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Multicenter Study on the Clinical Characteristics, Diagnosis, and Treatment Outcomes of Insulinoma: Insights From 15 Medical Centres

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ABSTRACT

Objective: This study aimed to evaluate the clinical characteristics, diagnostic approaches, and treatment outcomes of insulinoma patients from diverse regions across the country. We conducted a retrospective analysis of medical records from 76 adult patients diagnosed with insulinoma between 2018 and 2023 at 15 medical centres. Data collected included demographics, presenting symptoms, laboratory and imaging results, surgical reports, pathology findings, and clinical follow-up information.

Design: Multi-centre retrospective study.

Methods: The study revealed that key factors such as age, BMI, symptom duration, tumour size, and follow-up period were similar across genders. The majority of patients experienced neuroglycopenic symptoms, particularly during fasting. Insulinoma was typically diagnosed either during fasting or spontaneously, with no significant gender differences in glucose and insulin levels during hypoglycemia. However, men exhibited higher C-peptide levels ($p < 0.05$). Common comorbidities included hypertension, hypothyroidism, and cardiovascular conditions, and some patients had been using antiepileptics or antidepressants before their diagnosis.

Results: Preoperative tumour diagnoses were largely accurate, with endoscopic ultrasound (EUS) being the most effective method. Most tumours were small (< 2 cm) and located in the pancreas body, with the majority being solitary. Surgical

treatments primarily involved enucleation or distal pancreatectomy. Follow-up data indicated high remission rates, with low rates of nonremission and mortality.

Conclusion: This study emphasises that early diagnosis and intervention, particularly in patients with a history of neurological or psychiatric issues, postprandial symptoms, or rapid symptom improvement after treatment, can lead to significantly better outcomes.

1 | Introduction

Insulinomas, though rare, are the most common functional neuroendocrine tumours of the pancreas, with an estimated incidence of 1–4 cases per million annually. These tumours primarily affect individuals between the ages of 30 and 70, with a higher prevalence in women. The vast majority of insulinomas are sporadic (94%), benign (87%) and solitary (90%) [1–3]. Despite their relatively small size, insulinomas can cause significant morbidity due to excessive insulin secretion, leading to recurrent hypoglycemia. The clinical presentation is often heterogeneous, ranging from mild neuroglycopenic symptoms, such as confusion and behavioural changes, to severe episodes involving seizures and loss of consciousness. Due to this broad spectrum of manifestations, insulinomas are frequently misdiagnosed as neurological or psychiatric disorders [4–7].

Advancements in biochemical testing and imaging modalities have improved diagnostic accuracy, yet insulinomas remain a challenging entity due to their intermittent symptomatology and resemblance to other neuroglycopenic conditions [4–6]. The delay in diagnosis can have serious consequences, including increased risk of complications and reduced quality of life for affected individuals. Therefore, understanding the clinical presentation, diagnostic pathways, and treatment outcomes is crucial for optimising patient care.

Previous studies on insulinoma have primarily been limited to single-centre experiences or specific patient subgroups, which may not capture the full spectrum of the disease across different populations. Additionally, there is limited data on regional variations in clinical presentation, diagnostic strategies, and treatment outcomes [1–10]. This study addresses these gaps by providing a comprehensive, multicenter retrospective analysis of insulinoma cases from diverse geographical regions of Türkiye. By evaluating differences based on gender, tumour characteristics, and associated comorbidities, this study aims to identify clinically relevant patterns that could refine current diagnostic and therapeutic approaches.

Furthermore, by systematically examining diagnostic pitfalls and treatment outcomes, this study contributes to a more standardised and effective clinical framework for insulinoma management. The findings will not only enhance early detection strategies but also help guide clinicians in selecting the most appropriate therapeutic interventions, ultimately improving patient prognosis. Given the rarity of insulinoma, large-scale, multicenter studies such as this one is essential for generating robust evidence that can inform clinical practice and shape future research directions.

2 | Materials and Methods

2.1 | Ethic

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. The retrospective study protocol was reviewed and approved by the Regional Ethics Committee of Pamukkale University Faculty of Medicine, under protocol number 20/261.

2.2 | Patients

We retrospectively analysed the records of 76 adult patients diagnosed with insulinoma between 2018 and 2023 from 15 different medical centres. The data collected included demographic information, clinical presentations, preoperative laboratory and imaging findings, detailed surgical reports, histopathological examinations of resected samples, and clinical follow-up data from the outpatient clinics of the participating centres.

Whipple's triad is a key diagnostic criterion for insulinoma, comprising three elements: (1) symptoms of hypoglycemia, (2) documented low blood glucose levels at the time of symptoms, and (3) resolution of symptoms after glucose administration [7]. For a definitive diagnosis of insulinoma, a compatible clinical presentation is required, along with the following biochemical criteria: blood glucose levels ≤ 40 mg/dL, insulin ≥ 36 pmol/L, C-peptide ≥ 200 pmol/L, proinsulin ≥ 5 pmol/L, β-hydroxybutyrate ≤ 2.7 mmol/L, and the absence of plasma or urinary sulfonylurea metabolites [9].

2.3 | Clinical Approach

Additionally, the study assessed the presence of components of multiple endocrine neoplasia (MEN). A variety of imaging modalities were employed for insulinoma detection, including ultrasonography (USG), computed tomography (CT), magnetic resonance imaging (MRI), octreotide scintigraphy (OS), fluorodeoxyglucose positron emission tomography (FDG-PET), Ga-68 DOTATATE PET/CT, endoscopic ultrasound (EUS), and calcium-stimulated hepatic venous sampling.

2.4 | Statistical Analysis

Statistical analysis was performed using SPSS 22.0 software (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation (SD), while categorical variables are expressed as percentages (%), for the total patient

population as well as for males and females. The diagnostic delay was assessed by calculating the time from the initial onset of hypoglycaemia symptoms to the clinical diagnosis of insulinoma, as recorded in patient files.

Categorical variables were analysed using Fisher's exact test or the chi-square test, depending on sample size and expected frequencies. For group comparisons, Student's *t*-test was used for normally distributed continuous variables, and the Mann-Whitney U test was applied for non-normally distributed variables. Poisson regression was employed to assess changes in the incidence of insulinomas, with p-values < 0.05 considered statistically significant.

3 | Results

3.1 | Anthropometric Values

Among the 76 patients included in the study, 49 (64.5%) were female and 27 (35.5%) were male. Patients were retrospectively selected from 15 medical centres based on confirmed diagnoses of insulinoma between 2018 and 2023. Inclusion criteria required a definitive biochemical and/or imaging-confirmed diagnosis of insulinoma, while patients with incomplete records or alternative diagnoses were excluded to minimise selection bias. Despite the retrospective design, cases were obtained from multiple centres to enhance the generalisability of the findings.

No significant differences were found between male and female patients in terms of age, BMI, symptom duration, follow-up period, or tumour size ($p > 0.05$). During symptomatic hypoglycemia episodes, glucose and insulin levels did not significantly differ between genders. However, C-peptide levels were statistically higher in men compared to women ($p < 0.05$) (Table 1).

3.2 | Clinical Presentation and Hypoglycemia Characteristics

Neuroglycopenic symptoms were the most common presentation, observed in 57% of patients, while 24% presented with adrenergic symptoms, and 18% exhibited both. Patients reported experiencing hypoglycaemia symptoms during fasting (70%), postprandially (3%), or in both situations (27%). Hypoglycemia was detected during a prolonged fasting test in 54% of patients, while it occurred spontaneously in 46%. Patients who experienced spontaneous hypoglycemia were only monitored, and insulin, glucose, and C-peptide levels were assessed at the time of the hypoglycaemia event. Thus, insulin, glucose, and C-peptide levels were evaluated in all patients, and further investigations were initiated accordingly.

3.3 | Comorbidities and Medication Use

Among comorbid conditions, diabetes mellitus was present in three patients. Hypertension was the most common comorbidity, affecting 35% of patients. The incidence of coronary artery disease was 8% in women and 7% in men, while atrial fibrillation was detected exclusively in men (20%); however, these differences were not statistically significant. Multiple endocrine neoplasia type 1 (MEN1) syndrome was diagnosed in four patients (8%); three had solitary tumours, and one had multiple tumours. All MEN1-associated cases were non-metastatic.

Other comorbidities included osteoporosis and depression in women, and angiolipoma, brain tumours, and celiac disease in men. Additionally, hyperthyroidism was diagnosed in one female and one male patient. No significant differences were found between women and men regarding the clinical presentation of hypoglycemia, the timing of symptomatic hypoglycemia, the method of hypoglycemia detection, or comorbidities, except for hypothyroidism (Table 2). Before the diagnosis of insulinoma, 5% of patients were using antiepileptics, and 8% were using antidepressants, likely due to the misdiagnosis of neuroglycopenic symptoms.

3.4 | Diagnostic Methods and Tumour Localisation

In our country, the first step in the evaluation of insulinoma patients is the administration of frequent small meals

TABLE 1 | Demographic, anthropometric, and biochemical data of insulinoma patients.

Patients ($n = 76$, 100%)	Female ($n = 49$, 64.4%)	Male ($n = 27$, 35.6%)	*p* value
Age (year)	47.55 ± 13.31	49.96 ± 16.52	NS
BMI (kg/m^2)	28.24 ± 5.72	30.05 ± 7.19	NS
Duration of Symptoms (month)	22.60 ± 31.81	23.22 ± 37.28	NS
Follow-Up Period (month)	46.65 ± 57.20	39.52 ± 53.60	NS
Tumour Diameter (mm)	14.89 ± 0.47	19.96 ± 8.20	NS
At the Time of Hypoglycemia			
Blood Glucose Level (mg/dL)	37.15 ± 9.10	38.05 ± 7.87	NS
Insulin Level (mU/L)	28.11 ± 25.14	33.95 ± 23.87	NS
C- Peptide Level (μg/L)	3.64 ± 2.05	4.73 ± 1.97	$p < 0.05$

Note: Data are given as mean ± standard deviation (SD). One-way ANOVA, Student *t* test.
Abbreviations: BMI, Body mass index; NS, Not significant.

TABLE 2 | Features of hypoglycaemia symptoms and comorbidities on admission.

	Female		Male		Total		
Clinical presentation of hypoglycemia	**n**	**%**	**n**	**%**	**n**	**%**	***p* value**
Neuroglycopenic symptoms	25	51.1	18	66.6	43	56.6	NS
Adrenergic symptoms	13	26.5	5	18.5	18	23.7	NS
Both symptoms	11	22.4	3	11.1	14	18.4	NS
Data not available	0	0	1	3.8	1	1.3	NS
Time of symptomatic hypoglycemia							
Fasting	36	73.5	17	63.0	53	69.7	NS
Postprandial	1	2.0	1	3.7	2	2.6	NS
In both situations	12	24.5	9	33.3	21	27.7	
Detection of hypoglycemia							
Spontaneously	25	51.1	10	37.0	35	46.1	NS
During prolonged fasting test	24	48.9	17	63.0	41	53.9	NS
Comorbidities	**37/49**	**75.5**	**15/27**	**55.5**	**52/76**	**68.4**	
Hypertension	11	29.7	7	46.6	18	34.6	NS
Hypothyroidism	9	24.3	0	0	9	17.3	< 0.05
Coronary artery disease	3	8.2	1	6.7	4	7.7	NS
Diabetes mellitus	2	5.4	1	6.7	3	5.8	NS
Men1 syndrome	1	2.7	3	20.0	4	7.7	NS
Atrial fibrillation	0	0	3	20.0	3	5.8	NS
Other	11	29.7	0	0	11	21.1	

Abbreviation: NS, Not significant.

containing carbohydrates. For insulinoma patients experiencing persistent and severe hypoglycemia, the first-line medical treatment is diazoxide. However, due to occasional supply issues in our country, close blood glucose monitoring and dextrose infusion are used to maintain euglycemia during the diagnostic evaluation and preoperative period. In this study, the preoperative definitive diagnosis (DD) rate was 98.7%. The most frequently used imaging modality was endoscopic ultrasound (EUS), followed by computed tomography (CT) and magnetic resonance imaging (MRI). While EUS was the most frequently used diagnostic method in both genders, the diagnostic rate with CT was higher in men, whereas MRI and ultrasonography (USG) had higher diagnostic rates in women. The number and percentage of techniques used are presented in Table 3.

3.5 | Tumour Characteristics

Insulinomas were predominantly located in the body and tail of the pancreas, with only two cases (one female and one male) found in the head. In one patient, tumour localisation could not be identified using imaging methods. Most tumours (66 cases) were solitary, while eight cases were multiple. Metastases were detected in nine out of 76 patients, with the most common sites being regional lymph nodes and the liver. Additionally, one patient had metastases in both locations, and another had lung metastases (Table 4). Among the metastases, one was multiple, while the others were solitary insulinomas. MEN components were not detected in any of these cases.

3.6 | Tumour Size and Surgical Management

Regarding tumour size, 58 cases (76%) measured less than 2 cm, while 18 cases (24%) were larger than 2 cm. No statistically significant differences were observed between women and men in terms of tumour localisation, number, metastasis site, or size. Four patients declined surgery. Enucleation and distal pancreatectomy were the predominant surgical techniques employed in this study, while pancreaticoduodenectomy was performed in only five cases. The type of surgery was unspecified for five patients (7%). No statistically significant difference was observed between women and men regarding the type of surgery (Table 5).

3.7 | Follow-Up and Prognosis

Among the patients who were followed for an average of 44 months, the remission rate was 91%, non-remission was 4%, and the mortality rate was 5% (Table 6). During the follow-up period, one patient died due to insulinoma-related causes, while three patients died from other causes. Overall, following surgery, hypoglycaemia symptoms resolved in 90% of patients.

In this study, long-term outcomes related to insulinoma could not be obtained, as our follow-up period was less than 4 years. However, it has been reported that the majority of recurrences and postoperative complications associated with insulinoma typically occur within the first few years after surgery. Therefore, although the follow-up period in our study is less than

TABLE 3 | Results of methods used to detect insulinoma.

Techniques	Female		Male		Total		DD	*p* value
	n	%	n	%	n	%	%	
EUS	24	48.9	13	48.1	37	**48.7**	**82.2**	NS
Ga-68 PET/CT	14	28.6	8	29.6	22	**28.9**	**78.6**	NS
CT	22	44.8	15	55.5	37	**48.7**	**62.8**	< 0.05
MRI	18	36.7	6	22.2	34	**44.7**	**58.6**	< 0.05
FDG PET	2	4.1	0	0	2	**2.6**	**50.0**	NS
USG	4	8.1	4	14.8	8	**10.5**	**19.5**	< 0.05

Abbreviations: CT, Computerised tomography; DD, Definitive diagnosis; EUS, Endoscopic ultrasound; FDG- PET, fluorodeoxyglucose positron emission tomography; Ga 68- PET/CT, Ga-68 dotatate PET/CT scan; MRI, Magnetic resonance imaging; NS, Not significant; USG, Ultrasonography.

TABLE 4 | Location, number and characteristics of insulinoma.

Tumour Location	Female ($n = 49$)		Male ($n = 27$)		Total ($n = 76$)		*p* value
	n	%	n	%	n	%	
Head	1	2.2	0	0.0	1	1.4	NS
Body	21	42.8	9	33.3	30	39.4	NS
Tail	12	24.4	9	33.3	21	27.6	NS
Data not available	15	30.6	9	33.3	24	31.6	
Number							
Solitary	42	85.7	24	88.8	66	86.8	NS
Multiple	6	12.2	2	7.4	8	10.5	NS
Data not available	1	2.1	1	3.8	2	2.7	NS
Metastasis site	**7**	**14.2**	**2**	**7.4**	**9**	**11.8**	
Liver	1	14.3	1	50.0	2	22.2	NS
Lymph node	3	42.8	1	50.0	4	44.4	NS
To both places	1	14.3	0	0	1	11.1	NS
Lung	1	14.3	0	0	1	11.1	NS
Data not available	1	14.3	0	0	1	11.1	NS

Abbreviation: NS, Not significant.

TABLE 5 | Preferred methods of surgery.

Type of Surgery	Female ($n = 46$)		Male ($n = 26$)		Total ($n = 72$)		*p* value
	n	%	n	%	n	%	
Tumour enucleation	21	45.6	12	46.1	33	45.8	NS
Distal pancreatectomy	18	39.2	11	42.3	29	40.2	NS
Pancreaticodoudenectomy	4	8.7	1	3.9	5	7.0	NS
Not reported	3	6.5	2	7.7	5	7.0	

Abbreviation: NS, Not significant.

4 years, it still provides clinically meaningful data regarding the short- and medium-term outcomes of surgical and medical treatments. Additionally, since insulinoma is a rare disease, establishing larger datasets with longer follow-up periods remains a challenge for many centres. Further studies on this subject are needed.

In our study, it is believed that the small subset of patients (approximately 10%) who did not achieve complete resolution of hypoglycemia after surgery had various underlying causes. Some of these patients were diagnosed with metastatic insulinoma, which is associated with malignant disease and low surgical cure rates. In other patients, the persistence of hypoglycemia was thought to be due to incomplete resection caused by the tumour's location or multifocality. Sometimes, despite preoperative imaging, difficulties can arise in detecting small tumours or widespread nesidioblastosis intraoperatively.

TABLE 6 | Disease course during follow-up.

	Female ($n = 47$)		Male ($n = 24$)		Total ($n = 71$)		
Prognosis	**n**	**%**	**n**	**%**	**n**	**%**	***p* value**
Remission	43	91.6	21	87.5	64	90.1	NS
Non-Remission	2	4.2	1	4.2	3	4.2	NS
Mortality	2	4.2	2	8.3	4	5.7	NS

Abbreviation: NS, Not significant.

3.8 | Pathological Findings

Pathological examination of surgical samples revealed that the Ki-67 proliferation index was below 3 in 38 patients (30 female, eight male), between 3 and 20 in 23 patients (11 female, 12 male), and greater than 20 in one male patient. The mitotic index was less than 2 in 41 cases and greater than 2 in 13 cases. A high Ki-67 proliferation index and mitotic index were detected in one patient, a male with metastatic cancer, which was associated with reduced survival.

3.9 | Statistical Analysis Considerations

Selection Bias: To minimise selection bias inherent in retrospective studies, patients were included based on predefined eligibility criteria from multiple centres. However, the potential for bias in data completeness and variations in diagnostic approaches across institutions remains a limitation.

3.9.1 | Statistical Methods

Categorical variables were analysed using Fisher's exact test or the chi-square test, depending on sample size and expected frequencies. Group comparisons were performed using Student's *t*-test for normally distributed continuous variables and the Mann-Whitney U test for non-normally distributed variables. Poisson regression was employed to evaluate potential changes in insulinoma incidence over time, as it allows for modelling count data while adjusting for potential confounders.

3.9.2 | Missing Data Handling

Cases with missing critical variables were excluded from analysis. However, minor missing data points were managed using multiple imputation methods to reduce bias.

3.9.3 | Power Analysis

Given the rarity of insulinoma, a formal power analysis was not performed before data collection. However, post hoc calculations indicated that the sample size of 76 patients provided sufficient power to detect statistically significant differences in key variables such as C-peptide levels, comorbidities, and surgical outcomes.

By incorporating these methodological considerations, this study offers a robust analysis of insulinoma characteristics, diagnosis, and management while acknowledging its inherent limitations.

4 | Discussion

Insulinomas are rare neuroendocrine tumours of the pancreas, with reported incidence rates varying by region. While epidemiological studies indicate a lower prevalence in Europe and Australia (0.7–1.2 cases per million per year), higher rates have been documented in Japan and the United States (3.3 and 4.0 cases per million per year, respectively) [4, 9–12]. However, no epidemiological studies have been conducted in our country, making the true prevalence of insulinoma unknown. Our study provides the first comprehensive, multicenter analysis of insulinoma cases in the Türkiye, offering valuable insights into clinical presentation, diagnostic challenges, and treatment outcomes.

Our findings confirm that insulinoma is more common in women (64.5%) and is typically diagnosed in middle-aged individuals (mean age: 48 years). These results align with previous studies reporting a female predominance and a mean age of onset around 50 years [12]. The mean symptom duration before diagnosis in our cohort was 22 months, consistent with the literature, which reports delays of 18–30 months [20]. The delay in diagnosis is often attributed to the episodic nature of hypoglycemia and the frequent misdiagnosis of neuroglycopenic symptoms as psychiatric or neurological disorders. In our study, 5% of patients had been prescribed antiepileptics and 8% antidepressants before their insulinoma diagnosis, highlighting the risk of misclassification.

4.1 | Hypoglycemia Patterns and Diagnostic Considerations

Hypoglycemia in insulinoma patients predominantly occurs during fasting; however, some patients experience symptoms postprandially or in both states. Our findings indicate that fasting hypoglycemia was the most common presentation (70%), followed by a combination of fasting and postprandial hypoglycemia (27%), and exclusive postprandial hypoglycemia in 3% of cases. These results are consistent with previous reports, such as those by Placzkowski et al., who found fasting hypoglycemia in 73% of cases, mixed hypoglycemia in 21%, and postprandial hypoglycemia alone in 6%. [13–15], Interestingly,

our data also support the observation that postprandial hypoglycemia is more frequently seen in men. This finding suggests that insulinoma should be considered in the differential diagnosis of patients presenting with postprandial symptoms, even in the absence of fasting hypoglycemia.

4.2 | Comorbidities and Their Clinical Relevance

The presence of comorbid conditions in insulinoma patients is increasingly recognised, with hypertension being the most frequently reported. In our study, hypertension was the most common comorbidity (35%), aligning with recent findings suggesting a link between insulinoma and increased catecholamine release or hyperinsulinemia-induced sodium retention [16–22]. Other cardiovascular comorbidities, such as coronary artery disease (8%) and atrial fibrillation (6%), were also observed in our cohort. While the impact of recurrent hypoglycemia on cardiovascular morbidity in insulinoma patients remains unclear, the observed prevalence of these conditions supports the need for further investigation into their pathophysiological association.

In addition to cardiovascular conditions, our study identified several other comorbidities, including osteoporosis, depression, celiac disease, and thyroid disorders. The presence of MEN1 was observed in 8% of our cases, which is within the expected prevalence range of 6%–13% for insulinoma-associated MEN1 syndrome [23]. Additionally, while insulinoma in diabetic patients is rare, we identified three cases of diabetes coexisting with insulinoma, supporting previous case reports that describe this uncommon association [21].

4.3 | Tumour Localisation and Preoperative Imaging

Accurate preoperative localisation of insulinomas is crucial for effective surgical management. Consistent with previous literature, our study found that EUS was the most sensitive imaging modality, with a tumour detection rate of 82% [22]. While some studies have reported insulinomas as being more frequently located in the pancreatic tail [22, 24, 25], our findings revealed that the pancreatic body (39%) was the most common site, followed by the tail (28%). These variations suggest potential regional differences in tumour distribution or differences in imaging detection sensitivity.

4.4 | Tumour Characteristics and Metastatic Potential

Most insulinomas are small and solitary, with a low potential for metastasis [1–4, 8–10, 12, 13, 20, 24–28]. In our study, 76% of tumours measured < 2 cm, while 24% were > 2 cm, a size that is often associated with increased malignant potential [28–31]. Nine out of 76 patients (12%) had metastatic disease, primarily involving the liver and regional lymph nodes. These findings align with previous reports indicating that 8%–10% of insulinomas exhibit malignant behaviour [31].[309] Despite the presence of metastatic cases, our surgical outcomes were favourable, with a high remission rate (90%), a low recurrence rate (4%), and a mortality rate of 6%. The relatively low mortality observed, even in metastatic cases, suggests that early detection and surgical intervention play a critical role in improving patient prognosis.

4.5 | Clinical Implications and Future Directions

Our study highlights several critical aspects of insulinoma diagnosis and management. The frequent misdiagnosis of neuroglycopenic symptoms as psychiatric or neurological disorders underscores the need for increased clinical awareness. Given that a subset of patients presented with postprandial hypoglycemia alone, clinicians should consider insulinoma in patients with unexplained postprandial symptoms. Additionally, the high prevalence of hypertension and other cardiovascular comorbidities warrants further investigation into the long-term effects of insulinoma-related hyperinsulinemia on cardiovascular health [5–9, 14, 16–20, 29–36].

4.6 | Study Limitations

The primary limitation of our study is its retrospective nature, which may introduce selection bias and limit long-term prognostic insights. Additionally, while our multicenter data set provides a large and diverse patient population, further prospective studies are needed to validate our findings and explore potential regional variations in insulinoma presentation and management.

5 | Conclusion

This study provides the first multicenter analysis of insulinoma cases in our country, offering valuable insights into its clinical characteristics, diagnostic challenges, and treatment outcomes. Our findings reinforce the importance of early recognition and accurate localisation of insulinomas, particularly in patients with atypical presentations. Given the significant morbidity associated with delayed diagnosis, a heightened clinical suspicion and a multidisciplinary approach are essential for optimising patient outcomes. Future research should focus on refining diagnostic criteria, exploring the long-term cardiovascular risks associated with insulinoma, and standardising treatment protocols to improve patient care.

Author Contributions

Ş.T., G.F.Y., data collection, data analysis, writing of original draft, supervision, writing-review and editing. Z.Y., F.A.M., S.K., S.Ç., M.S.E., B.O.P., A.Ö.Y., K.U., O.B., S.S.Z., İ.E., M.G., F.M.C., S.F., Ş.B.P., B.Ç., H.Ö., G.Ü.K., M.E., Ş.Ç., İ.Ç.K., E.A., S.Y.: data collection, data analysis, and editing. All authors approved the final version of the paper.

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Data Availability Statement

Data available on request from the corresponding author.

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