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Metabolic Control, Quality of Life, and Body Image in Patients with Glycogen Storage Disease Type Ia

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A

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Glycogen storage disease is a group of inborn errors of metabolism, with type Ia being the most common form of the disorder. Glycogen storage disease type Ia (GSDIa) is a multisystemic condition in which individuals have various complications secondary to an inability to properly break down glycogen and to perform gluconeogenesis. Complex management is then necessary for patients and includes dietary modification, frequent cornstarch usage, and evaluation for additional complications such as hepatic adenomas, hypertriglyceridemia, and kidney disease. Previous studies have found lower scores in quality of life and body image in GSDIa patients; however, the specific factors influencing this relationship remain unknown. In this study, 24 adult participants (n=24) with glycogen storage disease type Ia completed a survey including measures of health-related quality of life, body image, and metabolic control. Results found that quality of life was significantly lower than the general population on both the physical and mental component scores ($t=-3.11$, $p=0.005$; $t=-2.21$, $p=0.03$). Additionally, body image was significantly lower on all subscales: Weight ($t=-5.88$, $p<0.001$), Appearance ($t=-5.67$, $p<0.001$), and Attribution ($t=-2.38$, $p=0.02$). In general, significance was not reached when examining roles that certain metabolic and demographic factors play in health-related quality of life and body image. Therefore, the relationship between these factors

is most likely complex. Overall, the current study confirms previous findings of lower health-related quality of life and body image in this population and provides preliminary evidence on potential factors influencing this phenomenon.

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INTRODUCTION

The glycogen storage diseases are a group of disorders characterized by abnormalities in various enzymes that are involved in glycogen synthesis and/or degradation. Each subtype of glycogen storage disease have varying enzymatic deficiencies, in turn leading to varying phenotypic expression. Glycogen storage disease type Ia, also known as von Gierke disease, is due to deficiency of glucose-6-phosphotase (G6Pase) activity (Hendriksz & Gissen, 2015). G6Pase is expressed in the liver and is responsible for catalyzing final reactions of glycogenolysis and gluconeogenesis. The lack of activity of the G6Pase protein leads to a decrease in glucose output from the liver during fasting. Furthermore, the build-up of glucose-6-phosphate leads to increased G6P in glycolysis and increased lactate production. The gene that encodes G6Pase is called *G6PC* and is located on chromosome 17q21 (Ozen, 2007; Wolfsdorf & Weinstein, 2003). GSDIa is inherited in an autosomal recessive manner; therefore, individuals with GSDIa have bi-allelic pathogenic variants in *G6PC*.

Metabolic derangements of GSDIa include severe fasting hypoglycemia, lactic acidosis, hypertriglyceridemia and hyperuricemia. The clinical features of this condition are multisystemic and may include seizures, lethargy, and failure to thrive. In addition to low glucose levels, there is also buildup of glycogen in these patients, leading to hepatomegaly. Patients with GSDIa may exhibit short stature and characteristic facial features including a round “doll”-like face with full cheeks (Kishnani et al., 2014). Complications arise in the context of poor metabolic control and manifest as hepatic adenomas, renal disease, severe hypoglycemia potentially leading to brain damage, osteoporosis/osteopenia, and anemia (Kishnani et al., 2014). According to ACMG guidelines on management of GSD type I, care for these patients should occur in the context of a multidisciplinary team with expertise in glycogen storage disease (Kishnani et al., 2014). Various specialists should be involved, including nephrology, hepatology, hematology, genetics, and cardiology, in addition to metabolic disease specialists. Additionally, the specific diet required for these individuals is a lactose, galactose, sucrose, and fructose free diet. This is further managed through the use of frequent cornstarch dose given every 3 to 4 hours, during the day and at night, often times necessitating use of

a G-tube. Understandably this form of management then can have a significant impact on the daily routines of individuals with GSDIa.

Researchers have suggested that further information on the relationship between metabolic control, body image, and quality of life would be useful to elucidate potential influencing factors of quality of life of patients with GSD (Flanagan et al., 2015). This research could provide insight for direction of adherence to diet and mental health care discussions for these patients. Because metabolic control as a factor influencing quality of life and body image in these patients has not been evaluated in depth before, the current study aims to further examine this question by eliciting information on the relationship between metabolic control, body image, and quality of life (QoL) in adult patients with glycogen storage disease type Ia. The authors hypothesize that individuals with better self-assessed and objective measures of metabolic control will have better quality of life and body esteem.

METHODS

Data was collected via a survey, using the system Qualtrics (Qualtric, Provo, UT) and consisting of four parts: demographics, metabolic control, quality of life, and body image.

To evaluate for level of metabolic control, patients completed questions regarding amount of complications they report per week, what they are using for treatment of complications and hypoglycemia, and what their own perceived level of metabolic control was. Level of control in the study is defined as the degree to which individuals follow management and dietary guidelines. Participants were asked if they consider themselves to be under good metabolic control and to rate their level of metabolic control on a scale of 1 to 10, with 10 representing highest level of control. Participants were also asked about their frequency and dosage of cornstarch used and whether they take *Glycosade*™. The metabolic control section consisted of 21 questions in total.

Short-Form 36 Version 2® (SF-36v2®) Health Survey from OPTUM QualityMetric, Inc was used to measure Health-Related Quality of Life (HRQoL) in adult patients with GSDIa (Ware & Sherbourne, 1992). SF-36v2® is a 36 item validated and reliable measure of health-related quality of

life in the adult population. Subscales include physical functioning, role physical, bodily pain, general health perception vitality, social functioning, role emotional, and mental health. The mental component score (MCS) and physical component score (PCS), which are summary measures for mental and physical aspects of health-related quality of life, were used in analysis in the current study. Scores on the measure were standardized and converted to a 0-100 scale for analysis (Maruish; Ware & Sherbourne, 1992).

Body image was measured using the Body Esteem Scale (Mendelson, Mendelson, & White, 2001). The Body Esteem Scale is a validated measure analyzing level of satisfaction or dissatisfaction with one's body and is comprised of three subscales. These subscales include Attribution, Weight, and Appearance. The Attribution subscale relates to the individuals perceptions on how others view their body. The Weight subscale represents their own perceptions about their weight and their satisfaction with their body. The Appearance subscale deals with how people perceive their own physical appearance and facial features. The scale consists of 30 items, answers for which take the format of a 5-point scale (0-4) (Mendelson et al., 2001). Of note, this measure was translated into Spanish by one of the researchers and the measure has not been previously validated in this language before.

A link to the survey was posted to the Association of Glycogen Storage Disease US website (https://agsdus.org), Glucolatino listserv, and glycogen storage disease patient Facebook groups, and a recruitment flyer was sent via mail to patients currently enrolled in the GSD program at McGovern Medical School at UTHealth. The survey was available in both English and Spanish. Inclusion criteria for this study included any patient with a diagnosis of GSDIa who was over the age of 18, who clicked on the survey link and who consented to participate. Exclusion criteria included individuals who do not fall into the aforementioned categories or who do not have a diagnosis of GSDIa. Finally, the study was only available to individuals who speak either English or Spanish. Originally, parents of children with GSD type Ia and adolescents aged 13-17 with GSDIa were included in the study, however these groups were removed due to low sample size and response rate.

Overall, specific response rate was unable to be calculated due to a lack of information about how many individuals who fit the criteria saw the link to the survey, but did not choose to complete it.

Statistical analysis was completed using the software Stata (v13.1, College Station, TX, USA). SF-36 and the Body Esteem Scale were scored using the recommended methods and compared to population norms (Maruish; Mendelson et al., 2001). Body image and QoL were compared to the US general population using one sample t-tests. Rank sum was used to evaluate sub-groups due to the small sample size. Significance was assumed at a Type I error rate of 5%.

RESULTS

Twenty-four adult patients with a diagnosis of GSDIa completed the survey. All surveys were fully completed except in one individual who did not complete the Body Esteem Scale (n = 23). The sample consisted of 5 male (21%) and 19 female participants and a majority identified as being Caucasian (88%, n=21) and from the United States (58%, n=14). Of individuals who reported being from the United States, the most commonly represented state was Texas (21%, n=3), followed by New York (14%, n=2). The age of participants ranged from 20-57 years old (median = 31). Three of the 24 participants (13%) completed the survey in Spanish.

The median age of diagnosis for the sample was 0.5 years, with the range being from birth to 20 years old. One could argue about verity of diagnosis for the individuals diagnosed at 20 years and 19 years respectively due to the severity of the condition, however removal of these individuals from analysis did not significantly impact statistical results and therefore they were included. Average height of the sample was 158 cm with the average weight being 68.9 kg. One individual did not provide their weight and therefore sample size for weight and BMI are 23. Average BMI was 27.3 kg/m^2 (SD = 6) with 11 (48%) having a 'healthy' BMI (18.5-24.9 kg/m^2) and 12 (52%) having a BMI classified as being overweight (>25 kg/m^2). No individuals had a BMI falling in the underweight category.

Table 1. Demographic characteristics

	Count	Frequency (%)	Mean (SD)	Median (IQR)
Gender				
Male	5	20.8%		
Female	19	79.2%		
Current Age			32.1 (9.1)	31 (25-38)
Age of Diagnosis (years)			2.7 (5.4)	0.5 (0.3-1.8)
Height (cm)			158.4 (7.7)	157.7 (153.2-164.1)
Weight (kg) n = 23			68.9 (16.9)	70.3 (56.0-78.0)
BMI n=23			27.3 (6.0)	25.8 (22.2-30.6)
Race				
Caucasian	21	87.5%		
Asian	2	8.3%		
Other	1	4.2%		
Ethnicity				
Non-Hispanic	20	83.3%		
Hispanic	4	16.7%		
Country				
United States	14	58.3%		
Mexico	2	8.3%		
Canada	2	8.3%		
Spain	1	4.2%		
Germany	1	4.2%		
Portugal	1	4.2%		
Argentina	1	4.2%		
Denmark	1	4.2%		
Israel	1	4.2%		
State				
Texas	3	21.4%		
New York	2	14.3%		
Michigan	1	7.1%		
South Carolina	1	7.1%		
Colorado	1	7.1%		
New Jersey	1	7.1%		
Illinois	1	7.1%		
Wisconsin	1	7.1%		
Illinois	1	7.1%		
Virginia	1	7.1%		
Alabama	1	7.1%		

A majority of individuals reported checking their glucose at home (75%, n=18). Of those individuals, 56% (n=10) of them reported checking their glucose when they think that they are low, and 33% (n=6) checking multiple times a day. 11% (n=2) reported that they check their glucose once a day. Two individuals (8%) reported receiving tube feedings, with both individuals using g-tubes. Twenty individuals reported taking cornstarch (83%), with 18 providing some level of information on their cornstarch schedule. Of these 18, 10 individuals (55%) noted that they had sleep interrupted due to having to wake up to take cornstarch. Other reported medications used by the sample including 25% (n=6) who take *Glycosade*™ and 50% (n=12) who take allopurinol.

A majority of individuals reported having 1 to 5 low blood sugars a week (67%, n=16), with 21% (n=5) being unsure how many they had. One individual each reported having no, 6 to 10, and >10 episodes of hypoglycemia a week. In terms of complications related to GSD 54% (n=13) of the sample reported having liver masses/hepatic adenomas, 25% (n=6) having osteoporosis, 46% (n=11) having kidney problems/kidney stones, 67% (n=16) having hypoglycemia every week at least once a week, and 92% (n=22) have high cholesterol or high triglycerides. Using those five complications listed, the mean number of complications for the sample was 2.8 with a standard deviation of 1.3.

Given scale of one to ten with ten being the highest control and one being the lowest, the mean self-perceived level of control for the sample was 5.9 with a standard deviation of 1.6. When looking at frequency of responses, no individuals reported scores of 1, 2, 9, and 10 (Figure 1). The most common reported score was 4 (26%). Additionally, 54% (n=13) consider themselves to be under good metabolic control (Table 2).

Table 2. Clinical characteristics and measures of control

	Count	Frequency (%)	Mean (SD)	Median (IQR)
Do you check your glucose at home?	18	75%		
Do you receive tube feedings?				
No	22	91.7%		
Yes	2	8.3%		
How often do you check your glucose?				
Multiple times a day	6	33.3%		
Once a day	2	11.1%		
When I think I am low	10	55.6%		
How many LBS's do you have per week?				
None	1	4.2%		
1 to 5	16	66.7%		
6 to 10	1	4.2%		
>10	1	4.2%		
Not sure	5	20.9%		
Complications reported				
Liver masses/hepatic adenomas	13	54.2%		
Osteoporosis	6	25.0%		
Kidney problems/Kidney stones	11	45.8%		
Low blood sugars every week	16	66.7%		
High cholesterol or triglycerides	22	91.7%		
Number of complications (see above for list of complications)			2.8 (1.3)	3 (2.0-3.5)
On a scale of 1 to 10 rate your level of metabolic control (10 being best control)			5.9 (1.6)	6.0 (4.0-7.0)
Do you consider yourself to be under good metabolic control?				
No	11	45.8%		
Yes	13	54.2%		

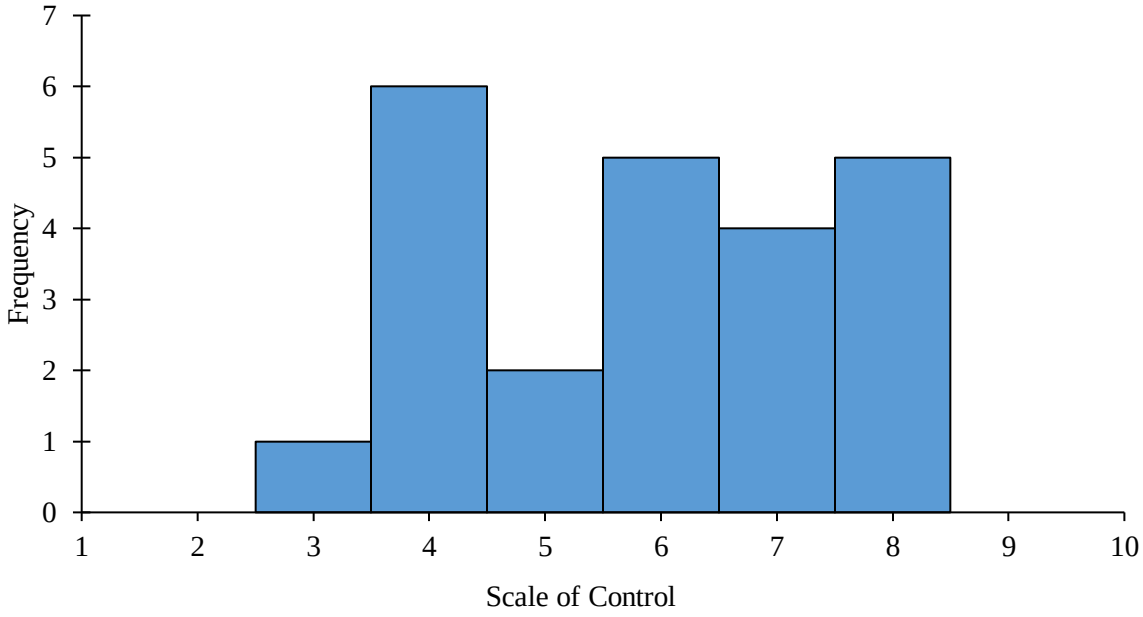

Figure 1. Scale of Control
Frequency of response regarding self-perceived level of control on a scale of 1 to 10, with 1 representing poorest control and 10 representing best control. Most individuals fell in the middle values, with no responses falling in levels 1, 2, 9, or 10.

Adult patients with glycogen storage disease type Ia were found to have lower health-related quality of life scores than the general population using the physical component score (PCS) ($t=-3.11$, $p=0.005$) and the mental component score (MCS) ($t=-2.21$, $p=0.03$) (Table 3). There was no statistically significant difference in quality of life found between males and females in both PCS ($p=0.594$) and MCS ($p=0.414$) (Table 4).

In reference to body image, adult patients with GSDIa were found to have statistically significantly lower scores than the general population in all three subscales of body esteem: Weight ($p<0.001$), Appearance ($p<0.001$), and Attribution ($p=0.02$). (Table 3). When stratifying based on gender, females were found to be significantly lower than gender norms in Weight ($p=0.002$) and Appearance ($p=0.005$), but not Attribution ($p=0.09$). Similarly when comparing males in the sample to gender norms, they scored significantly lower in the Appearance subscale ($p=0.04$), but not the Weight ($p=0.07$) or Attribution subscale ($p=0.12$).

Table 3. QoL and body esteem compared to population controls

Scales	Count	Mean (SD)	Median (IQR)	t-score	p-value
SF-36	n=24				
Physical Component Score (PCS)		46.1 (8.6)	47.1 (41.9-51.9)	-3.11	**0.005**
Mental Component Score (MCS)		42.8 (11.3)	43.7 (35.3-51.1)	-2.21	**0.03**
Body Esteem Scale (BES)	n=23				
Weight		1.4 (0.9)	1.5 (0.6-1.8)	-5.88	**<0.001**
Appearance		1.4 (1.0)	1.3 (0.6-2.2)	-5.67	**<0.001**
Attribution		1.8 (0.9)	1.8 (1.0-2.3)	-2.38	**0.02**

When examining factors related to metabolic control and their influence on outcome measures including the MCS and PCS subscales of QoL, the Weight, Appearance, and Attribution subscales of the BES, and self-reported control on a scale of one to ten, a majority of factors were found to have no effect (Table 4). Men and women did not report significantly different scores in quality of life, body esteem, of scale of control. Checking glucose at home, taking cornstarch, taking *Glycosade*™, waking up at night, and receiving tube feedings were not significantly associated with scores on QoL, BES, or perceived metabolic control (Table 4). Individuals who considered themselves to be under good metabolic control reported significantly higher responses on scale of control ($p<0.001$). Taking allopurinol was significantly associated with scale of control, such that individuals who take allopurinol reported higher levels of self-perceived control ($p=0.0155$). Individuals taking allopurinol and/or *Glycosade*™ had higher control than those who took neither ($p=0.009$). However, there was no difference seen between individuals taking one or the other and those taking both ($p=0.1255$). Taking both allopurinol and *Glycosade*™ was also significantly associated with BMI, such that individuals who take both have on average higher BMI's that individuals who take one or the other ($p=0.009$) and those who take neither ($p=0.008$). There was no difference in BMI seen between individuals who took neither allopurinol nor *Glycosade*™ and those who took one or the other ($p=0.437$). This relationship was also seen in reference to the Weight subscale of the BES. Individuals who took both *Glycosade*™ and allopurinol reported poorer scores

of the Weight subscale than individuals that took one or the other (p=0.014) and those who took neither (p=0.0497).

Table 4. Potential factors influencing outcome measures

Gender					
	Male (n=5)		**Female (n=19)**		**p-value**
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
MCS	40.5 (9.0)	42.7 (38.8-44.3)	43.4 (11.9)	44.3 (34.7-52.5)	0.594
PCS	48.9 (12.1)	50.9 (42.1-55.5)	45.4 (7.7)	47.0 (41.9-50.7)	0.4136
Weight	1.68 (1.26)	1.5 (0.89-2.25)	1.28 (0.86)	1.5 (0.36-1.75)	0.5673
Appearance	1.36 (0.94)	1.3 (1.2-1.7)	1.38 (0.99)	0.90 (0.40-2.30)	1.00
Attribution	1.8 (1.11)	1.6 (1-2)	1.74 (0.90)	1.80 (1.00-2.40)	0.7752
Scale of control	7.0 (1.0)	7.0 (6.0-8.0)	5.6 (1.65)	5.5 (4.0-7.0)	0.0866

Do you consider yourself to be under good metabolic control?					
	No (n=11)		**Yes (n=13)**		**p-value**
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
MCS	39.3 (12.4)	37.8 (26.1 - 51.9)	45.8 (9.8)	44.3 (38.8 - 50.4)	0.284
PCS	45.9 (9.4)	47 (36.3 - 50.7)	46.3 (8.2)	48.1 (42.1 - 52.8)	0.728
Weight	1 (0.7)	1.5 (0.1 - 1.5)	1.7 (1)	1.6 (0.9 - 2.3)	0.103
Appearance	1.1 (0.9)	0.8 (0.4 - 2.1)	1.6 (1)	1.7 (0.9 - 2.3)	0.271
Attribution	1.8 (0.6)	2 (1.6 - 2.2)	1.7 (1.1)	1.6 (1 - 2.6)	0.705
Scale of control	4.5 (1.0)	4 (4 - 6)	7.1 (1)	7 (6.5 - 8)	**<0.001**

Do you check your glucose at home?					
	No (n=6)		**Yes (n=18)**		**p-value**
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
MCS	38.1 (14.5)	39.3 (24.8-50.3)	44.4 (10.0)	44.3 (37.7-51.9)	0.3173
PCS	45 (8.5)	44.6 (41.9-50.9)	46.5 (8.8)	47.6 (42.1-52.9)	0.6407
Weight	1.25 (1.13)	1.13 (0.25-1.75)	1.4 (0.90)	1.50 (0.88-1.75)	0.6388
Appearance	0.9 (1.08)	0.60 (0.30-0.90)	1.53 (0.90)	1.50 (0.80-2.30)	0.1169
Attribution	1.67 (0.98)	1.70 (1.00-2.60)	1.78 (0.98)	1.80 (1.20-2.20)	0.9466
Scale of control	5.3 (1.97)	5.0 (4.0-7.0	6.1 (1.5)	6.0 (5.0-7.0)	0.3711

Do you take cornstarch?					
	No (n=4)		Yes (n=20)		p-value
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
MCS	37.6 (15.2)	37.7 (28.3-47.0)	43.9 (10.5)	44.3(35.3-51.1)	0.4386
PCS	38.8 (11.8)	33.5(31.8-45.7)	47.6 (7.3)	47.7 (42.5-51.9)	0.1213
Weight	1.72 (1.23)	1.81(0.94-2.50)	1.29 (0.89)	1.50 (0.56-1.69)	0.2753
Appearance	1.13 (1.27)	0.62 (0.32-1.95)	1.42 (0.92)	1.30 (0.75-2.20)	0.4614
Attribution	1.55 (1.15)	1.70 (0.60-2.50)	1.79 (0.90)	1.80 (1.10-2.20)	0.8458
Scale of control	5.0 (2.6)	4.0 (3.0-8.0)	6.0 (1.5)	6.0 (4.5-7.0)	0.3755

Do you take allopurinol?					
	No (n=12)		Yes (n=12)		p-value
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
MCS	41.5 (10.7)	42.3 (34.8-50.3)	44.1 (12.2)	42.7 (36.7-54.0)	0.6033
PCS	44 (8.9)	43.6 (35.7-51.7)	48.3 (8.0)	47.7 (43.2-53.1)	0.2481
Weight	1.48 (0.54)	1.50 (1.44-1.75)	1.25 (1.23)	0.81 (0.31-2.13)	0.2826
Appearance	1.42 (0.86)	1.30 (0.75-2.20)	1.33 (1.09)	1.25 (0.40-2.20)	0.8397
Attribution	1.78 (0.89)	1.80 (1.10-2.30)	1.72 (0.99)	1.80 (0.90-2.40)	0.8847
Scale of control	5.0 (1.5)	4.0 (4.0-7.0)	6.67 (1.4)	3.0 (2.0-4.5)	**0.0155**

Do you take *Glycosade*™?					
	No (n=18)		Yes (n=6)		p-value
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
MCS	42.2 (11.1)	42.9 (35.9-51.9)	44.6 (12.7)	48.6 (34.7-50.4)	0.6892
PCS	46 (9.3)	46.1 (41.9-52.8)	46.5 (6.7)	47.7 (41.9-50.2)	0.9734
Weight	1.44 (0.96)	1.50 (0.88-1.8)	1.15 (0.89)	1.25 (0.38-1.75)	0.7885
Appearance	1.41 (0.98)	1.25 (0.70-2.30)	1.28 (1.01)	1.30 (0.40-1.80)	0.8413
Attribution	1.81 (0.98)	1.90 (1.00-2.40	1.57 (0.79)	1.60 (1.00-2.20)	0.6155
Scale of control	5.8 (1.78)	6.0 (4.0-8.0)	6.0 (1.26)	6.5 (5.0-7.0)	0.858

DISCUSSION

This study aimed to provide more information about quality of life and body image in individuals with glycogen storage disease type Ia and also to examine the role that various factors of metabolic control play in these measures. Results found that quality of life and body image are both

impaired in adult patients with GSDIa and have provided preliminary data on factors that could influence this relationship.

Previous studies have examined quality of life in patients with glycogen storage disease type I. An Italian multisite study performed by Sechi et al. in 2014 found that patients with GSD type I reported lower scores on general health perception and social functions and better scores in bodily pain and mental health in comparison to previously published normal control values for the measure (Sechi et al., 2014). However, unlike the current study, they did not find any statistically significant differences in comparison to US norms for the physical and mental composite scores. Reasons for this difference include that perhaps Italian patients with GSDI have better quality of life than individuals in the US, or it could reflect an overall higher baseline quality of life in Italian individuals in the general population unrelated to having GSD. Overall, our data supports the general conclusions from Sechi et al. that adult patients with GSD report lower quality of life than the general population and also increases the generalizability of these findings, given that the original study included only Italian individuals.

Flanagan et al. examined eating disorder symptoms, eating attitudes, and body esteem using validated questionnaires and interviews in a previous study on body image in patients with all subtypes of GSD. They reported body esteem scores in children and adults lower than the population norm (Flanagan et al., 2015). When looking at specific subscales however, only Attribution was statistically significant, while in the current study participants reported significantly lower scores on all subscales. Therefore, our data similarly confirms their results that adult patients with GSD have lower levels of body esteem than the general population.

To the best of our knowledge this was the first study to examine why individuals with GSDIa have low quality of life and body image. Measures relating to demographics and metabolic control were evaluated to determine the nature of their relationship to outcome measures. For demographic factors, only gender was found to play a role. Females, in general, reported lower self-perceived control than males; however, this result was not statistically significant. Previous studies of the

general population have found that women self-report lower physical and mental health status than men (Bertakis et al, 2000). Our data seems to support this trend in the GSD population as well.

In reference to factors of metabolic control, individuals who use g-tubes had generally lower scores on the Attribution subscale of the BES. External devices have been shown to impact body image due to visibility of the device (Bolton, Lobben, & Stern, 2010). Therefore, these individuals could feel as though others are judging them for the g-tube, thereby lowering their body esteem. Of note, this trend was not significant, and only 2 individuals reported using g-tubes and therefore this data should be interpreted with caution. Additionally, taking *Glycosade*™ was not found to impact QoL and body image, which supports results of previous studies that have found that *Glycosade*™ does not impact QoL (Correia et al, 2008; Rousseau-Nepton et al, 2018).

Complications reported were also found to be a significant factor in QoL and body image. They were found at similar levels to what has previously been reported in individuals with glycogen storage disease as adults (Talente et al., 1994). As expected, almost every listed complication was significantly associated with overall number of complications reported. However, this statistical significance was not reached for high cholesterol/triglycerides. This association may not have been seen due to the large number of individuals with high cholesterol in the general population. Interestingly, high cholesterol has been previously linked with obesity and high BMI in the general population, however this relationship was not found in our sample (Mokdad et al., 2003). In terms of the role these complications may play in body esteem and quality of life, having low blood sugars at least once a week every week and having kidney stones/kidney problems were both found to be significant in their role in body esteem. Particularly, individuals who reported having either complication were found to have statistically significantly poorer scores on the Attribution subscale of the BES, suggesting these complications may play a role in QoL and body image.

Overall, while significant associations were found that influence perceived level of control, QoL, and body image in patients with GSDIa, there were no individual factors seen to strongly drive

the low QoL and body image in this population. Therefore, the relationship between factors of metabolic control and QoL and body image is most likely complex.

Results of the study also highlight the difference in objective and subjective measures of metabolic control. For example, individuals taking allopurinol, an objective sign of poor control, reported better self-perceived control than those who did not. Taking medication may be influencing perceived control or symptom relief, with a consequent sense of well-being. Studies on other chronic conditions have seen medical adherence related to higher perceived control, as well (Broadbent, Donkin, & Stroh, 2011). From this, one could recommend increased focus on medical adherence due to the relationship between taking allopurinol and perception of control. The importance of subjective experience in various avenues is well-characterized. Subjective perceptions have been shown to have more of an effect on predicting disordered eating than objective measures of weight (Wilson, Tripp, & Boland, 2005). Additionally, subjective experience has been shown to be an important factor in QoL in the general population (Diener & Suh, 1997). It is important to recognize that while individuals may have objectively poorer metabolic control, their subjective control may be high, allowing them to have higher QoL and body image than what would be expected based solely on objective measures.

Current guidelines for management of GSD type I include care by a team aware of the psychosocial considerations of the condition and discuss referral to a social worker or similar specialist if issues become apparent (Kishnani et al, 2014; Rake et al, 2002). This study supports results from previous studies finding that patients with GSDIa have lower quality of life and body image than the general population. It is then important for guidelines to address this subject in future management guidelines in more detail. There also likely exists a complex relationship in the development of low quality of life and body image in these patients. Therefore, targeted intervention to address concerns regarding body image and QoL would not be helpful and should instead be offered for all patients. Additionally, results of the study highlight the importance of objective versus subjective control and that objective control should not be the sole factor in determining individuals at

risk for issues related to QoL and body image. Future research should be performed evaluating accuracy in perception of metabolic control and the weight of objective versus subjective control in outcomes for these individuals. Additional research should also examine these findings in the context of a larger sample and for other subtypes of GSD, as complications of each differ (Chen & Weinstein, 2016). Overall, while psychosocial concerns may become apparent in childhood and adolescence in these patients, it is necessary to bring awareness to the fact that adult patients also report difficulty with body image and quality of life and therefore management in this context should be present throughout the lifetime.

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