Mediterranean Journal of Pharmacy & Pharmaceutical Sciences
ISSN: 2789-1895 online
www.medjpps.com
doi: 10.5281/zenodo.21833611
ISSN: 2958-3101 print

ORIGINAL RESEARCH article

The impact of drug interactions on biochemical parameters in Libyan patients with diabetes and hyperlipidemia

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Received: 03-04-2026, **Accepted**: 01-08-2026, **Published online:** 07-08-2026

HOW TO CITE THIS

Abrika OSS, et al. The impact of drug interactions on biochemical parameters in Libyan patients with diabetes and hyperlipidemia. Mediterr J Pharm Pharm Sci. 2026; 6(3): 33-39. [Article number: 259]. https://doi.org/10.5281/zenodo.21833611

Keywords: Diabetes mellitus, drug-drug interactions, drug-related problems, hyperlipidemia, polypharmacy

Abstract: Polypharmacy, defined as the concurrent use of five or more medications, is highly prevalent among older adults because of the increasing burden of chronic diseases such as diabetes mellitus and hyperlipidemia. In these patients, polypharmacy may complicate disease management, mask clinical manifestations, alter biochemical parameters, and reduce medication adherence, ultimately compromising therapeutic outcomes. Drug-related problems, defined as events or circumstances involving drug therapy that interfere with desired health outcomes, are common in this population because of multiple comorbidities and inappropriate prescribing. This study evaluated the effects of diabetes mellitus, hyperlipidemia, and their coexistence, as well as potential drug-drug interactions, on selected biochemical parameters. Libyan patients were categorized into three groups: Diabetes mellitus, hyperlipidemia, and mixed (patients with both conditions). Fasting blood glucose and glycated hemoglobin levels were significantly higher in the diabetes group than in the hyperlipidemia and mixed groups. Lipid profile parameters were significantly elevated in the hyperlipidemia group compared with the other groups. Liver function tests and serum electrolyte levels remained within normal reference ranges, with no significant differences among the study groups. Within the mixed group, patients receiving insulin plus atorvastatin exhibited a modest but significant increase in total cholesterol and high-density lipoprotein cholesterol compared with those receiving metformin plus atorvastatin. In contrast, triglyceride and low-density lipoprotein cholesterol levels showed no significant differences. The present findings demonstrate distinct biochemical profiles among patients with diabetes mellitus, hyperlipidemia, and their coexistence, while suggesting that the evaluated drug combinations exert limited effects on lipid metabolism.

Introduction

Polypharmacy, commonly defined as the concurrent use of five or more medications, is highly prevalent among older adults due to the increasing burden of chronic diseases such as diabetes mellitus and hyperlipidemia [1, 2]. Age-related physiological changes affecting drug absorption, metabolism, and excretion increase the susceptibility of elderly patients to adverse drug reactions, drug-drug interactions, and other drug-related problems [3-6]. In patients with diabetes and dyslipidemia, polypharmacy can complicate disease management, obscure clinical symptoms, alter laboratory parameters, and reduce medication adherence, thereby compromising therapeutic outcomes [7-10]. Drug-related problems (DRPs), defined as events that

interfere with desired health outcomes, are particularly common in this population due to multiple comorbidities and inappropriate prescribing practices [5, 6, 11, 12]. Common DRPs include non-adherence, inappropriate dosing, unnecessary drug therapy, and adverse drug reactions, all of which can negatively affect glycemic control, lipid management, and cardiovascular outcomes [13-15]. Tools such as the Beers Criteria and STOPP/START guidelines have been developed to reduce potentially inappropriate medications and improve medication safety in older adults [16, 17]. Understanding drug interactions and their effects on biochemical parameters is essential for optimizing pharmacotherapy in elderly patients with diabetes and hyperlipidemia. Regular medication review and rational prescribing are therefore critical strategies to minimize DRPs, improve patient safety, and enhance overall clinical outcomes [18, 19]. The objective of this study is to assess how drug interactions affect key biochemical parameters in patients with diabetes and hyperlipidemia. Identify common drug combinations in diabetic and hyperlipidemic patients. Assess the frequency and types of potential drug interactions and to evaluate changes in key biochemical parameters related to drug interactions.

Materials and methods

This cross-sectional observational study was conducted in Sebha, southern Libya, from May 2024 to June 2025. A total of 450 Libyan patients aged 45 - 70 years were included. The patients were divided into three groups: Diabetes mellitus (DM), hyperlipidemia (H-lipid), and mixed (both conditions), with 150 participants in each. Data were obtained from the regional medical insurance system. Biochemical markers analyzed included serum electrolytes (Na^+, K^+, Ca^{2+}, and Cl^-), lipid profile (total cholesterol, triglycerides, HDL, and LDL), liver function (total bilirubin and alkaline phosphatase), and glycemic indicators (fasting blood sugar and glycated hemoglobin, HbA1c).

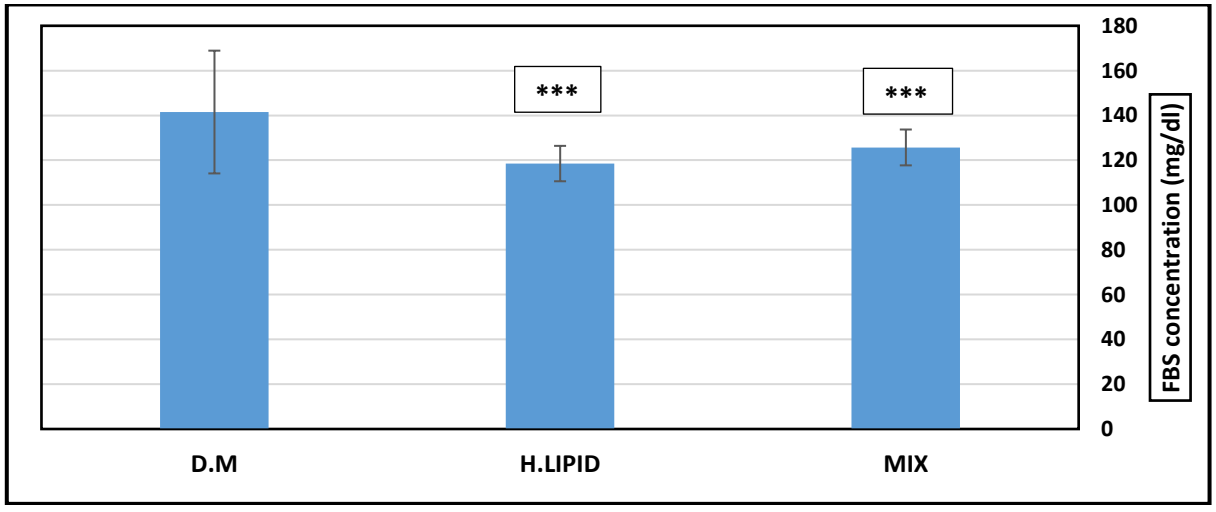
Ethical considerations: Personal data were anonymous, and no identifying or sensitive information was collected from the participants (022-MJ-2106-07).

Statistical analysis: Statistical comparisons among groups were performed using one-way analysis of variance (ANOVA), with significance set at $p < 0.05$.

Results

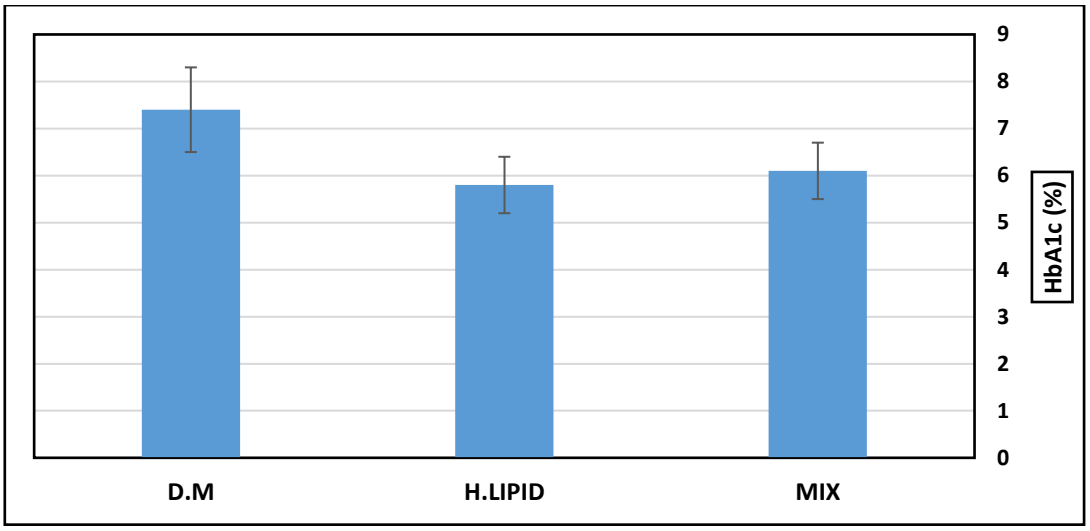
Fasting blood sugar (FBS) levels: The DM group had significantly higher mean FBS (141.5 ± 27.4 mg/dL) compared to the H. lipid (118.4 ± 7.9 mg/dL) and mixed groups (125.7 ± 8 mg/dL) ($p = 0.001$). No significant difference was observed between the H. lipid and mixed groups (**Figure 1**).

Figure 1: The average fasting blood sugar levels in the participants



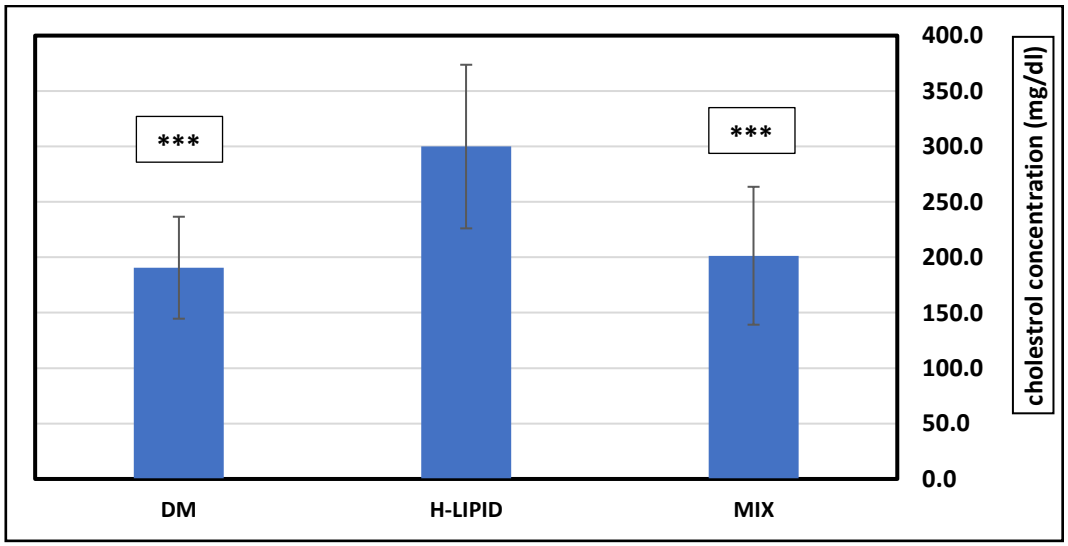
Concentration of glycosylated hemoglobin: The mean HbA1c was highest in the D.M. group (7.4 ± 0.9%), compared to the H. lipid (5.8 ± 0.6%) and mixed (6.1 ± 0.6%) groups. The increase in HbA1c in the DM group was statistically significant versus the H. lipid (p = 0.023) and mixed (p = 0.014) groups, while no significant difference was observed between the H. lipid and mixed groups, as illustrated in **Figure 2**.

Figure 2: The average glycosylated hemoglobin in the participants



Concentration of cholesterol: The mean cholesterol levels were 190.6 ± 46.0 mg/dL in the DM group, 299.9 ± 73.8 mg/dL in the H-lipid group, and 201.4 ± 62.2 mg/dL in the mix group. Total cholesterol was significantly higher in the H-lipid group compared to the DM and mix groups (p = 0.001), while no significant difference was observed between the DM and mix groups, as shown in **Figure 3**.

Figure 3: The average cholesterol concentration in the participants



Concentration of triglycerides: Triglyceride levels were highest in the H-lipid (173.0 ± 27.5 mg/dl) and mix (168.1 ± 12.4 mg/dl) groups compared to the DM group (125.2 ± 23.1 mg/dl). Significant differences were observed between the DM and H-lipid and mix groups (p = 0.001), whereas the H-lipid and mix groups did not differ significantly, as shown in **Figure 4**.

LDL-cholesterol concentration: The H-LIPID group had significantly higher LDL levels (171.8 ± 35.5 mg/dl) compared to the mixed group (121.3 ± 24.5 mg/dl) and the DM group (117.2 ± 29.3 mg/dl) (p = 0.001). No significant difference was observed between the DM and mixed groups (p = 0.828), as shown in **Figure 5**.

Figure 4: The average cholesterol concentration in the participants

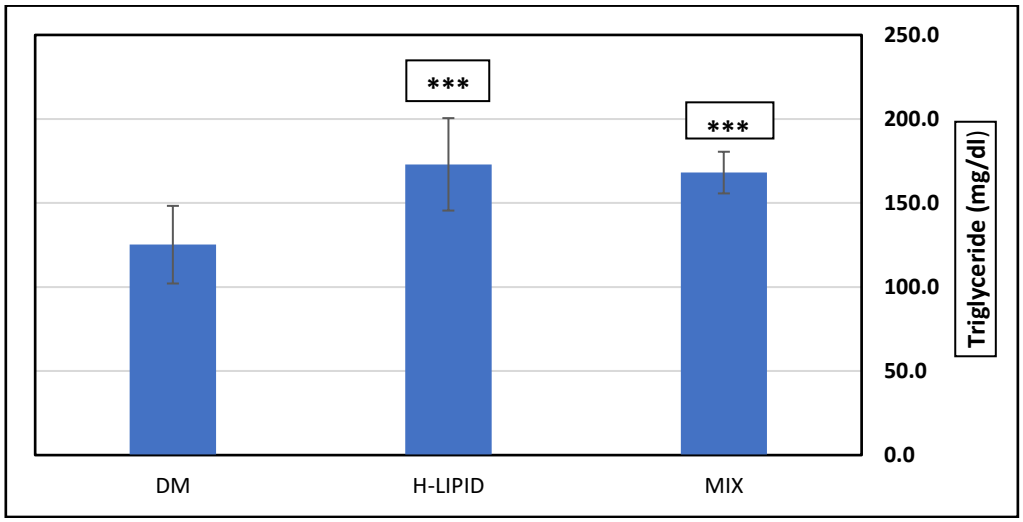
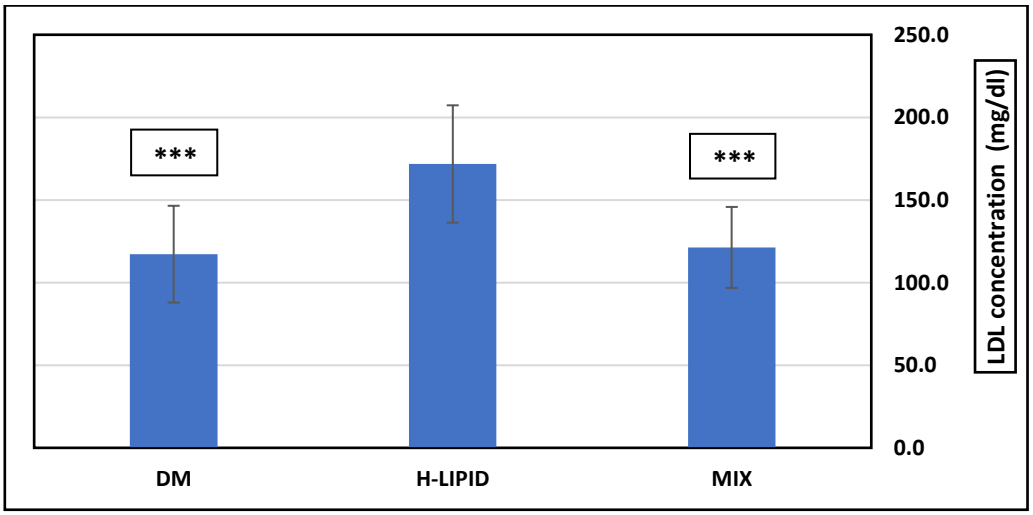
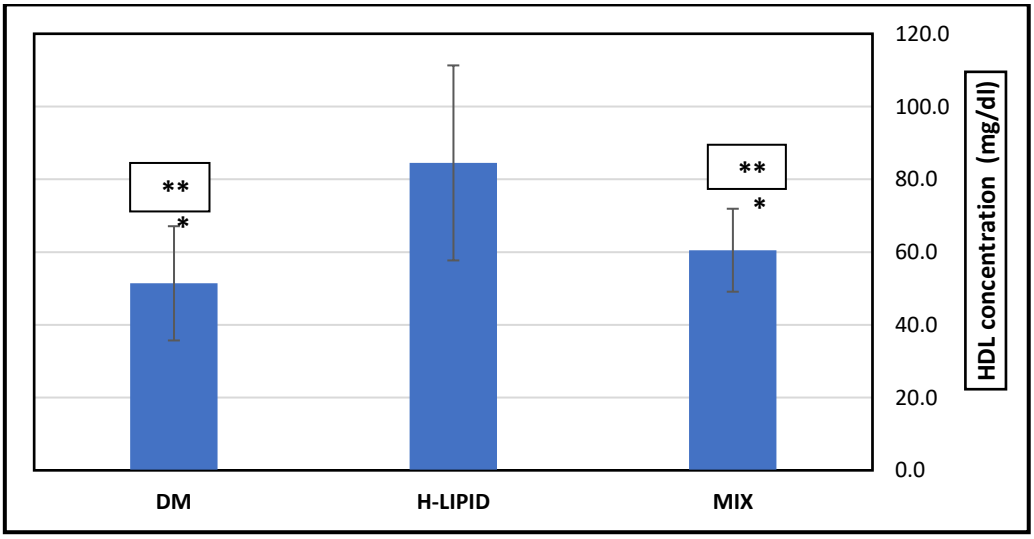


Figure 5: The average LDL-cholesterol concentration in the participants



Concentration of high-density lipoprotein (HDL): The mean HDL levels were 51.4 ± 15.7 mg/dL in the DM group, 84.5 ± 26.8 mg/dL in the H-lipid group, and 60.5 ± 11.4 mg/dL in the mixed group. HDL was significantly higher in the H-lipid group compared to the DM and mixed groups ($p = 0.001$), while no significant difference was observed between DM and mixed groups, as shown in **Figure 6**.

Figure 6: The average HDL-cholesterol concentration in participants



Total bilirubin concentration: The serum total bilirubin levels were similar across all groups: DM (1.56 ± 0.4 mg/dL), H-lipid (1.60 ± 0.4 mg/dL), and mixed (1.51 ± 0.6 mg/dL), with no significant differences observed.

Serum alkaline phosphatase concentration: The mean serum alkaline phosphatase levels were similar across all groups: DM (122 ± 29.9), H-LIPID (125 ± 13.6), and MIXED (124 ± 30.9). No statistically significant differences were observed between the groups, as shown in **Table 2**.

Table 2: Concentration of total bilirubin and alkaline phosphatase in the serum

Group	H-lipid	Diabetic	Mixed
T. Bilirubin	1.60 ± 0.4	1.56 ± 0.4 P = 0.21	1.51 ± 0.6 p = 0.93
Alkaline phosphatase	125 ± 13.6	122 ± 29.9 p = 0.53	124 ± 30.9 p = 0.76

Concentration of electrolytes in the serum: **Table 3** shows that serum electrolyte concentrations were within the normal range, with no significant differences observed among the groups (Na, K, Ca, and Cl).

Table 3: Concentration of electrolytes in the serum

Electrolyte	H-lipid	Diabetic	Mixed
Sodium	137.4 ± 5.6	133.8 ± 15.8	136.5 ± 8.2
Potassium	4.33 ± 0.61	4.32 ± 0.62	4.33 ± 0.61
Calcium	8.7 ± 0.46	8.8 ± 0.54	8.9 ± 0.58
Chloride	102.7 ± 2.5	103.1 ± 3.5	100.8 ± 5.9

Drug-drug interaction: The study evaluated drug-drug interactions in patients with diabetes and hyperlipidemia (mixed group, n = 150) receiving different treatments. Patients were divided into three subgroups: Insulin plus atorvastatin (n = 23), metformin plus atorvastatin (n = 121), and other drugs. Results showed a slight but significant increase in total cholesterol (p = 0.041) and HDL cholesterol in the insulin-treated group compared to the metformin-treated group. No significant differences were observed in triglycerides or LDL cholesterol between the groups, as shown in **Table 4**.

Table 4: Difference between the two groups in triglycerides and LDL cholesterol

Treatment	Atorvastatin/insulin N = 23	Atorvastatin/metformin N = 121	P value
Triglycerides	170.1 ± 10.6	166.4 ± 11.8	0.951
Cholesterol	204.3 ± 27.0	183.7 ± 31.0	0.041
HDL - cholesterol	65.1 ± 12.0	56.8 ± 18.0	0.037
LDL - cholesterol	124.6 ± 16.0	119.1 ± 23.0	0.253

Discussion

Metformin primarily lowers blood glucose by decreasing hepatic glucose production and enhancing insulin sensitivity, whereas statins (e.g., atorvastatin, simvastatin, rosuvastatin) primarily lower cholesterol but may slightly increase blood glucose and HbA1c due to minor effects on insulin sensitivity and pancreatic β-cell function [20]. Pharmacokinetically, statins and metformin do not significantly interact, as metformin is mainly renally excreted and statins are metabolized via the CYP450 system. However, pharmacodynamic interactions are possible, where the glucose-lowering effect of metformin can counteract the mild hyperglycemic effect of statins. In this study, FBS was significantly higher in the DM group than in the mixed (DM plus hyperlipidemia) or hyperlipidemia-only groups, while no significant difference was observed between the

mixed and hyperlipidemic groups. This suggests that metformin mitigates any minor glucose-raising effect of statins, supporting the relative safety of combination therapy in clinical practice. Similarly, glycosylated hemoglobin (HbA1c) levels were highest in the DM group (7.4 ± 0.9%), lower in the mixed group (6.1 ± 0.6%), and lowest in the hyperlipidemic group (5.8 ± 0.6%). The intermediate HbA1c in the mixed group likely reflects a balance between metformin's glucose-lowering effect and the modest hyperglycemic effect of statins. Previous studies support this: Statins may modestly increase HbA1c, but the cardiovascular benefits outweigh this small glycemic risk, especially when patients are on metformin [21-24]. Overall, our findings emphasize that combination therapy of metformin and statins is clinically safe regarding glycemic control in patients with diabetes and dyslipidemia.

Conclusion: This study highlights important variations in glycemic and lipid profiles among patient groups and indicates that the overall lipid profile in hyperlipidemia was elevated, particularly cholesterol and LDL, compared to the mixed group. This suggests a possible therapeutic interaction between the diabetes treatment and the lower lipid profile in the mixed group. Combined pharmacotherapy for diabetes and hyperlipidemia does not adversely affect liver function or electrolytes.

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Acknowledgements: The authors would like to express their sincere appreciation to the Fezzan Health Insurance Authority for its valuable assistance in data collection. The authors also extend their heartfelt gratitude to Wadi Alshaty University for providing the opportunity to conduct this research and for its continuous support throughout the study.
Authors' contributions: OSSA conceived and designed the study and performed data analysis. AMA collected the data. NMI contributed to data analysis. OSSA & NMI drafted the manuscript. All authors approved the final version of the manuscript and agreed to be accountable for its contents.
Conflict of interest: The authors declare the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Ethical issues: The authors have considered ethical issues, including plagiarism, informed consent, data fabrication or falsification, and double publication or submission.
Data availability statement: The raw data that support the findings of this article are available from the corresponding author upon reasonable request.
Generative AI disclosure: No Generative AI was used in the preparation of this manuscript.