Case Study – Diabetes Mellitus

Suspected Diagnosis and Initial Testing

The NHS reported that between 2011 and 2019, the percentage of adult men who were diagnosed with type 2 diabetes mellitus was 9% - making it one of the most prevalent chronic diseases in the UK. Furthermore, over 90% of diabetes cases in adults are type 2, indicating that this would be the most likely type (NHS, 2022). The patient presented with many risk factors and symptoms that led to suspicion of diabetes. The World Health Organisation (2020) states that the risk factors of type 2 diabetes include physical inactivity, age, and obesity.

A global study has shown that the mean age of type 2 diagnosis in men is 45.1 years, and the mean BMI is 25.2 (Carrillo-Larco et al., 2023). Both figures are similar to the patient demographics, supporting the likelihood that the patient may be suffering from this disease. The patient's lack of exercise may have led to weight gain and Amanat et al. (2020) explain that exercise can lead to decreased levels of glycosylated haemoglobin (HbA1c), a defining factor of diabetes. However, it could be argued that the lack of exercise may have been initially due to fatigue associated with the onset of diabetes as this is a common symptom (Nazarko, 2023). Hypertension is another factor as it is known to be common in diabetic patients (de Boer et al., 2017).

Nazarko (2023) explains how the patient's symptoms also correspond to suspicion of type 2 diabetes. Insulin is a key hormone responsible for regulating blood glucose levels. It is produced by beta pancreas cells and operates by binding to insulin receptors that signal to the body to either convert the glucose to energy or store it as triglycerides. In type 2 diabetes, the body becomes insulin-resistant, and the beta cells become dysfunctional. This can lead to symptoms such as polyuria due to the body attempting to reduce levels of glucose that are no longer regulated by insulin by passing it in urine. This leads to polydipsia as the patient will feel the need to drink more to replace the lost fluid. The patient is presenting both of these symptoms.

Urine dipstick tests are quick, with a turnaround time of only a few minutes, and inexpensive. They can be used as point-of-care testing to get a fast indication of whether the suspicion of type 2 diabetes is correct. In type 2 diabetes, the patient will likely be passing more protein in their urine (Jeon & Kim, 2021). Glucose levels will also likely be elevated in the urine. Ketones can also be tested with a urine dipstick test which is integral in screening for ketoacidosis, an urgent complication of diabetes (World Health Organisation, 2020). Therefore, a urine dipstick test is a quick way of confirming to the doctor that diabetes may be present, indicating which further tests to conduct, as well as ruling out a medical emergency.

Initial and Further Test Results

Urine dipstick testing is beneficial in aiding the fast clinical assessment of patients with suspected or confirmed diabetes. This patient showed positive results for urine glucose, protein, bilirubin, and ketones. The expected outcomes for these tests in healthy patients are negative.

In healthy patients, there is usually little to no glucose passed in the urine. The renal tubule is responsible for reabsorbing almost all the glucose in the glomerular filtrate, however, if the amount of glucose present in the filtrate is too high, the renal tubule cannot absorb it all and it is passed in urine (Liman & Jialal, 2023). Type 2 diabetes mellitus can lead to issues with maintaining glucose homeostasis and therefore can lead to high levels of plasma glucose known as hyperglycaemia (Li et al., 2023). The rise in plasma glucose can therefore cause a rise in urine glucose levels (glucosuria), showing that this patient's urine glucose result can indicate type 2 diabetes mellitus.

It has been shown that proteinuria can be an indication of inflammation correlating to insulin resistance and therefore type 2 diabetes mellitus (Jeon & Kim, 2021), further showing that the urine tests support the hypothesis of type 2 diabetes mellitus.

Studies have shown that elevated bilirubin levels may be present in patients with type 2 diabetes mellitus as it can correlate with a lower risk of diabetes-related complications, however, elevated bilirubin levels may also indicate liver issues and therefore liver function tests could be recommended (Zhu et al., 2017).
Ketones present in the urine may be indicative of diabetic ketoacidosis (DKA), a serious complication of diabetes and medical emergency. Ketones are caused by uncontrolled lipolysis due to insulin deficiency and therefore the excessive production of ketones (Dhatariya, 2016). DKA is not common in cases of type 2 diabetes mellitus, but it is still possible and therefore should be tested (Eyth et al., 2018). Although there are ketones present, they are not within the range for DKA of over 2+, therefore indicating that the patient is not suffering from DKA (Misra & Oliver, 2014). It is essential to determine this as it can greatly impact the clinical management of the patient.

The results from the urine testing likely prompted the further tests undertaken as they can also be used to confirm the suspicion of diabetes as well as aid in determining the severity and therefore clinical management of the patient.

Testing levels of glycosylated haemoglobin (HbA1c) is commonly used in assessing long-term blood sugar control. Plasma glucose attaches to the haemoglobin component of red blood cells (RBCs) creating HbA1c. The level of glucose in the blood corresponds to the number of RBCs impacted. The average lifespan of RBCs is 90 days and therefore, testing HbA1c levels gives an overview of the past 90 days of blood glucose control (Naik & Eyth, 2023). This is often used to monitor known diabetics as well as aiding in diagnosis and is beneficial as it is not largely impacted by recent dieting and has less intra-individual variability than plasma glucose testing. The World Health Organisation (2020) states the diagnostic cut-off value is 48 mmol/mol. This patient was tested thrice with each result being above the cut-off value indicating diabetes. The severity of the HbA1c result can indicate will be able to easily manage their disease with exercise and diet alone.

An oral glucose tolerance test (OGTT) can be used to aid diabetes diagnosis. It requires an initial fasting glucose blood test to be taken before the patient receives a standardised oral dose of glucose. A follow-up glucose blood test is taken 2hrs post

glucose dose. It is useful in determining if the patient cannot store and use glucose properly- indicating possible pancreatic beta cell function and insulin resistance (Eyth et al., 2018). The clinical ranges for this test are described by the NHS (2019) and shown below in Table 1.

Table 1: A table to show the clinical outcome cut-offs for OGTT as described by the NHS (2019).

Outcome	OGTT 0hrs (mmol/L)	OGTT 2hrs (mmol/L)
Normal	<6.1	N/A
Impaired fasting glycaemia	6.1 – 6.9	< 7.8
Impaired glucose tolerance	<7.0	7.8 – 11.0
Diabetes Mellitus	≥7.0	≥11.1

The patient has an OGTT 0hr result of 7.6mmol/L and an OGTT 2hr result of 9.7mmol/L. This means that they do not fit into any defined category. It may be beneficial to rerun this test, however, it has been shown that this test can be unreliable due to it being affected by many factors. For example, the patient's diet and exercise in the days leading to the test and drugs such as corticosteroids can influence the results (Eyth et al., 2018).

Random and fasting glucose tests were performed in addition to the OGTT and both results were elevated when compared to the given reference ranges. Plasma glucose levels are often elevated in type 2 diabetic patients due to the body's poor regulation of glucose because of insulin resistance and impaired insulin production from pancreatic beta cells. Fasting glucose levels are known to rise over time as pancreatic beta cells become more impaired over time (Yang et al., 2023). Therefore, both these results complement the suspicion of the patient suffering from type 2 diabetes mellitus. The World Health Organisation (2020) also states how fasting plasma glucose results can be used to assess type 2 diabetes management and when to start medication as opposed to controlling with diet and exercise.

There are many complications of diabetes such as chronic recurring infections and sores of the feet and lower legs, diabetic retinopathy, diabetic kidney disease, coronary heart disease, and diabetic neuropathy (World Health Organisation, 2020). The kidney function tests undertaken (EGFR, Na, K, Cl, creatinine, and urea) were all

within the given reference range, indicating that the patient is not suffering from diabetic kidney disease as a complication. The full blood count results were also all within the given reference ranges and there was no mention of any physical sores of the lower legs. If the count of white blood cells was elevated (neutropenia), this could indicate the patient has an infection, however, this is not the case and therefore ruling out this complication (Frater, 2020). These assessments of possible complications help to evaluate the progression of the disease and therefore help inform clinical management of the patient.

Prognostic Outcome and Potential Therapies

The prognosis for type 2 diabetes mellitus varies between individual cases and it is important to look at all the facts presented in this case to understand this patient's prognosis and treatment options.

Firstly, this patient is diagnosed with diabetes later in life at the age of 48. Studies regarding diabetic death rates in the EU have shown that patients diagnosed with diabetes at age 50 (a similar age to the patient) die an average of 5 years earlier in comparison to a non-diabetic. In contrast, 50-year-old diabetics who were diagnosed at the age of 30 have a life expectancy 13 years shorter than a non-diabetic person (Kaptoge et al., 2023). This information suggests that the patient has a better prognosis due to developing the condition at a later stage of life.

Diabetes is often associated with comorbidities and complications (Farmaki et al., 2021). Assessing the possible presence of these is vital in understanding the progression of the condition, the treatments needed, and the prognosis. Upon assessment of the test results and symptoms, there does not seem to be any indication that the patient is suffering from any complications however it is stated that the patient has hypertension. Hypertension is reported to affect more than two-thirds of type 2 diabetes patients. Hyperglycaemia from diabetes can lead to elevated activity of the sympathetic nervous system, in turn leading to more muscle growth and fluid retention that can cause high blood pressure. Hypertension coinciding with diabetes increases

a patient's risk of heart disease, therefore, it is recommended to keep blood pressure below 140/85mmHg. This means it would be beneficial to the patient if their blood pressure is controlled. There are various medications available to help control blood pressure such as statins and diuretics. There is a possibility that these medications can impact blood sugar levels but with a strict routine this can be managed and the benefits to the cardiovascular system outweigh the negative impacts (Ferrannini & Cushman, 2012).

Other possible complications of diabetes are described by Farmaki et al. (2021). They can be divided into acute and chronic complications. Acute complications tend to have a quicker onset such as diabetic ketoacidosis, hypoglycaemia, and hyperglycaemia. Each of these is reversible, however, they can have serious effects, especially if left untreated. Hyperglycaemia is the leading cause of serious and life-threatening complications and can develop if the patient does not maintain strict diet control or medication regimen. On the other hand, chronic conditions often take more time to develop. They can impact the function of most organs in the human body such as retinopathy of the eyes, nephropathy of the kidneys, neuropathy of the nervous system, and macroangiopathy of the cardiovascular system. It is reported that most morbidity in type 2 diabetes patients is due to complications with the cardiovascular system. It could be recommended to perform cardiac risk assessments tests such as for brain natriuretic peptide (BNP) and lipid tests to ensure the patient is not developing this complication (Takeuchi & Sata, 2012). The blood test results provided include renal function tests for urea, creatinine, and the estimated glomerular filtration rate (EGFR). These were all within the normal reference range, indicating the patient is not suffering from diabetic nephropathy (Gounden et al., 2023). Due to the lack of evidence of a diabetic complication, the patient may not require any treatments excluding those to directly treat the diabetes.

The World Health Organisation (2020) describes a management protocol flowchart for newly diagnosed type 2 diabetes mellitus patients using fasting or random glucose test results. Initially, it is stated that the fasting blood glucose result is ≥7mmol/L and <18mmol/L, the patient should be counselled on their diet and physical activity and reviewed in 3 months. The patient for this case study fits into this category.

Studies have shown that maintaining a healthy lifestyle including diet control and regular exercise can dramatically reduce the risk of chronic and acute diabetic complications. This approach is often used as the initial therapy for diabetes as it can aid glycaemic control as well as lowering other risk factors such as weight and blood pressure (Zhang et al., 2019). Furthermore, studies have shown that weight loss can also lead to remission of type 2 diabetes mellitus in approximately 80% of individuals. This makes diet and exercise key in not only managing the condition but treating it also. However, it is noted that maintaining a strict lifestyle long-term can be challenging and patients may be diagnosed with the condition if they cannot sustain it (Magkos et al., 2020).

The World Health Organisation (2020) then states that if the patient is not achieving their goals with a healthy lifestyle, then a course of 500mg of metformin once a day should begin alongside lifestyle counselling. Metformin is a biguanide drug that works by decreasing liver glucose production, therefore lowering blood glucose levels, and enhancing insulin sensitivity (Jacobs & Corcoran, 2023). If this treatment does not yield the sought results after 3 months, the metformin should be increased to 1000mg once a day, increasing to twice a day in a further 3 months if treatment is not working. After this, it is recommended to add 80mg of gliclazide once a day. (World Health Organisation, 2020). This drug is used to increase the production of insulin from the beta pancreatic cells (Al-Omary, 2017). If treatment is still not working, the World Health Organisation (2020) then states that the patient should be counselled on the use of insulin injections as a treatment.

Overall, the prognosis for this patient looks promising due to their late onset of diabetes as well as the lack of evidence suggesting the development of any further complications. Despite having slightly high blood pressure, this patient has a history of having an active lifestyle and may be successful in treating their condition through lifestyle management.

Bibliography

- Al-Omary, F.A.M. (2017) 'Gliclazide', *Profiles of Drug Substances, Excipients and Related Methodology*, pp. 125–192. doi:10.1016/bs.podrm.2017.02.003.
- Amanat, S. *et al.* (2020) 'Exercise and Type 2 Diabetes', in *Physical Exercise for Human Health* .
- Carrillo-Larco, R.M. *et al.* (2023) 'Mean age and body mass index at type 2 diabetes diagnosis: Pooled analysis of 56 health surveys across income groups and world regions', *Diabetic Medicine*, 41(2). doi:10.1111/dme.15174.
- de Boer, I.H. *et al.* (2017) 'Diabetes and hypertension: A position statement by the American Diabetes Association', *Diabetes Care*, 40(9), pp. 1273–1284. doi:10.2337/dci17-0026.
- Dhatariya, K. (2016) 'Blood ketones: Measurement, interpretation, limitations, and utility in the management of diabetic ketoacidosis', *The Review of Diabetic Studies*, 13(4), pp. 217–225. doi:10.1900/rds.2016.13.217.
- Eyth, E., Basit, H. and Swift, C. (2018) *Glucose Tolerance Test*. Treasure Island, Florida : StatPearls Publishing. Available at: https://europepmc.org/article/nbk/nbk532915 (Accessed: 05 March 2024).
- Farmaki, P. *et al.* (2021) 'Complications of the type 2 diabetes mellitus', *Current Cardiology Reviews*, 16(4), pp. 249–251. doi:10.2174/1573403x1604201229115531.
- Ferguson, L.D. *et al.* (2017) 'Men across a range of ethnicities have a higher prevalence of diabetes: Findings from a cross-sectional study of 500 000 uk biobank participants', *Diabetic Medicine*, 35(2), pp. 270–276. doi:10.1111/dme.13551.
- Ferrannini, E. and Cushman, W.C. (2012) 'Diabetes and hypertension: The bad companions', *The Lancet*, 380(9841), pp. 601–610. doi:10.1016/s0140-6736(12)60987-8.
- Frater, J.L. (2020) 'How I investigate neutropenia', *International Journal of Laboratory Hematology*, 42(S1), pp. 121–132. doi:10.1111/ijlh.13210.
- Gounden, V., Bhatt, H. and Jialal, I. (2023) *Renal Function Tests*. Treasure Island, Florida : StatPearls Publishing. Available at: https://www.ncbi.nlm.nih.gov/books/NBK507821/#:~:text=Tests%20of%20ren

al%20function%20can,the%20presence%20of%20renal%20impairment. (Accessed: 07 March 2024).

- Jacobs, T.F. and Corcoran, C. (2023) *Metformin*. Treasure Island, Florida : StatPearls Publishing. Available at: https://www.ncbi.nlm.nih.gov/books/NBK518983/ (Accessed: 07 March 2024).
- Jeon, J. and Kim, J. (2021) 'Dipstick proteinuria and risk of type 2 diabetes mellitus: A nationwide population-based Cohort Study', *Journal of Translational Medicine*, 19(1). doi:10.1186/s12967-021-02934-y.
- Kaptoge, S. *et al.* (2023) 'Life expectancy associated with different ages at diagnosis of type 2 diabetes in high-income countries: 23 million person-years of observation', *The Lancet Diabetes & Endocrinology*, 11(10), pp. 731–742. doi:10.1016/s2213-8587(23)00223-1.
- Li, J., Yang, J. and Hong, T. (2023) 'Delineating the transcriptional atlas for impaired insulin secretion: A window into type 2 diabetes pathophysiology', *Journal of Diabetes Investigation*, 14(11), pp. 1231–1233. doi:10.1111/jdi.14060.
- Liman, M.N.P. and Jialal, I. (2023b) *Physiology, Glycosuria*. Treasure Island, Florida : StatPearls Publishing. Available at: https://www.ncbi.nlm.nih.gov/books/NBK557441/ (Accessed: 04 March 2024).
- Magkos, F., Hjorth, M.F. and Astrup, A. (2020) 'Diet and exercise in the prevention and treatment of type 2 diabetes mellitus', *Nature Reviews Endocrinology*, 16(10), pp. 545–555. doi:10.1038/s41574-020-0381-5.
- Misra, S. and Oliver, N.S. (2014) 'Utility of ketone measurement in the prevention, diagnosis and management of diabetic ketoacidosis', *Diabetic Medicine*, 32(1), pp. 14–23. doi:10.1111/dme.12604.
- Naik, R. and Eyth, E. (2023). Treasure Island, Florida : StatPearls Publishing. Available at: https://europepmc.org/article/nbk/nbk549816 (Accessed: 05 March 2024).
- Nazarko, L. (2023) 'Type 2 diabetes: causes, diagnosis', *Nursing Times*, 119(10).
- NHS (2019) *Diagnosis of Diabetes Mellitus*, *NHS choices*. Available at: https://mft.nhs.uk/the-trust/other-departments/laboratory-medicine/biochemistry/specimen-requirements-and-reference-

ranges/reporting-of-results/diagnosis-of-diabetes-mellitus/#:~:text=A%20fasting%20venous%20plasma%20glucose,the%20degree%20of%20glucose%20intolerance. (Accessed: 05 March 2024).

- NHS (2022) *Health Survey England Additional Analyses, Ethnicity and Health, 2011-2019 Experimental statistics*, *NHS choices*. Available at: https://digital.nhs.uk/data-and-information/publications/statistical/health-survey-england-additional-analyses/ethnicity-and-health-2011-2019-experimental-statistics/diabetes (Accessed: 29 February 2024).
- Takeuchi, H. and Sata, M. (2012) 'The relationship among brain natriuretic peptide (BNP), cholesterol and lipoprotein', *Heart Asia*, 4(1), pp. 11–15. doi:10.1136/heartasia-2011-010042.
- World Health Organisation (2020) *Diagnosis and Management of Type 2 Diabetes* [Preprint]. Available at: https://iris.who.int/bitstream/handle/10665/331710/WHO-UCN-NCD-20.1-eng.pdf?sequence=1 (Accessed: 29 February 2024).
- Yang, W., Jiang, W. and Guo, S. (2023) 'Regulation of macronutrients in insulin resistance and glucose homeostasis during type 2 diabetes mellitus', *Nutrients*, 15(21), p. 4671. doi:10.3390/nu15214671.
- Zhang, Yanbo *et al.* (2019) 'Combined lifestyle factors and risk of incident type 2 diabetes and prognosis among individuals with type 2 diabetes: A systematic review and meta-analysis of prospective cohort studies', *Diabetologia*, 63(1), pp. 21–33. doi:10.1007/s00125-019-04985-9.
- Zhu, B. *et al.* (2017) 'Effect of bilirubin concentration on the risk of diabetic complications: A meta-analysis of Epidemiologic Studies', *Scientific Reports*, 7(1). doi:10.1038/srep41681.