of compatibility testing with DMF not by a general type of glove. Gloves should be checked prior to use and changed if contaminated, damaged, used for a long period of time or if there is any concern that there is a puncture or that the gloves may be compromised. Aprons, long sleeved protective clothing, splash goggles and appropriate footwear should also be provided that will resist chemical effects. Respiratory protective equipment (RPE) may be necessary to supplement engineering controls where vapour exposures cannot be adequately controlled, and during emergency spill response situations; however, selection of the proper RPE, fit testing, training, cartridge change schedules, cleaning and maintenance are all vital.

The illustrative Case 01 highlights the importance of prompt response to dermal contamination. After having gloves and forearm area slightly splashed, the worker should immediately remove the contaminated gloves, wash affected skin with soap and water, report the incident, and get an occupational-health review. A delay in changing gloves, e.g., the estimated 20-minute delay as detailed in the illustrative record, might allow more time for possible dermal exposure.

What are medical surveillance and biological monitoring?Medical surveillance and biological monitoring are what?

Workers who are regularly engaged in tasks related to DMF, such as mixing, open transfer, coating, cleaning, maintenance, and spill response, should be medically monitored. The goal of surveillance is to identify exposures or potential exposures and to remove individuals from additional exposures (when needed) and to assess workplace controls. Should not be used as an exposure prevention substitute.

Individuals who are being considered for placement in DMF-related work should have an occupational history, history of previous liver

disease or alcohol consumption, use of medications or supplements, metabolic risk factors, abnormal liver test results in the past, and any potential non-occupational hepatotoxic exposures documented at time of baseline evaluation. Tests may be ordered as baseline such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), bilirubin, and others as indicated by the clinical situation.

Follow-up should be provided periodically based on the intensity and frequency of exposure, monitoring at the workplace, and medical advice. Employees who are performing high exposure activities may need more frequent evaluations than those who are doing low or intermittent exposure activities. Monitoring should involve assessment of symptoms, liver function and biological monitoring when clinically appropriate.

The urinary NMF and AMCC are frequently selected biomarkers for occupational exposure to DMF. Typically, NMF is indicative of relatively recent exposure, and is measured at the end of a shift or workday. Exposure may be detected over a longer time period and can be useful if collected on a post-exposure schedule that is appropriate. Interpretation depends on the consideration of sampling time, work pattern, dermal-exposure potential, creatinine correction, laboratory analytical method and applicable national / laboratory biological-exposure guidance values.

Before the shift urinary NMF was found to be 8.2 mathrm(mg/g) creatinine, and approximately 16 hours later, urinary AMCC was found to be 32.1 mathrm(mg/g) creatinine. The levels of NMF and AMCC after 7 days off DMF related activities were respectively 4.1 mathrm(mg/g) creatinine and 7.8 mathrm(mg/g) creatinine. This temporal decline is related to decreased exposures following work reassignment, but does not create a cause and effect relationship.

Results of liver functions in the illustrative case revealed mild elevation of ALT, AST, and GGT, but with normal bilirubin, ALP, and INR. Supportive temporal evidence of improvement following removal from DMF-related tasks must be used in conjunction with clinical assessment and reasonable exclusion of alternative causes to make a diagnosis of liver injury caused by DMF. Examples of these include viral hepatitis, alcoholic liver disease, hepatotoxicity due to medications and supplements, metabolic dysfunction-associated steatotic liver disease, autoimmune liver disease, biliary disease, and other occupational or non-occupational exposures.

Case-Based Medical Priorities

The 10-worker data set can be used to prioritize follow-up, and should be noted that several findings are not complete, pending, or preliminary.
Occupational-health review is warranted for cases 01, 03, 04, and 09, characterized by repeated or high intensity of exposure history, moderate-to-marked abnormalities of liver enzymes, and/or elevated or positive liver-biomarker results. The following tests should be performed again promptly on these workers: repeat liver function tests, biomonitoring, detailed assessment of exposure, alcohol and drug history, evaluation of viral hepatitis, specialist referral if indicated. The clinical evaluation should be conducted and the workplace exposure controls should be reviewed before the person is removed from DMF related work.

Serialization of liver-function tests, additional biological monitoring, exposure assessment for the specific tasks, and a review of chemical handling, ventilation, and glove use and cleaning may be needed for Cases 05, 06, and 07. However, temporary removal from the exposure may support an occupational contribution, with improvement interpreted in the context of other potential causes.

It is probably advisable to interpret results with caution for cases 02, 08 and 10 as exposure information or biomonitoring results are incomplete, unavailable, negative or inconclusive and metabolic conditions like obesity, diabetes or fatty liver can lead to ongoing liver-enzyme abnormalities. While these cases should be investigated medically and at work, the information available does not prove that DMF is responsible for liver abnormalities.

Corrective Actions and Remedies

If a spill, glove contamination, a failure in ventilation or a potential for exposure has occurred, immediate steps should include stopping or controlling the source of the exposure, removal of contaminated gloves or clothing, washing exposed skin, first aid as necessary, documentation of the event, and occupational-health assessment. Temporarily remove workers with any symptom, or clinically significant liver-test abnormality, from the task of handling DMF until medical clearance is obtained.Remove temporarily from handling of DMF until medical clearance is obtained for workers who develop symptoms or liver-test abnormalities that are clinically significant.
All reported incidents should be investigated to establish the cause of the incident. Exposure should be investigated to determine if it was caused by open handling, poor ventilation, lack of local exhaust capture, use of inappropriate glove material, failure to replace gloves promptly, poor training, lack of closed transfer equipment, inadequate supervision, or failure to follow established guidelines. The corrective actions should involve improvements like: closed transfer systems, local exhaust ventilation audit, re-evaluate glove compatibility, replace gloves when they are contaminated, improve spill response, refresh training, and strengthening supervision.

The workplace should also have a confidential process, without retaliation, for employees to report if they have been exposed to chemicals, if they have symptoms that they believe may be caused by chemicals, if there has been a chemical spill, if their PPE is damaged, or if they have ventilation issues. Any medical information that is provided must be kept confidential and be handled by qualified occupational-health staff. Chemical inventory, SDSs, training attendance, PPE distribution and glove specifications, ventilation maintenance, workplace air monitoring, biological monitoring, incident reports, and medical surveillance outcomes should be recorded.

When a worker has been diagnosed by a competent clinician as having a work-related illness the employer must ensure that he/she has access to suitable treatment, follow up, safe work re-assignment, work rehabilitation and any compensation mechanisms provided for by the relevant labour and occupational health legislation. Claims should not be based on survey information only, but also on verified clinical information, on evidence of exposure, on employment records and on assessment based on the relevant law.

Interpretation and Study Limitation

This assessment is for a 10-worker case table and one detailed illustrative DMF exposure record. Novel terms like “partial,” “pending,” “expected improvement,” “possible,” and “highly probable” are included in some case classes, and should not be considered final diagnoses without supporting original laboratory reports, clinical records, complete exposure history, and ruling out reasonable alternative diagnoses.

Based on the findings, therefore, there is reason for concern regarding occupational-health issues that are amenable to workplace inspection and exposure evaluation, as well as prevention measures and workplace medical surveillance. They also cannot determine if the level of DMF exposure is high or low, or if liver damage is common or uncommon, or if liver damage is a problem in the factory, or if people are not legally compliant.

Limitations

There are some important limitations associated with this assessment. First, the dataset is limited to 10 workers, and therefore does not reflect the prevalence, severity or distribution of DMF exposure or liver abnormalities in the broader worker population. The results should be viewed as occupational-health issues within individual cases, and not as a measure of the risk in a factory.

Secondly, the information on exposure in some cases was incomplete, and was based in part on job descriptions, reported work practices or early classification of exposure as partial, pending, uncertain or inconclusive. There was no personal air monitoring, task-based exposure assessment, DMF concentration measurement in the workplace air, nor was there a complete dermal-exposure assessment conducted. The true level of exposure, the length of time exposed and the path of exposure thus could not be reliably estimated.

Conclusion

According to this case-based assessment, workers who work with dimethylformamide (DMF) could be exposed to preventable occupational health hazards by breathing it or by absorbing it into their skin. Some of these sources of exposure may be higher if: workers are exposed to chemicals during open transfer, mixing, coating, cleaning, spill handling, there is inadequate ventilation, damaged or contaminated gloves, or inadequate worker training. For selected workers, abnormal urinary DMF metabolites and liver-function tests increase the risk of an occupational contribution to liver injury. The small number of cases, incomplete exposure history and non-specific nature of liver-enzymes abnormalities however, prevents the diagnosis of liver disease caused by DMF in all workers who use the product without additional clinical and work exposure evaluation.

According to the Bangladesh Labour Act, 2006 (amended), and the Bangladesh Labour Rules, 2015, employers are legally obliged to ensure the health, safety and welfare of their employees. This should encompass the identification of chemical hazards, the provision of safety information and hazard communication, adequate provision of ventilation, minimisation of open handling of solvents, provision of appropriate PPE, creation of training, investigation of chemical incidents and spills, and maintaining OH&S records in the workplace where DMF is being employed. Employers should not assume that masks or respirators are sufficient, and should offer chemically compatible gloves, protective clothing, washing facilities, or an eyewash or shower if required, as well as ensuring that PPE is promptly replaced when it is contaminated.

Employers should establish a medical-surveillance programme for employees working with DMF. This programme must involve pre-employment health assessment, periodic liver-function tests, appropriate timing of biological monitoring (e.g. urinary N-methylformamide (NMF) and N-acetyl-S-(N-methylcarbamoyl)cysteine (AMCC)), confidential clinical review, and temporary cessation of exposure, where medically appropriate. Employees should not be afraid to make any complaints about symptoms, spills, damaged ventilation, or issues with PPE. In the event of clinically supported illness the worker is to be provided with treatment, safe reassignment, rehabilitation, and consideration for compensation or other legal remedies, as may be provided by the provisions of the labour and social-protection laws in Bangladesh.

Pharmacists can be a key player in the detection and alleviation of potential liver toxicity which may result from DMF. Pharmacists should make sure that the medicines that are prescribed, any over-the-counter medicines, herbal medicines, supplements, alcohol use and other potential hepatotoxic exposures are reviewed in hospital, community and occupational health settings. This is important as medicines like high dose Paracetamol, Anti-Tuberculous drugs, some Antibiotics, Antiepileptic medicines & some Herbal medicines can cause or exacerbate liver damage and can also cause abnormal blood tests of ALT, AST or GGT which may be confused as liver damage. Pharmacists should advise employees to not self-medicate, particularly taking unnecessary pain killers/antibiotics/herbal products as this can lead to back up in the medical system; and should direct workers to seek medical evaluation immediately if symptoms such as unexplained/fatigue, nausea, abdominal pain, dark urine, loss of appetite or jaundice develop.

In general, the prevention of DMF-related disease in Bangladesh demands a coordinated effort with the involvement of the employers, workers, pharmacists, physicians, industrial hygienists, factory inspectors and regulatory bodies. Implementing Bangladesh labour-safety regulations, improved engineering controls, dermal-protection measures, worker education in easily understood language, biological monitoring that is reliable, and pharmacy-led medication review can help prevent exposures and aid in early detection of liver-related health issues.

Third, not all workers had results for urinary N-methylformamide (NMF) or N-acetyl-S-(N-methylcarbamoyl)cysteine (AMCC) testing. Biomarker results were reported with some laboratories not providing details of the analytical method used, quality-control procedures, biological exposure reference values, urine dilution details or the exact timing of urine collection. It can only be compared within a worker group, since the concentrations of NMF and AMCC are highly dependent on sample timing, recent work activities, dermal contact and creatinine correction.

Fourth, liver-function abnormalities are non-specific. Many factors other than occupational exposure to DMF can lead to elevated levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and/or gamma-glutamyl transferase (GGT). Other possible alternative explanations are metabolic dysfunction-associated steatotic liver disease, obesity, diabetes, alcohol consumption, viral hepatitis, use of drugs or supplements, autoimmune liver disease, biliary disease and other occupational or environmental hepatotoxic exposures. While some case records showed that the selected alternative causes were not present or not as likely, full diagnostic workup was not performed in all cases.

Fifth, temporary improvement following temporary discontinuance of DMF related activities can support an occupational contribution but will not establish causation in and of itself. It is possible that over time liver enzymes and urinary biomarkers may become lower for reasons other than workplace reassignment, for example, due to diet changes, alcohol, medications, recovery from illness, or normal biological variation. Re-exposure test was not done or recommended as it would be an unnecessary health risk.

Sixth, the detailed information provided for case 01 was made clear to be illustrative training data, and not verified clinical information from any specific patient. Thus, data on its exposure history, biomonitoring data, liver-test values, and apparent improvement following reassignment should not be viewed as evidence of disease or used with the other cases to establish disease frequency or exposure-response relationships.

Lastly, there is a lack of a comparison group of unexposed, long-term follow-up, universal clinical examination for all participants, and independent workplace hygiene inspection. These restrictions make it impossible to draw any definitive statements of cause, dose-response relationships, legal liability or the percentage of liver abnormalities caused by DMF exposure. However, the patterns found warrant further investigation using the appropriate biological monitoring, personal air sampling, dermal exposure assessment, clinical follow-up, and/or improved workplace exposure control.

References

[1] Redlich CA, Beckett WS, Sparer J, et al. Liver disease associated with occupational exposure to the solvent dimethylformamide. Annals of Internal Medicine. 1988;108(5):680–686. doi:10.7326/0003-4819-108-5-680.

[2] European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Drug-induced liver injury. Journal of Hepatology. 2019;70(6):1222–1261. doi:10.1016/j.jhep.2019.02.014.

[3] Fontana RJ, Liou I, Reuben A, et al. AASLD practice guidance on drug, herbal, and dietary supplement–induced liver injury. Hepatology. 2023;77(3):1036–1065. doi:10.1002/hep.32689.

[4] Chalasani NP, Maddur H, Russo MW, Wong RJ, Reddy KR. ACG Clinical Guideline: Diagnosis and management of idiosyncratic drug-induced liver injury. American Journal of Gastroenterology. 2021;116(5):878–898. doi:10.14309/ajg.0000000000001259.

[5] Chalasani NP, Hayashi PH, Bonkovsky HL, et al. ACG Clinical Guideline: The diagnosis and management of idiosyncratic drug-induced liver injury. American Journal of Gastroenterology. 2014;109(7):950–966. doi:10.1038/ajg.2014.131.

[6] Hoofnagle JH, Björnsson ES. Drug-induced liver injury—types and phenotypes. New England Journal of Medicine. 2019;381(3):264–273. doi:10.1056/NEJMra1816149.

[7] Danan G, Benichou C. Causality assessment of adverse reactions to drugs—I. A novel method based on the conclusions of international consensus meetings: Application to drug-induced liver injuries. Journal of Clinical Epidemiology. 1993;46(11):1323–1330. doi:10.1016/0895-4356(93)90101-6.

[8] Danan G, Teschke R. RUCAM in drug and herb induced liver injury: The update. International Journal of Molecular Sciences. 2016;17(1):14. doi:10.3390/ijms17010014.

[9] Lee WM. Drug-induced hepatotoxicity. New England Journal of Medicine. 2003;349(5):474–485. doi:10.1056/NEJMra021844.

[10] Ostapowicz G, Fontana RJ, Schiødt FV, et al. Results of a prospective study of acute liver failure at 17 tertiary care centers in the United States. Annals of Internal Medicine. 2002;137(12):947–954. doi:10.7326/0003-4819-137-12-200212170-00007.

[11] Saillenfait AM, Sabaté JP, Gallissot F. Dimethylformamide-induced liver damage in workers: A review of the literature. Toxicology. 1997;123(1–2):1–15. doi:10.1016/S0300-483X(97)00105-1.

[12] Kawai T, Zhang ZW, Takeuchi A, et al. Methylformamide and N-acetyl-S-(N-methylcarbamoyl)cysteine in urine as biological markers of occupational exposure to dimethylformamide. International Archives of Occupational and Environmental Health. 1992;63(7):451–456. doi:10.1007/BF00379081.

[13] Chang HY, Wang JD, Yang CS, et al. Dimethylformamide exposure and liver function among synthetic-leather workers. Journal of Occupational and Environmental Medicine. 2004;46(11):1177–1183. doi:10.1097/01.jom.0000145418.19389.aa.

[14] Wu TN, Yang GY, Shih TS, et al. Liver damage and occupational exposure to dimethylformamide. Scandinavian Journal of Work, Environment & Health. 1994;20(6):407–412. doi:10.5271/sjweh.1388.

[15] Dimethylformamide-induced liver damage among synthetic leather workers. Archives of Environmental Health. 1991;46(3):161–166. doi:10.1080/00039896.1991.9937444.

[16] Chivers T, et al. Abnormal liver function associated with occupational exposure to dimethylformamide and glutathione S-transferase polymorphisms. Biomarkers. 2005;10(6):464–474. doi:10.1080/13547500500333648.

[17] The potential health risks of N,N-dimethylformamide: An updated review. Journal of Applied Toxicology. 2024. PubMed record available at: https://pubmed.ncbi.nlm.nih.gov/38339870/

[18] Human Biomoitoring Initiative (HBM4EU): Human Biomonitoring Guidance Values Derived for Dimethylformamide. 2022. PubMed record available at: https://pubmed.ncbi.nlm.nih.gov/35736906/

[19] Occupational Safety and Health Administration. Dimethylformamide: Safety and Health Topics. United States Department of Labor. Available at: https://www.osha.gov/chemicaldata/

[20] National Institute for Occupational Safety and Health. Dimethylformamide. NIOSH Pocket Guide to Chemical Hazards. Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/niosh/npg/

[21] International Agency for Research on Cancer. Dimethylformamide. In: IARC Monographs on the Identification of Carcinogenic Hazards to Humans, Volume 115: Some Industrial Chemicals. Lyon: IARC; 2018. Available at: https://monographs.iarc.who.int/

[22] American Conference of Governmental Industrial Hygienists. 2024 TLVs and BEIs: Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH: ACGIH; 2024.

[23] European Chemicals Agency. Dimethylformamide: Substance Information and Harmonised Classification and Labelling. Helsinki: ECHA. Available at: https://echa.europa.eu/substance-information

[24] International Labour Organization. Safety in the Use of Chemicals at Work: Code of Practice. Geneva: ILO; 1993. Available at: https://www.ilo.org/

[25] International Labour Organization. Occupational Safety and Health Convention, 1981 (No. 155). Geneva: ILO; 1981. Available at: https://normlex.ilo.org/

[26] International Labour Organization. Chemicals Convention, 1990 (No. 170). Geneva: ILO; 1990. Available at: https://normlex.ilo.org/

[27] Teschke R, Eickhoff A. The role of causality assessment in drug-induced liver injury. International Journal of Molecular Sciences. 2015;16(6):13078–13106. doi:10.3390/ijms160613078.

[28] Björnsson ES. Hepatotoxicity by drugs: The most common implicated agents. International Journal of Molecular Sciences. 2016;17(2):224. doi:10.3390/ijms17020224.

[29] Andrade RJ, Chalasani N, Björnsson ES, et al. Drug-induced liver injury. Nature Reviews Disease Primers. 2019;5:58. doi:10.1038/s41572-019-0105-0.

[30] Navarro VJ, Lucena MI. Hepatotoxicity induced by herbal and dietary supplements. Seminars in Liver Disease. 2014;34(2):172–193. doi:10.1055/s-0034-1379303.

[31] World Health Organization. WHO Guidelines on the Pharmacological Treatment of Persisting Pain in Children with Medical Illnesses. Geneva: WHO; 2012.

[32] Government of the People's Republic of Bangladesh. The Constitution of the People's Republic of Bangladesh. Relevant Articles: 8(2), 15, 18, 20, 31 and 32. Available at: https://bdlaws.minlaw.gov.bd/

[33] Government of the People's Republic of Bangladesh. Bangladesh Labour Act, 2006 (Act No. XLII of 2006), as amended. Relevant provisions should be cited according to the current official version. Available at: https://bdlaws.minlaw.gov.bd/

[34] Government of the People's Republic of Bangladesh, Ministry of Labour and Employment. Bangladesh Labour Rules, 2015, as amended. Available at: https://mole.gov.bd/ এবং https://dife.gov.bd/

[35] Government of the People's Republic of Bangladesh. The Pharmacy Ordinance, 1976 (Ordinance No. XIII of 1976). Available at: https://bdlaws.minlaw.gov.bd/

[36] Bangladesh Labour Act, 2006, ch. VII, Section 79.