



Health-Related Quality of Life in Children and Adolescents with Type 1 Diabetes

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Authors' contributions

This work was carried out in collaboration between all authors. Author EK designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors PP and VM managed the analyses of the study. Author VM managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2017/31345

Editor(s):

(1) Nicolas Padilla-Raygoza, Department of Nursing and Obstetrics, Campus Celaya Salvatierra University of Guanajuato, Mexico.

Reviewers:

(1) Gonzalo Emiliano Aranda Abreu, Universidad Veracruzana, Centro de Investigaciones Cerebrales, Mexico.
(2) Armando Cuéllar Cuéllar, Havana University, Cuba.

Complete Peer review History: <http://www.sciencedomain.org/review-history/18199>

Received 31st December 2016

Accepted 7th March 2017

Published 15th March 2017

Review Article

ABSTRACT

Purpose: The evaluation of the children's quality of life has been established and applied to those suffering from chronic diseases concerning mainly the appreciation of the effectiveness of health care provision. The incidence of Type 1 diabetes has increased recently, posing a challenge to healthcare specialists, while it is considered to be a significant stress factor for the family.

Methods: A review of epidemiological studies was conducted within the Medline and Cinahl databases. Following the application of the eligibility criteria, we identified 17 appropriate studies.

Results: Youth with type 1 diabetes report remarkably similar quality of life to a nondiabetic youth population. Later age of onset of diabetes, good metabolic control, fewer hyperglycemic episodes, lower glycosylated hemoglobin (HbA1c) levels and intensified insulin therapy are associated with a better health-related quality of life (HRQOL). Educational intervention for adolescents with type 1

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diabetes and family support could be a safeguard against possible deterioration in QoL and glycemic control over time.

Conclusions: Chronic diseases affect not only the child's life but also its families'. For this reason there is a need for well- educated and specialized nurses to support and lead the families to the effective management of the disease.

Keywords: Quality of life; children; adolescents; type 1 diabetes.

1. INTRODUCTION

Type 1 diabetes is the most prevalent metabolic disease of children affecting approximately 150 million people worldwide and it is estimated that new cases will be double by the year 2025 [1]. Increasing numbers of youth with diabetes require intensive treatment programs to reduce the risk of complications. Moreover, intensive regimens increase the burdens placed on daily issues and relationships of children and their families. The chronic complications of type 1 diabetes mellitus that refer to parents and pediatric patients with diabetes may be prevented by optimal glycemic control. However achieving good control in children with diabetes is complex and time consuming. Time, education, personal motivation and active ongoing communication between patients' families and caregivers, are required [2,3].

The health-related quality of life (QoL) has been increasingly recognized as an important health indicator for children and the general population and particularly for those with chronic conditions such as diabetes. A major challenge both for health professionals and patients, is to maximize quality of life, in the context of effective therapeutic intervention [4]. Adolescents are at risk of poorer metabolic control and life adjustment difficulties, due to the fact that rapid biological changes occur during this period of life and the need to cope with this chronic disease. These considerable demands may interfere with adolescents' ability to negotiate important developmental tasks including the ability to achieve good psychological adjustment and improve overall quality of life [5,6].

The main goals of diabetes care in children and adolescents are to achieve good metabolic control, normal growth and development, as well as psychosocial development and support of young patients and their families to deal with diabetes. It is important to evaluate overall the quality of life of the child with diabetes, considering disease management, physical

symptoms, and normal developmental milestones, including school performance and socio-emotional development [7]. The relationship however, between QoL and psychosocial issues, diabetes treatment regimens and metabolic control in adolescents is controversial. For this reason, the specialist diabetes nurse, especially as coordinator, constitutes the link between the family and the healthcare specialists. The health professionals should encourage the family members to participate in the children-adolescent's therapeutic care plan in order to sustain optimal levels of quality of life [8,9].

1.1 Aim

The present review of the issue aims to summarize the existing scientific knowledge regarding the association between Type 1 diabetes and quality of children's life.

2. METHODS

A review of the literature on the effect of type 1 diabetes in children's life was performed. The following question (Population, Intervention, Comparison, Outcome, PICO) was applied: "Given the existing epidemiological evidence, the question arises as to whether there is a connection between type 1 Diabetes and health-related quality of life". We drew up a review protocol in advance, following standards outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses, The PRISMA Statement [10]. Furthermore, a comprehensive bibliographic search was carried out using the MEDLINE (Medical Literature Analysis and Retrieval System Online, or MEDLARS Online) and CINAHL (Cumulative Index to Nursing and Allied Health Literature) databases for the years 2001-2014 and the published interface key terms used were "Health-related quality of life, children, adolescents, type 1 Diabetes". Retrieved studies were checked against a list of eligibility criteria while the references of each retrieved study were also checked for additional studies that met the eligibility criteria.

Existing prior eligibility criteria to restrict studies were defined. Epidemiological studies (of any study design) referring to children and published in English after 2001, were included only when they referred to quality of life in children and adolescents with type 1 diabetes. Studies not meeting these criteria were excluded from the review. The following data were extracted from each study: Main characteristics, study population, study local measures of effects and confidence intervals for each outcome.

3. RESULTS

Fig. 1 demonstrates the numbers of studies identified and excluded in each phase of the search. Manual searching of references provided an additional study that met the broad eligibility criteria. Ultimately, seventeen studies were deemed suitable for inclusion in the review.

Table 1 summarizes the main findings of the seventeen studies included in the review of the issue. The review of the issue included two population-based studies, three cross-sectional studies, three case studies, one quasiexperimental study, four clinical trials, one pilot (ongoing cohort study) and three cohort studies. Birkebaek et al. [11] in Denmark, presented a study which compared the quality of life in a Danish population of 700 children and adolescents with type 1 Diabetes treated with either CSII or MDI. The results showed better levels of quality of life on children and adolescents that used continuous subcutaneous insulin injection for a long period of time more than one year. In particular, children and adolescents on MDI for more than one year reported more diabetes related symptoms, but less treatment problems, and worse generic functioning in all subscales compared with those on CSII. Parents also reported concerns when their children were on CSII treatment compared with MDI [11].

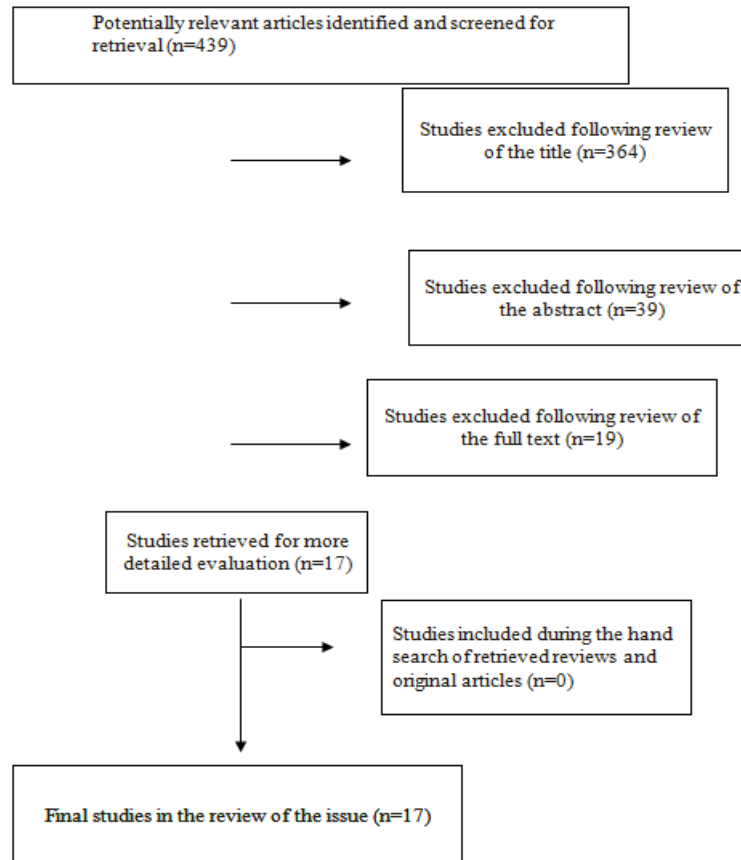


Fig. 1. Literature search and strategy outcomes, Prisma flowchart

Table 1. Summary of the characteristics of studies included in the review of the issue

Author	Study design	Measures	Study population	Age	Outcomes
Birkebaek et al., 2014 (Denmark)	Population- based study	Questionnaires: Pediatric Quality of Life Inventory Diabetes PedsQL DM and Generic Module PedsQL GCS	n =700 children and adolescents with Type 1 Diabetes.295 CSII, 405 MDI	8-17	Children treated for more than one year the CSII group scored significantly higher on all PedsQL GCS subscales compared with the MDI group, except for “social functioning”. No significant differences between children on CSII or MDI treated less than one year were found for any of the PedsQL GCS subscales.
Froisland et al., 2013 (Norway)	Population-based study	DISABKIDS questionnaires.DCGM-37,DDM-10	937 children and adolescents with Type 1 Diabetes and their parents	8-19	Lower HRQOL scores were significantly associated with higher HbA1c and, being a girl in this population-based study of young people with type 1 diabetes. Experiencing diabetes ketoacidosis was significantly associated to lower HRQOL scores. There were no significant differences in scores between users of insulin pump and multi-injection treatment in this young population on intensive insulin treatment.
Stahl et al., 2012 (Germany)	Case study	Questionnaire KINDL-R	n=629 children & adolescents with Type 1 Diabetes n=6813 children & adolescents	11-17	Self- and parent-reported total QoL did not differ between the patient group and the general population. The adjusted difference between the two samples in total QoL was $\beta=0.89$ in the self-reports and $\beta=-0.98$ in the parent-reports
Tahirovic et al., 2012 (Bosnia and Herzegovina)	Cross -sectional study	Questionnaire PedsQL 4.0 Generic Core Scales, PedsQL 3.0 Diabetes Module	n=65 children & adolescents	5-18	Children were assigned to one of two groups. In Group 1 were the children with HbA1c values <8% and Group 2 were children with >8%. The patients in Group 1, by pediatric patient had statistically better disease-specific HRQOL scores.

Author	Study design	Measures	Study population	Age	Outcomes
Abolfotouh et al., 2011 (Egypt)	A quasiexperimental study	Education intervention EPI Info Version 6.4 DQoL for Youth interview questionnaire	503 adolescents	14-16	Poorer QoL was significantly associated with older age, more hospital admissions in the last 6 months, higher levels of depression, poor self-esteem, and poor self-efficacy.
Kalyva et al., 2011 (Greece)	Case study	Questionnaire PedsQL 4.0 Generic Core Scales, PedsQL 3.0 Diabetes Module	n=117 children & adolescents with Type 1 Diabetes n=128 children & adolescents	5-18	Results indicated that later age of onset of diabetes, less hyperglycemic episodes, lower glycosylated hemoglobin HbA1c, older age, and male gender were associated with better general HRQoL and diabetes-specific HRQoL.
Mednick L et al., 2010 (England & Wales)	Pilot Study(ongoing prospective study)	Insulin Pump Therapy Satisfaction Questionnaire [IPTSQ]	22 children with type 1 diabetes and their parents	10–18	Parent–child satisfaction were highly correlated ($r = .53$) and children’s pump satisfaction was significantly positively correlated with diabetes- related quality of life ($r = .51$).
Naughton et al., 2008 (United States)	Cross-Sectional Study	Questionnaire PedsQL, Diabetes Health Questionnaire	2188 children & adolescents with type 1 diabetes	8-22	Primary insurance source, the use of insulin injections vs an insulin pump, a hemoglobin A1c value of at least 9%, were correlated with lower levels of health-related quality of life. Strong connection was found between the age - sex of the patient and the quality of life with males among the older groups to present higher levels of HRQOL.
Botello-Harbaum M et al., 2008 (United States)	Prospective study	Diabetes Quality of Life scale (DQOL), Authoritative Parenting Index, Diabetes Responsibility and Conflict Scale, Diabetes Family Responsibility Scale (DFRS)	69 patients with type 1 diabetes	11-16	Diabetes-related quality of life was significantly associated with parent responsiveness. The age of the child and parent–child conflict were found significant factors affecting quality of life.
Hassan et al., 2006	Clinical Trial	Questionnaires: CDI-S, Hollinshead Four-Factor	222 children & adolescents with Type 1 Diabetes	8-17	Higher SES was associated with better glycemic control ($p<.0005$) and QOL

Author	Study design	Measures	Study population	Age	Outcomes
(United States)		Index of Social Status, PedsQL 4.0 Generic Core Scales, PedsQL 3.0 Diabetes Module			($p < .0005$).
Valenzuela et al., 2006 (United States)	Clinical Trial	Questionnaires :CDI-S, Hollinshead Four-Factor Index of Social Status, BASC-SRP Behavior Assessment System for Children's Self-Report of Personality, BASC-Parent Rating Scale, PSS Perceived Stress Scale, BDI Beck Depression Inventory, FES Family Environment Scale, PedsQL 4.0 Generic Core Scales, PedsQL 3.0 Diabetes Module	160 children & adolescents with Type 1 Diabetes	5-17	Present findings indicate that insulin pump therapy does not have negative implications for HRQOL. Child, family and parent adjustment variables were significantly related to HRQOL, whereas other demographic and clinical variables were relatively less important.
Graue et al., 2005 (Norway)	Case study	Questionnaires: PBI, Parental Bonding Instrument, Parental Involvement Scale, CHQ-CF87, Child Health Questionnaire, DQOL-Y, Diabetes Quality of Life Questionnaire	n=115 adolescents with Type 1, n:9345 healthy adolescents	5-17	Age, gender, a higher degree of parental care and involvement, and a lower perception of parental control explained 52% of the variation in diabetes life-satisfaction.
Wagner et al., 2005 (Germany)	Clinical Trial	Questionnaire KINDL-R	68 children & adolescents with Type 1 Diabetes 1502 healthy school children	8-16	Lower HbA1c <8% and intensified insulin therapy >3 injections/day were associated with a better HRQOL in different domains ($p < 0.05$)
Hesketh et al., 2004 (Australia)	Prospective Cohort Study	Questionnaires: Child Health Questionnaire PF-	n=117 children & adolescents with Type 1 Diabetes	5-18	Adolescents reported significant improvements on the Family Activities

Author	Study design	Measures	Study population	Age	Outcomes
		50, Child Health Questionnaire CF-80.			($p < 0.001$), Bodily Pain ($p = 0.04$), and General Health Perceptions ($p = 0.001$) scales and worsening on the Behavior ($p = 0.04$) scale.
Whittemore R et al., 2003 (United States)	Cross- Sectional Study	Diabetes Quality of Life- Youth Scale (DQOLY), Children's Depression Inventory(CDI), Issues in Coping with IDDM- Child Version Scale, Diabetes Family Behavior Scale (DFBS), Depression Parent Version Scale (CES-D)	56 children & their parents	8-12	Parent depressive symptoms ($\beta = -0.27$, $p < 0.05$), child depressive symptoms ($\beta = -0.42$, $p < 0.01$), warm and caring family behaviors ($\beta = 0.37$, $p < 0.01$) found as important factors correlating with quality of life.
Laffel et al., 2003 (United States)	Clinical Trial	Questionnaires: PedsQL, Family Conflict Scale	100 children & adolescents with Type 1 Diabetes	8-17	PedsQL responses from youth with type 1 were stable over 1 year and similar to norms from a healthy standardization sample for all three scales of the PedsQL.
Hoey et al., 2001 (Europe, Japan, and North America)	Cohort Study	Questionnaire: DQOL, Diabetes Quality of Life	n=2101 adolescents with Type 1 Diabetes	10-18	Mean HbA1c was 8.7%. Lower HbA1c was associated with lower impact ($p < 0.001$), fewer worries ($p < 0.05$), greater satisfaction ($p < 0.001$) and better health perception ($p < 0.001$) for adolescents.

Froisland et al. (2013) examined the HRQOL in children and adolescents with diabetes type 1 which preferred the intensive insulin treatment, in Norway. Quality of life was related to metabolic control and female gender, but not to mode of intensified insulin treatment. Fathers scored higher than mothers on total score and most subscales. Also, they were not found significant differences in scores users of a pump compared to MDI treatment [12].

Stahl et al. [13] in Germany, conducted a research in which the majority of the children used intensified insulin therapy. Children and adolescents with type 1 diabetes reported "excellent" general health compared to non-diabetic children, whereas the parent-rated general health was worse than that in the control group. As for the health-related quality of life, the total QoL reports (children/adolescents-parents) were the same between the patient group and the general population. The adjusted difference (SE) between the two samples in total QoL was $\beta = 0.89$ (0.52; $P=0.087$) in the self-reports and $\beta = -0.89$ (0.53; $P=0.066$) in the parent-reports [13].

In another study from Bosnia and Herzegovina, Tahirovic et al. (2012) examined the association between general and disease specific health related quality of life (HRQOL) scores and metabolic control in children with type 1 diabetes. The children were assigned into two groups. In Group 1 were included children with HbA1c values $<8\%$ and in Group 2 were children with $>8\%$. The patients in Group 1, mostly children, reported significantly better disease-specific HRQOL scores in comparison with Group 2. Moreover strong correlation was found between the total HRQOL scores and HbA1c in both groups [14].

A quasiexperimental study from Abolfotouh et al. [15] assessed the impact of an educational intervention on the total diabetes QoL. 503 adolescents with type 1 diabetes participated in the study, separated in two groups (experimental and control). Over a period of four months, four 120-minute sessions of an educational program were applied to the experimental group of adolescents with type 1 diabetes. The older age, the number of hospital admissions in the last 6 months, higher levels of depression, poor self-esteem and self-efficacy were significant determinants of lower quality of life. Deterioration in all domains of QoL presented in both groups, however this deterioration was significantly less severe in the intervention group [15].

Whittemore et al. [16] used cross-sectional data from the Coping for Health in Living with the Diabetes (CHILD) study, aiming to identify factors associated with quality of life and metabolic control in school-aged children with type 1 diabetes, which were on intensive treatment. Evidence revealed that parent depressive symptoms ($\beta = -0.27$, $P < 0.05$), child depressive symptoms ($\beta = -0.42$, $P < 0.01$), warm and caring family behaviors ($\beta = 0.37$, $P < 0.01$) found as important factors correlating with quality of life. More precisely children who reported fewer depressive symptoms, and had parents with less depressive symptoms, reported higher quality of life. Moreover children, who perceived more warm and caring from their family regarding diabetes management, were more likely to report higher quality of life [16].

Kalyva et al. [17] conducted a research study in Greece to evaluate health related quality of life (HRQOL) in children and adolescents with type 1 diabetes compared to healthy peers. The questionnaires that were used in the study assessed both child and parents' reports. As expected the findings showed that the non-diabetic group reported higher levels of HRQOL than the children with T1DM. Moreover, the later onset of diabetes, fewer hypoglycemic episodes, lower levels of Glycosylated Hemoglobin (HbA1c), older age and male gender, were significant factors for better general and diabetes-specific HRQOL [17].

The cross-sectional SEARCH Study (2008) aimed to examine the connection between demographic and diabetes management factors and the health-related quality of life (HRQOL) of youths with type 1 diabetes. Data were collected from a sample of 2188 patients aged 8 to 22 years using the PedsQL scale. Evidence suggested that the primary insurance source, the use of insulin injections vs an insulin pump, a hemoglobin A1c value of at least 9%, were correlated with lower levels of health-related quality of life. Moreover a strong connection was found between the age - sex of the patient and the quality of life with males among the older groups to present higher levels of HRQOL [18].

According to Hassan et al. [19] the lower socioeconomic status (SES) was associated with depression and poor quality of life in children with type 1 diabetes. In the study participated 110 subjects with HbA1c $7.1\% \pm 0.7\%$ and 112 subjects with HbA1c $9.9\% \pm 1.6\%$. The results showed that 9.5% of poorly controlled children

were depressed, compared with 3% of well controlled. Moreover they found that higher SES was favorable to better glycemic control ($P < 0.005$) and QoL ($P < 0.005$) [19]. Another study from the University of Miami, conducted by Valenzuela et al. [20] assessed the impact of injection regimens and insulin pump therapy on health-related quality of life. Findings indicated that there was no connection between the insulin therapy prescribed and the quality of life. More precisely, neither insulin pump therapy nor injection regimens have negative impact on HRQOL [20].

In the study of Mednick, Cogen and Streisand (2004) also presented the satisfaction and subsequent quality of life among 22 children with type 1 diabetes and their parents, during the transition to insulin pump therapy. The results indicated that children and parents were strongly satisfied with the use of insulin pump therapy, especially due to the flexibility offered by the pump, related to eating and sleeping hours. The study revealed a strong correlation between the children's satisfaction due to the pump use and the diabetes-related quality of life ($r = .51$) [21].

Graue et al. [22] in their study referred to the role of parental care in type 1 diabetes management. They selected 115 diabetic adolescents, 9,345 healthy peers and 291 physically disabled youths. The parents of adolescents with type 1 diabetes were reported to be more involved in the daily care of the disease than parents in the control groups. Furthermore, factors such as age, gender and a higher degree of parental care and involvement found to be positively related with mental health and diabetes-life satisfaction. On the other hand, HbA1C and other clinical variables did not impair the HRQOL [22].

Botello-Harbaum et al. [23] conducted a study in order to assess the relationship of parent responsiveness and demandingness with diabetes-related quality of life among children and adolescents with type 1 diabetes. Baseline and 12-month follow-up self-report assessments were used, in terms of a behavioral interventional study to enhance adherence. From the 81 children which participated in the study, 69 were retained through the 12-month follow-up. The results suggested that diabetes-related quality of life was significantly associated with parent responsiveness. Furthermore other factors that found to affect quality of life were the age of the child and parent-child conflict as well [23].

Wagner et al. [24] reported that among the 68 children and adolescents with type 1 diabetes, lower levels of HbA1c (less than 8%) and intensified insulin therapy (more than three injections per day) was favorable to better health-related quality of life. As for the comparison between the healthy peers and diabetic population, the first reported higher scores of total HRQOL, but in some domains children and adolescents with diabetes scored higher [24].

A prospective cohort study from Hesketh, Wake and Cameron [25] explored the alterations in health-related quality of life in children with diabetes over a two-year period. The parents of the patients stated that there was no difference in children's HRQOL between baseline and follow up, whereas the adolescents reported significant improvement in several domains of the questionnaires (Family activities, physical pain, general health perceptions scales) and lower scores on the behavior item. Lower levels of psychosocial summary scores obtained from parents were also correlated with higher percentages of HbA1C [25].

Laffel et al. [26] assessed the reports of 100 children with type 1 diabetes and their parents' in order to identify factors associated with general quality of life. Among age, duration of the disease, gender, glycosylated hemoglobin and family involvement, the only important determinant was found to be the family conflict. Over a period of one year, comparing the data with a healthy control sample, there was no difference in the QOL.

A large international cohort study of 2101 adolescents with type 1 diabetes and their families, investigated the role of metabolic control in the quality of life. The study was conducted in 17 countries in Europe, Japan and North America, with 21 participating centers. The factors which were significantly associated with good metabolic control and predicted better quality of life were the lower impact of the disease, the fewer worries, the greater satisfaction and the better health perception [27].

4. DISCUSSION

As indicated through this review of the issue, the existing body of epidemiological evidence and the possible association between health-related quality of life and type 1 diabetes were brought together. Stahl et al. [13] and Laffel et al. [26] agreed with the main finding of our review,

supporting that the total QoL reports (children/adolescents-parents) for the health-related quality of life, were the same between the patient group and the general population, despite the challenges of modern therapy.

On the other hand, Wagner et al. [24] comparing the quality of life between healthy peers and the diabetic population, concluded that the previous reported higher scores. These results are in line with the observation of Kalyva et al. [17] in Greece, where the young patients considered that the chronic disease does not have any great effect on their life, despite the perspectives of their parents.

Parental care and involvement in the study of Graue et al. [22] found to be positively related with some areas of total quality of life, such as the mental health and the diabetes-life satisfaction. Whitemore et al. [16] underlined that the warm and caring family behaviors statistically correlate with higher quality of life [16]. Botello-Harbaum et al. [23] supported that diabetes related quality of life was significantly associated with parent responsiveness. These results indicate that parents function as agents of support and confidence, optimism and stability so that the children could cope with the stress related to the management of the disease. Although diabetes may occasionally provoke burdens on the daily family life, for this reason it is essential that parental support be provided in order to preserve effective management and cope with the demands of the disease [23].

As for the type of insulin regimen, Valenzuela et al. [20] suggest that insulin pump therapy compared to injections, does not have negative implications for the total quality of life and the study of Froisland et al. (2013) showed no significant differences between pump and MDI treatment [12,20]. On the contrary of Mednick et al. (2010) presented high levels of satisfaction from the pump use both at parents and children and a strong connection between intensive pump therapy and quality of life. They also noted that children had achieved improved metabolic control over their diabetes and improved carbohydrate counting as well. It is accepted that pump therapy provides health improvements and increases flexibility, but appropriate education, carbohydrate calculation and frequent glucose monitoring, are also required. As a result, interventions should be designed in order to encourage children and adolescents in the use of insulin pump [21]. Abolfotouh et al. [15] described an educational intervention

implemented on adolescents with type 1 diabetes. The results of this quasiexperimental study indicated that quality of life and glycemic control can be maintained over time, through appropriate and individualized education [15].

The majority of the surveys of the present review reveal that later age of onset of diabetes, sex, good metabolic control, less hyperglycemic episodes, lower glycosylated hemoglobin (HbA1c), intensive insulin therapy, primary insurance source are associated with a better health-related quality of life (HRQOL) [12,13,15,16,20,24].

Literature underlines the role of good metabolic control in the diabetes quality of life, even in developing and transitional countries [10]. Lower family socioeconomic status and depression are also connected with poorer glycemic control in pediatric type 1 diabetes. Both parent and child depressive symptoms can impair quality of life [13]. More specifically, depression may lead to poor management, frequent hospitalization and complications [17]. Well-controlled children with type 1 diabetes improve the quality of life in their families. As indicated by parents and health professionals in the study of Hoey et al. [27] (2001) higher HbA1c was significantly connected with higher family burden.

5. IMPLICATIONS/ RELEVANCE FOR DIABETES EDUCATORS

This study area is of high importance, due to the fact that the risk of long term complications is reduced with good metabolic control. It is, therefore, desirable to determine the correlation between good metabolic control and general quality of life during childhood and to identify whether preventable or treatable risk factors exist. It is obvious that chronic diseases affect not only the child's life but also its families'. For this reason there is an absolute need for well-educated and specialized nurses to support and lead the families to the effective management of the disease.

This review applies to epidemiologists, health care specialists and research community as interesting areas for further research work.

6. CONCLUSION

Chronic diseases affect not only the child's life but also its families'. For this reason there is a need for well- educated and specialized nurses

to support and lead the families to the effective management of the disease.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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