



THERAPEUTIC INERTIA IN A PATIENT WITH CARDIOMETABOLIC MULTIMORBIDITY AT A MINISTRY OF HEALTH PRIMARY CARE CENTER IN AZ-ZARQA, JORDAN: A CASE REPORT

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ABSTRACT

Background: Primary care settings in Jordan are highly populated with patients suffering from Cardiometabolic Multimorbidity which is a package of three conditions namely type 2 diabetes mellitus (T2DM) with hypertension and with dyslipidemia, and poses a significant burden to the patient and health system. Adding hypothyroidism and depressive disorder to the mix, clinical complexity increases and treatment inertia becomes a real challenge in meeting guideline recommended targets.

Case Presentation: This report present the case of a 52-year-old Jordanian woman with a seven-year disease course of T2DM, hypertension and new onset of overt hypothyroidism (TSH of 18.4 mIU/L) and depressive disorder (PHQ-9 score 14) who presented to her regional Primary Care Center, Ministry of Health, Az-Zarqa with persistent glycemic dyscontrol (HbA1c 10.2%). These 3 visits were spread across 12 months and had all shown HbA1c levels >9%, without there being evidence for any antidiabetic intensification. This was a "paradigmatic" example of therapeutic inertia as it has been documented after all 3 visits. A systematic management plan which would include initiation of HRT, initiation of levothyroxine, adjustment of antihypertensive therapy, depression screening and adding empagliflozin for antidiabetic intensification.

Outcome: HbA1c at 6-month follow-up was 7.8, blood pressure 132/82, TSH was normalized at 2.1 mIU/L, and the PHQ-9 was reduced to 5 at 6-month follow-up. The case describe the clinical and therapeutic dilemmas presented by cardiometabolic multimorbidity in the primary care setting, and highlight the importance of the family medicine specialist in working as a team to address the multimorbidity patient.

Conclusion: The treatment of cardiometabolic multimorbidity, hypothyroidism and depression should follow a systematic approach tailored for the individual patient, specifically considering therapeutic inertia, polypharmacy and mental health risks. Separate chronic disease management approaches and knowledge of chronic disease specialists among family physicians in Jordan primary care centers are desperately needed.

Keywords: therapeutic inertia; type 2 diabetes mellitus; hypothyroidism; depressive disorder; cardiometabolic multimorbidity; polypharmacy; primary care; Jordan; Az-Zarqa

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1. BACKGROUND AND INTRODUCTION:

Cardiometabolic multimorbidity (CMM), which is co-occurrence of two or more cardiometabolic conditions including type 2 diabetes mellitus (T2DM), hypertension and dyslipidemia, marks one of the greatest challenges faced by the primary health care sector today and as a key burden in the Eastern Mediterranean Region (EMR). In Jordan, the prevalence of T2DM in 2019 was estimated at 17.1% among adults, and 32.3% for hypertension rate, both of which were managed mainly in the primary health care (PHC) of the Ministry of Health (MoH) centers [1] with a disproportionately high burden in Jordan. The second more populous governorate in Jordan, Az-Zarqa, has over one-million residents, among whom a significant percentage of Syrian refugees are, and experiences especially severe service challenges, with continued low ratio of PHC physicians to patients, which falls short of recommended levels [2,3].

Therapeutic inertia (TI) – “the tendency to not begin treatment or not doing more when treatment goals aren't reached” [4] – has been found to be a common challenge to reaching optimal care for chronic disease in primary care. TI is reported to increase up to 40–60% in the primary care setting in T2DM, and is seen to be complex and multi-faceted, involving clinician, patient and system factors [4,5]. In health systems in low and middle income countries (LMICs) like Jordan, some disadvantages at the system level seem to dominate through factors like short consultations, restricted access to lab investigations, high patient turnover and poor continuity of care [2,3].

Thyroid dysfunction and depressive disorder makes CMM more complex in the clinical setting. In patients with T2DM, 15–23% have an underlying hypothyroidism, and hypothyroidism amplifies glycemic disturbances in DM2 by worsening insulin resistance, causing a greater tendency to weight gain, and possibly erroneously raising HbA1c due to an increase in red blood cell lifespan. [6,7] At the same time, a bidirectional relationship between T2DM and major depressive disorder (MDD) has also been proven; having had clinical depression two years prior to T2DM diagnosis increases the risk of future T2DM by roughly 60%, and incident depression by roughly

15–20% increases the risk of subsequent T2DM [8,9]. Other mechanisms through which depression worsens glycemic self-management include decreased adherence, lack of physical activity and hypothalamic–pituitary–adrenal (HPA) axis dysfunction [9].

Even then, the overall assessment and management of T2DM–hypertension–hypothyroidism–depression tetrad in the Jordanian MoH PHC centers is still rare, and physicians often face tight time limits for consultations and a lack of mental health referral systems. As far as we are aware, this particular clinical setting, with detailed exploration of therapeutic inertia and risk of polypharmacy, within the Jordanian PHC setting, has not been reported previously in a case report. This case is intending to emphasize the difficulties encountered in the case and to call to make changes in the structure of chronic disease management in the PHC centers of MoH in Jordan.

2. CASE PRESENTATION:

2.1 Patient Information and Clinical History: In March 2024, a 52-year-old Jordanian female (the patient) visited Az-Zarqa Directorate of Health, Al-Rusayfah Primary Health Care Centre, for an appointment on follow-up. Since 2017, she had been under care at the center and had received T2DM (diagnosed in 2017 for 7 years at presentation) as well as hypertension (diagnosed in 2018). She was a housewife, further educated to secondary level, had four children, did not use tobacco. She had a family history of T2DM in her mother side, premature coronary artery disease in her father (myocardial infarction at age 58).

The patient at the time of the index visit presented with a four-month history of progressive fatigue, cold intolerance, and weight gain (about 6 kg over five months), constipation, and generalized thinning hair. She also reported that for the past 8 weeks she had been experiencing a persistent low mood, anhedonia, hopelessness, and sleep problems, symptoms she hadn't shared with a health care provider, because of social stigma. She complained of micturition that was intermittent, associated with a fever and that led to urination over a large volume, describing it as indicative of uncontrolled hyperglycemia. She denied

chest pain, dyspnoea, having any focal neurological deficits or lower limb oedema.

2.2 Medication History and Reconciliation: The patient's previous medication included the prescription(s): 1. Metformin 1000 mg twice daily; 2. Glibenclamide 5 mg twice daily; 3. Amlodipine Besylate 5 mg once a day and 4. Enalapril 10 mg once a day. A review of the longitudinal medical record showed that her three successive HbA1C level measurements (most non-elderly adults target < 7.0% [ADA] [10]) were respectively and successively 9.4% in March 2023, 9.7% in September 2023, and 10.2% at the present visit, during which no corresponding intensification/elaboration of her antidiabetic therapy was documented in the record. This is clear therapeutic inertia over a long period of time.

The following drug-related issues were identified at the index visit: (a) the patient had stopped her glibenclamide approximately 2 months back as she felt it made her 'recurrently' feel hungry; (b) she was taking ibuprofen 400 mg as needed (2-3 times per week) which she bought on her own as a headache pain reliever, but this was not documented in the MoH record, representing a clinically significant drug–drug interaction when combined with enalapril (decrease its

antihypertensive effect and increase the risk of nephrotoxicity); and (c) self-reported calcium carbonate 500 mg twice daily for 2 years (no documentation of this in the MoH record), which represents a clinically significant interaction with levothyroxine (absorption interaction).

2.3 Physical Examination Findings: General examination revealed that she is an overweight woman in no acute distress. The anthropometric measurements are described in detail in Table 1. Blood pressure was 158/96 mmHg (average of 2 readings taken 5 minutes apart, taken from right arm in a sitting position); the heart rate was 64 beats per minute (regular); the temperature was 36.8°C; and oxygen levels were 98% on room air. The thyroid appeared mildly enlarged with a smooth surface but not tender or with nodules or bruits. On examination, there were no scales and other non-scarring hair loss was evident. Neurological examination revealed stony dullness of bilateral deep tendon reflexes. At this visit, there was no fundoscopic examination and the patient had said her last eye examination was more than three years ago. Foot examination showed a diminished vibration sense at the great toe bilaterally, with monofilament sense was intact (10 g Semmes–Weinstein). Peripheral pulses were present, and were symmetrical (table 1).

Table 1. Anthropometric and Vital Signs at Index Presentation

Parameter	Value	Reference / Target
Age	52 years	—
Weight	84.0 kg	—
Height	161 cm	—
Body Mass Index (BMI)	32.4 kg/m ²	Normal: 18.5–24.9 kg/m ²
Waist circumference	97 cm	IDF: <80 cm (female)
Blood pressure	158/96 mmHg	Target: <130/80 mmHg (ADA 2024)
Heart rate	64 bpm	60–100 bpm

2.4 Investigations: At the index visit, routine laboratory tests were ordered, with the results coming within 48 hours and presented in Table 2. Urine albumin-to-creatinine ratio (UACR) was 47.3 mg/g (Stage A2 albuminuria, the early stage of diabetic nephropathy). On the electrocardiogram (ECG) normal sinus rhythm was seen, with no ischemic changes, left axis deviation and borderline voltage parameters of left ventricular hypertrophy. There was

no renal or hepatic dysfunction (eGFR was 72 mL/min/1.73 m², CKD G2 according to KDIGO classification for chronic kidney disease (CKD)). A raised LDL-C level was found at 4.1 mmol/L and TGs at 2.8 mmol/L features of hypothyroidism dyslipidemia.

Patient health questioner 9 (PHQ-9) was given in Arabic (validated Jordanian Arabic version): total score 14/27 which is consistent with moderate

depression. The patient endorsed items related to depressed mood, anhedonia, fatigue, sleep disturbance and concentration difficulties, and had a score of 1 for the item of self-harm (passive ideation). The average

answer for the Morisky Medication Adherence Scale (MMAS-8) was 4/8, which corresponds to medium–low adherence (table 2).

Table 2. Laboratory Investigations at Index Presentation and Six-Month Follow-Up

Investigation	Index (March 2024)	Visit (September 2024)	F/U Reference Range
HbA1c (%)	10.2	7.8	< 7.0 (ADA target)
Fasting plasma glucose (mmol/L)	12.7	7.4	< 7.0
TSH (mIU/L)	18.4	2.1	0.4–4.0
Free T4 (pmol/L)	8.2	14.6	12–22
Total cholesterol (mmol/L)	6.9	5.1	< 5.2
LDL-C (mmol/L)	4.1	2.3	< 1.8 (high-risk)
HDL-C (mmol/L)	0.9	1.1	> 1.2 (female)
Triglycerides (mmol/L)	2.8	1.6	< 1.7
Serum creatinine (µmol/L)	82	79	44–97
eGFR (mL/min/1.73 m ²)	72	75	≥ 60 (G1–G2)
UACR (mg/g)	47.3	29.1	< 30 (target)
Haemoglobin (g/dL)	11.8	12.9	12.0–16.0
Serum potassium (mmol/L)	4.1	4.3	3.5–5.0
Liver enzymes (ALT, U/L)	28	25	< 40
Blood pressure (mmHg)	158/96	132/82	< 130/80 (ADA)
PHQ-9 score	14	5	< 5 (remission)
MMAS-8 score	4/8	7/8	8 = high adherence

3. DIFFERENTIAL DIAGNOSIS AND DIAGNOSTIC REASONING:

The presenting symptom complex (fatigue - weight gain, cold intolerance, hair loss, constipation), led to the broad differential of: (1) worsening glycaemic control contributing to fatigue and lethargy, (2) depression as an independent contributor to fatigue and energy deficit; (3) uraemia (excluded by the normal creatinine and eGFR 72); and (5) iron-deficiency anaemia (prior significant iron-deficiency has been excluded by normal iron studies with elevated ferritin, and normal serum iron; and mild reduction in hemoglobin level at 11.8 g/dl, consistent with the normochromic normocytic anemia of hypothyroidism rather than iron-deficiency). Thyroid peroxidase (TPO) antibodies were then ordered and again returned quite high at 1,240 IU/mL, confirming Hashimoto's thyroiditis as the cause of hypothyroidism.

Depressive symptomatology needed to be distinguished from the hypothyroid associated mood changes, and from diabetes-specific distress. The

presence of the PHQ-9 score (14–moderate depression), independent history of anhedonia and hopelessness, and a positive family history of depression (mother's aunt) justified the diagnosis of co-existing major depression (DSM-5 criteria), rather than diagnosis of thyroid mediated mood disturbance. This was accompanied by a referral to the mental health liaison nurse working in PHC.

4. MANAGEMENT PLAN AND CLINICAL REASONING:

4.1 Antidiabetic Therapy Intensification:

Metformin 1000mg twice daily continued due to the presence of prolonged glycaemic dyscontrol (HbA1c 10.2%), type 2 diabetes duration 7 years, eGFR 72, albuminuria stage A2, high cardiovascular risk factors (hypertension and dyslipidemia) and a positive family history of premature CAD. The Glibenclamide was not resumed due to patient reported hypoglycaemic events and availability of more favorable agents in terms of safety and cardio-renal profiles. With SGLT-2 inhibitors having proven to have cardio-renal protective effects, they were initiated in line with the

2024 guidelines of the American Diabetes Association (ADA) for use in people with type 2 diabetes who have established cardiovascular risk factors, cardiovascular disease (CVD) patients with kidney dysfunction (eGFR < 45 mL/min) or heart failure [10]. The patient was educated about proper hydration, genitals care and the significance of increasing the ingestion of carbohydrates to prevent euglycemic diabetic ketoacidosis.

4.2 Thyroid Replacement: Levothyroxine (LT4) was started on at a low dose of 25 mcg daily and the dose titrated over time; this was done to address these factors, recognizing that it is preferable to titrate dosage in longstanding hypothyroidism. A recommendation was given that the patient should take the LT4 at least 4 hours apart from the calcium carbonate in order to avoid any possible interference in absorption. Repeat TSH/free T4 was planned at 6 weeks for any needed dose adjustment. For co-management of Hashimoto's thyroiditis, the endocrinology in Prince Hashem Military Hospital (Az-Zarqa) was referred to in line with the referral letter. However, the treating physician was aware of the possibility that the excess HbA1c could be due to the extent of the prolonged lifespan of erythrocytes in patients with hypothyroidism [6,7] and determined to reassess after normalization of thyroid function.

4.3 Depression Management: After consensus and in the presence of no contraindications in the ECG (no significant prolongation of the QTc interval interval), there were no other serotonergic drugs in the patient's treatment plan, and the renal function was adequate, sertraline 50 mg was prescribed once a day. However, Sertraline was chosen over tricyclic antidepressants due to their effects on the metabolism (weight gain, hyperglycemia) and anticholinergic side-effects which would add to the metabolic effects of hypothyroidism. Structured brief psychological support (problem-solving therapy - 4 sessions) were offered via the PHC mental health liaison nurse. A reassessment of the PHQ-9 was planned at four and 8 weeks.

4.4 Antihypertensive Optimization: For albuminuria A2 stage, enalapril was continued at 10mg daily due to its renoprotective benefit and this was escalated to 20mg at the four week visit where patient blood pressure was still above target. Amlodipine dosage

raised to 10mg. The patient was strongly advised to stop using the over-the-counter (OTC) ibuprofen, and prescribed with paracetamol 500 mg as a substitute for the OTC medicine for pain management. NSAIDs (non-steroidal anti-inflammatory drugs) were recorded as a clinical allergy/warning in the MoH record to ensure that NSAIDs were not prescribed again.

4.5 Statin Therapy and Cardiovascular Risk Reduction: Rosuvastatin (20mg once daily) has been started due to poor LDL-C (4.1 mmol/L), high estimated 10-year cardiovascular risk (estimated SCORE2-Diabetes >10%) and the known effect of hypothyroidism on worsening dyslipidemia. Recheck of lipid panel was scheduled for three months, based on the assumption that thyroxine would restore euthyroid state to the patient and would have its own effect on the lipid panel. Since there was no control over blood pressure, the low-dose aspirin (75 mg daily) was deferred for further analysis pending reassessment of blood pressure control.

4.6 Self-Management Education and Structured Follow-Up: The PHC nurse educator delivered the structured diabetes self-management education (DSME) in Arabic covering meal planning (mediterranean adapted), physical activity (set for 150 minutes moderate intensity activity per week), blood glucose self-monitoring (patient was given a glucometer, test strips), foot care and sick day rules. Follow-up was at two weeks (BP/adherence) and at six weeks (TSH/free T4, PHQ-9, BP), 12 weeks (HbA1c, lipid panel, UACR) and at 6 months (full panel). A checklist for care coordination was completed and the patient's care was recorded in PHC chronic disease register for proactive recall.

5. OUTCOMES AND FOLLOW-UP:

Energy levels, mood and general quality of life were significantly improved at the 6 month post patient visit (September 2024) as reported by the patient. She had seen all of the review appointments and scored an MMAS-8 = 7/8 (high adherence). In addition to the index values shown in Table 2, key clinical and laboratory outcomes at six months are based upon a subset of the data presented here. There was a clinically significant reduction in HbA1c from 10.2% to 7.8% (a decrease of 2.4% for clinical significance).

Blood pressure was 132/82 mmHg, meeting the ADA 2024 < 130/80 mmHg target. After three months of levothyroxine up-titration to 75 mcg/day, TSH became normalised. The depression symptomatology is reduced to almost remission on the PHQ-9 which dropped from 14 to 5. Achieved euthyroidism led to a significant reduction in LDL-C (from 4.1 to 2.3 mmol/L) alongside the effects of statin medications. UACR improved from 47.3 to 29.1 mg/g. The patient mentioned improvement in her symptoms of cold intolerance, a decrease in constipation and diminished hair loss. There was a modest loss of body weight of 3.2 kg, primarily as a result of the osmotic and modest caloric loss caused by empagliflozin, and also due to improved metabolic state with euthyroidism.

No adverse events were reported related to the pharmacotherapy that was begun. The patient had one asymptomatic, mild case of genitourinary candidiasis at week 8 which was treated with oral fluconazole, which is a known, but treatable side effect of SGLT-2 inhibitors. No hypoglycemic episodes were recorded after the glibenclamide was discontinued.

6. DISCUSSION:

6.1 Therapeutic Inertia in a Resource-Constrained

Primary Care Setting: The key clinical and systemic finding in the case was a therapeutic inertia of 12 months documented by repeatedly missing therapeutic targets as indicated by three sequential HbA1c levels above target, despite the patient's advanced diabetes. Fittingly, this is consistent with prevalence of TI published data, as McDaniel et al. [5] was able to identify TI using machine learning analysis of EHR in 40% of primary care patients with T2DM therefore highlighting the systemic nature of this problem. The contribution of system-level factors in the context of PHC at the MoH level in Jordan might include high patient flow (the Al-Rusayfah center also has two family medicine specialists patients attend, and about 2,800 registered patients with chronic disease), lack of communication with patient (HbA1C results sometimes only arrive after the patient has left the consultation), and lack of structured intensification protocol for chronic disease with integrated decision support alerts.

Patient related factors associated with TI in this instance were reluctance of patients to report

depression at their clinic visit (stigma), and the self-discontinuation of glybenclamide without advice from the treating physician, potentially causing the previous treating physician to assume that the symptom control was due to improved glycemic control. Our observations corroborate those of Isajev et al. (11), who found that clinical inertia, and patient-level barriers, were both independent predictors of inadequate T2DM management in Primary Care [11].

6.2 Hypothyroidism as a Compounding

Comorbidity: In this patient, the finding of overt Hashimoto's thyroiditis (TSH 18.4 mIU/L, TPO antibody >1,240 IU/mL) is important clinically and has two fold meanings, namely, a metabolic and an anti-metabolic connection. It was noted that T2DM patients with hypothyroidism had significantly higher HbA1c levels (HbA1c 10.1% vs. 5.48%) and poorer lipid profile than euthyroid T2DM patients in the study by Elhoussein et al. (6) in Scientific Reports. In this instance it is still not known if the high HbA1c (10.2%) was from real glycemic dyscontrol or if it was an artificially high reading which could have been due to erythrocyte survival the time of measurement. Alternatively, in hypothyroid patients, when there is a discrepancy between HbA1c levels and fasting glucose concentration as well as clinical symptoms, other glycemic markers like fructosamine and glycated albumin obtainable with a single blood draw should be used instead, as discussed in Cureus (2025) and the systematic review in PMC (2024) [7,12]. The significant reduction in HbA1C to 7.8% at 6 months, in tandem with attainment of euthyroidism highlights the role of thyroid function as a modifiable factor associated with glycemic control.

6.3 Depression and Glycaemic Self-Management:

The moderate depression (PHQ-9 14) which has gone previously undetected by the patient is a good example of phenomenon's that can happen in the care of T2DM. In the last review by de Groot, 2023, and a recent systematic review by Liu et al., 2024 [8,9] reported a bidirectional association between depression and T2DM with shared mechanisms such as decreased adherence to self-care and neuro-inflammation and dysfunction of the hypothalamic-pituitary-adrenal axis. The 2023 Standards of Care from the ADA strongly support annual screenings for depression in all individuals with diabetes using a

patient-friendly depression screening tool (PHQ-2 or PHQ-9) [10]. This recommendation had not been attended for this patient throughout visits, thus a gap in clinical governance of a PHC system that needs attention in the Jordanian MoH.

6.4 Polypharmacy and Drug Interaction Management:

When levothyroxine, sertraline, rosuvastatin and empagliflozin were added to metformin, amlodipine, and enalapril, the therapy was a seven drug regimen which is defined as polypharmacy (≥ 5 drugs in use at the same time). Three pre-existing drug interactions were also identified: (1) ibuprofen–enalapril (hyponatremia risk, decreased antihypertensive effects); (2) calcium carbonate–levothyroxine (abnormal absorption of levothyroxine, managed by separating the doses of these drugs in the same patient) and (3) potential empagliflozin interaction with enalapril requiring patient eGFR and potassium monitoring, because both drugs have natriuretic effects and risk of reducing blood volume. Nevertheless, polypharmacy in comorbid T2DM and depression has been correlated with greater adherence to antidepressant medications and a greater risk of adverse drug events, reinforcing the need for systematic medication reconciliation at every review [13].

6.5 Implications for Primary Care Policy in Jordan:

Regarding the exploration of chronic disease management in MoH PHC centers in Jordan that can be applicable in this case, here are some key implications: A multimorbidity management protocol should be routinely applied as a structure embedded within the national PHC chronic disease guidelines; this should include annual depression screening, thyroid function testing for high-risk groups and intensification prompts based on HbA1c level. In a study by Al-Hadeethi et al. (2022), authors evaluated whether Jordanian PHC centers are able to manage hypertension and found many inadequacies in adhering to guidelines, stocking of medicines and training their human resources [2]. The results obtained could easily be applied to the treatment of T2DM and CMM. Second, to support the role of the family medicine specialist to refer those with complex chronic disease to the correct health specialist, the

length of time spent with complex chronic disease consultations will need to be increased (a minimum of 20 minutes for multimorbidity reviews versus currently 7–9 minutes on average). Third, having a clinical pharmacist in the PHC team (even in rotation) would support clinical medication reconciliation and polypharmacy since it is supported in European and regional models in practice [14].

7. CONCLUSION:

This case report portrays a condition of multimorbidity involving the cardiometabolic system, namely type 2 diabetes mellitus (T2DM), hypertension (HT), overt hypothyroidism (Hashimoto's thyroiditis) and major depressive disorder (MDD) in a 52-year old Jordanian female patient who presented to a primary care center within the Ministry of Health (MoH) in the city of Az-Zarqa. The case shows three major mistakes in the primary care management of chronic conditions, namely: (1) that, despite persistently uncontrolled glycaemia, no action seemed to have been taken to change treatment, or to optimize glycemic control; (2) failure to screen for depression and hypothyroidism in a high-risk patient; and (3) incomplete medication reconciliation so that a clinically significant NSAID–ACE inhibitor interaction persisted without being recognized.

A holistic, multifaceted management plan with all four diagnoses led to six-monthly clinically significant and meaningful reduction in HbA1c by 2.4%, normalization of thyroid parameters and blood pressure, near remission of depression and better medication adherence. The case highlights the critical importance of the special role of the family medicine expert who has the time to provide care, the knowledge and tools to support decision-making, and the capacity to coordinate an interprofessional team, all of which are needed to manage patients with cardiometabolic multimorbidity in a non-elite, resource-limited public health system. Urgent calls for systemic interventions such as developing multimorbidity specific clinical pathways, required screening for depression and thyroid within Jordanian MoH PHC centers, and integration of clinical pharmacists in Jordanian PHC centers are needed.

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