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QUALITY OF LIFE AMONG TYPE 1 DIABETIC PATIENTS TREATED WITH NEUTRAL PROTAMINE HAGEDORN (NPH) INSULIN REGIMEN

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ABSTRACT

Background: *Type 1 Diabetes Mellitus (T1DM) requires lifelong insulin therapy for survival, glycemic control and prevention of acute and chronic complications. Neutral Protamine Hagedorn (NPH) insulin remains widely used in low- and middle-income countries because of its affordability and availability. NPH insulin has a peak action profile and may be associated with hypoglycemia, glycemic variability, treatment burden and reduced health-related quality of life.*

Objective: *This study aimed to assess quality of life parameters among patients with T1DM receiving NPH insulin in Pakistan.*

Materials and Methods: *This NPH-only analysis included 90 patients with confirmed T1DM receiving NPH insulin. Demographic and clinical characteristics, glycemic control, hypoglycemia frequency and severity, medication adherence, adverse drug reactions, SF-36 quality of life domains and Diabetes Quality of Life (DQOL) scores were analyzed descriptively. Continuous variables were reported as mean ± standard deviation while categorical variables were presented as frequency and percentage. No comparison with other insulin regimens was included.*

Results: *The mean age of NPH users was 27.5 ± 9.2 years and the mean duration of diabetes was 8.2 ± 5.1 years. Mean HbA1c was 8.2 ± 1.1%, fasting blood glucose was 165 ± 30 mg/dL and postprandial blood glucose was 240 ± 40 mg/dL. Follow-up HbA1c was 7.9 ± 0.9%. Hypoglycemia was common, with 39% reporting 1–2 episodes/month and 28% reporting ≥3 episodes/month. Severe hypoglycemia occurred in 24% of patients. The overall SF-36 score was 60.2 ± 9.1 while the overall DQOL score was 62.0 ± 8.6. The lowest quality of life scores was observed in the social domains.*

Conclusion: *T1DM patients receiving NPH insulin in Pakistan showed moderate quality of life, suboptimal glycemic control, frequent hypoglycemia and variable adherence. Routine quality of life assessment, hypoglycemia prevention and structured patient education should be integrated into care for NPH-treated T1DM patients.*

Keywords: *Type 1 Diabetes Mellitus, NPH insulin, quality of life, SF-36, DQOL, HbA1c, hypoglycemia, Pakistan.*

INTRODUCTION

Diabetes Mellitus Type 1 Diabetes Mellitus (T1DM) is a chronic autoimmune metabolic disease that is characterized by the destruction of pancreatic beta cells, resulting in an absolute deficiency of insulin and life-long dependence on exogenous insulin. Contrary to Type 2 Diabetes Mellitus, which is typically linked to insulin resistance and progressive beta-cell dysfunction,

T1DM, in general, necessitates insulin replacement since the time of diagnosis. The disease requires lifelong self-management which includes administration of insulin, monitoring of blood glucose, regulation of diet, adjustment of physical activity and the process of the recognition of hypoglycemia symptoms [1,2]. T1DM also influences the functioning of everyday life, emotional well-being, social participation, satisfaction with treatment and the overall quality of life.

Insulin therapy has been the mainstay of management of T1DM. Insulin therapy is aimed at recreating physiological insulin secretion as much as possible by covering both basal and prandial insulin secretion. Basal insulin is used to maintain the normal glucose levels between meals and at night, whereas prandial insulin is used to keep the normal glucose levels within the body after eating meals. Neutral Protamine Hagedorn (NPH) is an intermediate-acting human insulin that over a number of decades has been used as a basal insulin option. Although long-acting insulin analogues are available, NPH insulin continues to be used in developing countries because of their lower price and relatively high availability [3,4].

The further utilization of NPH insulin is especially applicable in such a country as Pakistan where a significant number of patients pay out of pocket to treat diabetes. The affordability of insulin, its availability and continuous access is a significant issue in the low- and middle-income context. Patients are unable to afford newer insulin analogues, glucose monitoring supplies or frequent specialist follow-up. NPH insulin remains a significant part of an everyday diabetes treatment, particularly in patients with restricted financial means [5,6].

NPH insulin possesses pharmacological weaknesses, which can affect patient experience. It is a variable absorption profile with a strong peak action. Such features can predispose to the development of hypoglycemia, especially when the meals are delayed, the physical activity increases suddenly or the action of insulin peaks at night. One of the complications of insulin therapy is called hypoglycemia. It can lead to sweating, shaking, palpitations, dizziness, anxiety, loss of consciousness or emergency hospitalization in life-threatening situations [7,8]. Even non-severe forms of hypoglycemia can instill fear and lower the confidence levels of insulin therapy.

Quality of life has emerged as a significant patient-reported outcome in the study of diabetes. HbA1c, fasting blood glucose, postprandial glucose and complication rates are traditional diabetes outcomes that are still important but not complete in capturing the lived experience of patients. A patient can have a quantifiable improvement in glycemic control and still feel fatigued, with burden in the therapy, anxious, fearful of hypoglycemia, socially restricted or dissatisfied with therapy. Accordingly, health-related quality of life offers more comprehensive knowledge of the effects of disease and treatment on physical, psychological, social and functional well-being [9,10].

A number of instruments have been employed in measuring the quality of life in diabetes. The SF-36 is a generic health-related quality of life measure that assesses domains of physical functioning, role limitation, bodily pain, general health, vitality, social functioning, emotional role and mental health. The Diabetes Quality of Life (DQOL) measuring instrument is more specifically concerned with diabetes related issues, impact of treatment, satisfaction and social or emotional impacts of living with diabetes [9,11]. These instruments assist clinicians and researchers to comprehend the results that cannot be measured using lab results alone.

Research has indicated that insulin therapy can have various effects on quality of life. Insulin therapy may alleviate hyperglycemia symptoms and decrease the risk of complications, although it can also raise treatment burden, anxiety associated with injections, fear of hypoglycemia and

psychological distress [12,13]. In other investigations, it is reported that patients who were insulin treated had lower mental component scores, implying that psychological and behavioral support should be provided in addition to pharmacological management [14]. A study of patients with T1DM treated with insulin analogues has also implied that improved glycemic control is related to improved DQOL scores [15].

Various clinical and social factors determine the quality of life of diabetic patients. They are age, gender, length of diabetes, body mass index, hypoglycemia, glycemic control, complications, comorbidities, adherence to treatment, level of education, income, family support and access to diabetes care [16,17]. The emotional health, the productivity of work, the education, family and social relationships may be impacted by the burden of daily self-care in chronic diseases like T1DM. The quality-of-life evaluation is particularly significant in patients, who undergo insulin regimens, which require close timing and monitoring.

There is a shortage of local evidence on the quality of life with the use of NPH insulin among patients with T1DM in Pakistan. The majority of diabetes studies in Pakistan are related to Type 2 diabetes, its prevalence, glycemic control, pharmacotherapy or complications. Among T1DM patients undergoing widely-used basal insulin therapy, less focus has been given to patient-reported outcomes. Given that NPH insulin continues to be a significant and cost-effective treatment, the need to understand quality of life among NPH users, can provide clinicians with clinical and psychosocial needs in this group [5,6,18].

The rationale of this study is that NPH insulin is still a widely-relevant intervention in Pakistan, yet patients taking NPH insulin may experience hypoglycemia, fluctuating glycemic levels, treatment burden and social or emotional restriction. The rationale behind conducting this NPH analysis was to evaluate the parameters of quality of life among T1DM patients receiving NPH insulin in Pakistan. The research is restricted to the NPH users and not a comparison of the NPH with any other insulin regimen. The aim is to describe the quality-of-life profile, glycemic status, burden of hypoglycemia, adherence and adverse drug reactions among patients with T1DM who are treated with NPH insulin.

Materials and Methods

This research is an NPH descriptive analysis that was carried out among patients with Type 1 Diabetes Mellitus in Pakistan. The current study has only considered patients who are undergoing NPH insulin. No comparison among various insulin regimens was done.

The population of the study was 90 patients with known T1DM who were on NPH insulin. Inclusion criteria included a confirmed diagnosis of T1DM, the use of NPH insulin as a part of their treatment regimen, the ability to answer the quality-of-life questionnaire. Patients who had Type 2 Diabetes Mellitus, were pregnant, in lactation, had severe acute illness or major comorbid conditions that might independently contribute to quality of life were excluded.

Demographic and clinical variables consisted of age, gender, body mass index, the duration of diabetes, hypertension, dyslipidemia and smoking status. Glycemic variables encompassed HbA1c and fasting glucose, postprandial glucose, follow-up HbA1c, follow-up fasting glucose and HbA1c reduction. Hypoglycemia was reported based on frequency and severity. Adherence to medication and adverse drug reaction were also reported.

The quality of life was measured by SF-36 domain scores and using diabetes-specific DQOL scores. SF-36 parameters comprised of physical, psychological, social, environmental and general quality of life scores. DQOL parameters were physical, mental, social, pain and general DQOL scores. The higher the scores, the higher the quality of life was.

Data analysis was done on a descriptive basis on SPSS Version 26 . Continuous variables were provided in the form of mean, standard deviation, whereas categorical variables were provided in the form of frequency and percentage. The aim of this paper was to describe a set of parameters of quality of life in NPH insulin users. The results were reported using detailed tables to outline the

clinical and quality of life profile of T1DM patients who took NPH insulin.

Results

A total of 90 patients with Type 1 Diabetes Mellitus receiving NPH insulin were included in this analysis. The results are presented according to baseline demographic and clinical characteristics, glycemic profile, hypoglycemia frequency and severity, SF-36 quality of life domains, DQOL domains, medication adherence and adverse drug reactions.

Table 1. Baseline Demographic and Clinical Characteristics of T1DM Patients Receiving NPH Insulin (n = 90)

Variable	NPH Insulin Users
Age (years)	27.5 ± 9.2
Male	55%
Female	45%
BMI (kg/m²)	20.9 ± 3.1
Duration of diabetes (years)	8.2 ± 5.1
Hypertension	25%
Dyslipidemia	20%
Smoking	15%

The mean age of NPH insulin users was 27.5 ± 9.2 years, indicating a young adult T1DM population. The mean duration of diabetes was 8.2 ± 5.1 years, showing that most patients had been living with T1DM for several years. Male participants represented 55% of the sample while females represented 45%.

Table 2. Glycemic Profile of T1DM Patients Receiving NPH Insulin

Glycemic Parameter	Mean ± SD
HbA1c (%)	8.2 ± 1.1
Fasting blood sugar (mg/dL)	165 ± 30
Postprandial blood sugar (mg/dL)	240 ± 40
Follow-up HbA1c (%)	7.9 ± 0.9
Follow-up fasting glucose (mg/dL)	138 ± 25
HbA1c reduction	−1.4 ± 1.0

The glycemic profile showed suboptimal metabolic control among NPH insulin users. Mean HbA1c was 8.2 ± 1.1%, fasting blood sugar was 165 ± 30 mg/dL and postprandial blood sugar was 240 ± 40 mg/dL. Follow-up HbA1c improved to 7.9 ± 0.9%, with a mean HbA1c reduction of −1.4 ± 1.0.

Table 3. Frequency of Hypoglycemia among T1DM Patients Receiving NPH Insulin

Hypoglycemia Frequency	Frequency	Percentage
No episodes	30	33%
1–2 episodes/month	35	39%
≥3 episodes/month	25	28%
Total	90	100%

Hypoglycemia was a prominent clinical issue among NPH users. Only 33% of patients reported no hypoglycemic episodes. In contrast, 39% reported 1–2 hypoglycemic episodes per month

while 28% reported three or more episodes per month.

Table 4. Severity of Hypoglycemia among T1DM Patients Receiving NPH Insulin

Severity of Hypoglycemia	Frequency	Percentage
Mild	30	33%
Moderate	38	42%
Severe	22	24%
Total	90	100%

Moderate hypoglycemia was reported by 42% of patients while severe hypoglycemia was reported by 24%. This indicates that hypoglycemic burden among NPH users was not limited to mild episodes and may have affected daily functioning, emotional well-being and treatment confidence.

Table 5. SF-36 Quality of Life Domain Scores among T1DM Patients Receiving NPH Insulin

SF-36 Domain	Mean ± SD	Interpretation
Physical domain	60 ± 11	Moderate physical quality of life
Psychological domain	62 ± 10	Moderate psychological well-being
Social domain	58 ± 12	Lowest domain score; social burden present
Environmental domain	61 ± 9	Moderate environmental health perception
Overall SF-36 quality of life	60.2 ± 9.1	Moderate overall quality of life

The overall SF-36 quality of life score was 60.2 ± 9.1. Among SF-36 domains, the social domain had the lowest score at 58 ± 12, followed by physical health at 60 ± 11. These results suggest moderate overall quality of life with meaningful social and physical limitations.

Table 6. DQOL Domain Scores among T1DM Patients Receiving NPH Insulin

DQOL Domain	Mean ± SD	Interpretation
Physical domain	61.3 ± 10.4	Moderate physical diabetes-related QoL
Mental domain	62.5 ± 9.8	Moderate mental diabetes-related QoL
Social domain	59.7 ± 11.2	Social concerns evident
Pain domain	64.2 ± 9.6	Relatively better pain-related score
Overall DQOL	62.0 ± 8.6	Moderate diabetes-related QoL

The overall DQOL score was 62.0 ± 8.6. The social domain was among the lower-scoring areas at 59.7 ± 11.2 while the pain domain showed a relatively better score of 64.2 ± 9.6. These findings indicate that diabetes-specific quality of life was moderate among patients receiving NPH insulin.

Table 7. Medication Adherence among T1DM Patients Receiving NPH Insulin

Adherence Level	Frequency	Percentage
High adherence	40	44.4%
Moderate adherence	34	37.8%

Low adherence	16	17.8%
Total	90	100%

High adherence was observed in 44.4% of NPH users. Moderate adherence was seen in 37.8% while low adherence was reported in 17.8%. This indicates that more than half of the patients had less than high adherence.

Table 8. Adverse Drug Reactions among T1DM Patients Receiving NPH Insulin

Adverse Drug Reaction Status	Frequency
Adverse drug reactions reported	22%
No adverse drug reactions reported	78%

Adverse drug reactions were reported by 22% of NPH users. Although most patients did not report adverse drug reactions, the presence of adverse reactions in more than one-fifth of the sample is clinically relevant.

Table 9. Summary Profile of Quality of Life and Clinical Burden among NPH Insulin Users

Parameter	Observed Finding
Overall SF-36	60.2 ± 9.1
Overall DQOL	62.0 ± 8.6
Lowest SF-36 domain	Social domain: 58 ± 12
Lowest DQOL domain	Social domain: 59.7 ± 11.2
HbA1c	8.2 ± 1.1%
Follow-up HbA1c	7.9 ± 0.9%
Any hypoglycemia	67%
Severe hypoglycemia	24%
High adherence	44.4%
Adverse drug reactions	22%

The overall pattern shows moderate quality of life among NPH insulin users, with social functioning being the most affected area. The clinical profile also shows suboptimal HbA1c, frequent hypoglycemia and variable adherence.

Discussion

This is an NPH-alone study that evaluated the quality-of-life profile of 90 patients with Type 1 Diabetes Mellitus using NPH insulin in Pakistan. The results indicated a moderate overall quality of life, an overall SF-36 score of 60.2 ± 9.1 and an overall DQOL score of 62.0 ± 8.6. The scores suggest that patients being treated with NPH were not reporting a massively poor quality of life but they were not experiencing an optimally good well-being either. Social functioning in both instruments was the most affected with a SF-36 social score of 58 ± 12 and a DQOL social score of 59.7 ± 11.2.

The social burden witnessed in this study is a clinically significant burden. T1DM involves regular insulin injections, meal planning, glucose monitoring, focus on physical activity and hypoglycemia awareness. These responsibilities may interfere with studies, work, family interactions and social participation. Past literature has pointed out that diabetes-related quality of life is multidimensional and encompasses physical, emotional and social factors and not just glucose levels [9,13]. The current results reinforce this perspective since social scores were one of the lowest qualities of life domains even though there were improvements in HbA1c in the follow-up.

The NPH group has a glycemic profile that appears to indicate suboptimal control. The mean HbA1c

level was 8.2 ± 1.1, with fasting blood glucose and postprandial blood glucose of 165 ± 30 mg/dL and 240 ± 40 mg/dL, respectively. Despite the fact that follow-up HbA1c improved to 7.9 ± 0.9% it was still above the commonly recommended levels of many adults with T1DM. Poor glycemic control in T1DM risk increases microvascular and macrovascular complications, as well as influences the symptoms, fatigue and concern about future health [1,11].

The DQOL results are aligned with the idea that there is a connection between glycemic status and perceived quality of life. The total DQOL score was 62.0 ± 8.6 and domain scores ranged between 59.7 ± 11.2 in the social domain up to 64.2 ± 9.6 in the pain domain. A comparison of the T1DM patients who received insulin analogues found that the DQOL scores were better in patients with HbA1c 8-percent or below [15]. Follow-up HbA1c in the current NPH-treated cohort was moderate but not high, in quality of life.

One of the most significant clinical burdens in the sample was hypoglycemia. Only 33% of NPH users reported no episodes of hypoglycemia, 39% reported 1-2 episodes per month and 28% reported 3 or more episodes per month. The prevalence of severe hypoglycemia was reported among 24% of patients. It is significant as hypoglycemia is known to have a detrimental impact on health-related quality of life, confidence in treatment and patient-reported outcomes [7,8]. In patients with NPH insulin, the peak action of the intermediate-acting insulin may add to the occurrence of hypoglycemic episodes, especially when meals are delayed, physical activity changes or a fall in the amount of glucose in the body overnight.

Median psychological score of 62 ± 10 on SF-36 and mental DQOL score of 62.5 ± 9.8 may also be partly explained by the fear of hypoglycemia. The patients with repeated hypoglycemia can develop the fear of falling asleep, exercising, travelling, attending social events or being alone. Others might purposefully lower the dose of insulin or increase the amount of food consumed to avoid occurrence of episodes which can aggravate glycemic control. This hypoglycemia fear/glycemic instability loop might be particularly applicable to patients who are treated with NPH insulin [7,20].

In this NPH-treated group, medication adherence was variable. There was high adherence among 40 patients (44.4%), moderate among 34 patients (37.8%) and low among 16 patients (17.8%). This implies that 55.6% of sample did not belong to the high-adherence group. Insulin adherence plays a critical role in T1DM but it is affected by cost, education, fear of hypoglycemia, injection burden, patient motivation and care provider support [4,12]. The identified adherence pattern could also be one of the reasons behind the observed HbA1c and quality of life profile of this group.

Two out of five NPH users reported adverse drug reactions. Though adverse reactions were not reported by the majority of patients, this percentage is significant since the adverse experience may decrease the satisfaction and adherence rates to the treatment. Even the slight or moderate issues related to the treatment, in the case of chronic diseases like T1DM, may accumulate over time and lead to treatment fatigue. Tolerability in patients is a significant aspect of insulin therapy assessment [2].

The current findings also should be analyzed in the Pakistani healthcare setting. NPH insulin is still clinically viable due to the fact that it is usually cheaper than the long-acting analogues. Affordability in low-resource settings may be the deciding factor on whether patients can afford to pursue insulin therapy. Affordability is not a guarantee of good results. Patients taking NPH insulin might need a more intensive education regarding injection time, meal planning, glucose monitoring and prevention of hypoglycemia. Research on insulin access and the management of diabetes in developing contexts stresses the importance of availability, affordability and continuity of care being central to diabetes outcomes [3,5,6].

The medium quality of life profile that has been observed in this research indicates that a regular patient-reported outcome assessment in clinics should be conducted. The data of SF-36 and DQOL can assist clinicians to determine patients who are struggling socially, physically or emotionally despite having routine clinical records

which mainly emphasize on HbA1c. Recent research on quality of life as measured by patient reports suggests that patient-reported outcomes be used to inform education and individualized care [16,18]. The social domain was persistently low in the given sample, which implies that patient counseling is not to be limited to insulin dose adjustment only but must be applied to school and work, family, social confidence and fear of hypoglycemia.

The results do indicate that patients who get NPH insulin should be closely monitored. NPH is a significant basal insulin option where cost is a critical consideration, yet safe and effective usage requires patient education, frequent monitoring and individualized treatment planning. Practical interventions can involve the provision of structured hypoglycemia education, review of dose timing, self-monitoring training, availability of glucose testing supplies, adherence counseling and family involvement.

The current NPH-only data bring in local data evidence in Pakistan compared to the global quality of life literature. Past research has indicated that quality of life in diabetes might be affected by metabolic control, hypoglycemia, complications, treatment regimen and sociodemographic factors [13,18]. There is not much evidence on quality-of-life parameters in relation to Pakistani patients with T1DM who are treated with NPH insulin. This can render the current analysis of interest to clinicians and researchers that are interested in patient-centered diabetes care in resource-constrained environments.

Limitations

There are certain limitations of this analysis. First, it enrolls only NPH insulin users and does not set comparative effectiveness with other insulin regimens. Second, the sample size was also restricted to 90 patients which can limit the generalizability. Third, data on quality of life and hypoglycemia were partly based on patient reporting and may have some recall bias. Fourth, the analysis was descriptive and did not involve NPH-only regression modeling due to the lack of raw individual-level data in this extracted paper. Fifth, socioeconomic status, affordability of insulin, detailed status of complication and frequency of glucose monitoring were not fully studied.

Future Directions

The future researchers are encouraged to conduct larger multicenter cohorts of patients with T1DM using NPH insulin in Pakistan. The longitudinal designs are required to evaluate the variations in SF-36 and DQOL scores over time. Predictors of quality of life in NPH users (including HbA1c, hypoglycemia, adherence, socioeconomic status, education, complications, insulin affordability and access to glucose monitoring), should also be evaluated in future research. Mixed-method research can prove useful in exploring the patient experiences, barriers to treatment, fear of hypoglycemia and social limitation in more depth.

Conflict of Interest

The authors declare no conflict of interest.

Conclusion

In Pakistan, patients with T1DM who were put on NPH insulin demonstrated moderately good overall quality of life, with their social functioning being the most impacted area. Significant clinical characteristics of this group were suboptimal glycemic control, frequent hypoglycemia, variable adherence and adverse drug reactions. Regular quality of life evaluation and systematic hypoglycemia-centered education should be implemented in the management of NPH-treated T1DM patients.

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