Language assessment in Egyptian children with sickle cell disease

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Background
Sickle cell disease (SCD) is a blood disorder; however, the central nervous system is one of the organs frequently affected by the disease. Brain insult can begin early in life and often leads to neurocognitive dysfunction. The progression of central nervous system abnormalities in SCD and its effect on language development have not been fully delineated.

Aim
To determine the effect of SCD on language development in Egyptian children with SCD in order to delineate this group as a possible high-risk group for language disorders. In this way, further proper assessment of these children will aid the initiation of an early intervention and prevention of these problems.

Participants and methods
A total of 24 children with SCD were subjected to the language assessment protocol of Ain Shams University Hospitals. These patients underwent language testing using the Standardized Arabic Language Test and hearing assessment including a basic audiological assessment and transient evoked otoacoustic emissions (TEOAEs) testing. The results obtained from this group were compared with the results of 17 normal children who were subjected to the same assessment protocol.

Results
The results of this study showed that the age of acquisition of both the first word and sentence was significantly delayed in children with SCD than their control group. The scores of intelligence quotient and language parameters were significantly lower in the group of children with SCD. The language age deficit was significantly higher in the SCD group than the control group. The expressive language abilities and pragmatics were significantly lower than semantics and receptive abilities in children with SCD. The age of onset of the disease and number of vaso-occlusive crisis showed a significant correlation with the intelligence quotient score and all the language parameters. In terms of audiological assessment, all children of both groups had normal audiograms and tympanograms, but the group of children with SCD showed reduced TEOAEs echo levels in comparison with their control. Moreover, there was a significant correlation between TEOAEs echo levels and language parameters in children with SCD.

Conclusion
SCD is considered as one of the important risk factor that can affect proper language development. Therefore, long-term follow-up of these children is necessary to detect deficits early in life to prevent delayed language development and poor academic achievement.

Keywords:
anemia, language assessment, language disorders, sickle cell, sickle cell disease

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Introduction

Sickle cell disease (SCD) is a hereditary red blood cell disorder that is characterized by the production of abnormal hemoglobin, chronic hemolytic anemia, and vascular occlusion, causing pain and irreversible organ damage [1]. SCD is a blood disorder; however, the central nervous system (CNS) is one of the organs frequently affected by the disease. Brain insult can begin early in life and often leads to neurocognitive dysfunction. The neurological consequences of SCD result from complications associated with hemolytic anemia, cerebral hypoxia, and stenosis of the major cerebral arteries [2]. The developing brain is particularly vulnerable to hypoxemia and ischemia, to which children with SCD are frequently exposed [3]. The most devastating complication of SCD is cerebral vascular infarction. Although most infarcts are not accompanied by overt neurological symptoms, 'so-called silent infarcts', they do appear to be associated

with reduced neurocognitive functioning [4]. These silent infarctions can produce neurocognitive deficits throughout the lifespan [5], which can result in reduced lifetime capacities for reading and spelling achievement, increased number of absences from school and work, and lower performance on intelligence quotient (IQ) tests [6].

Approximately one-fourth to one-third of children with SCD have some form of CNS effects from the disease, which typically manifest as deficits in the specific cognitive domains and academic difficulties [7]. Cognitive dysfunction in SCD children is well documented. Generally, the literature has shown deficits across a wide variety of cognitive domains, including intelligence, attention and executive function, memory, language, visuomotor, and academic achievement [4]. Previous research has pointed to language difficulties in children with SCD, as evidenced by decreased scores on tests of verbal intelligence [8], and, more specifically, reduced oral vocabulary [9] and verbal comprehension [10,11].

In addition to cognitive dysfunction in children with SCD, sensorineural hearing loss has been long recognized as a complication in these children [12]. Patients with SCD have a much higher incidence of this complication than the rest of the population [13], with a variable degree of severity [14].

For normal language development, normal sensory channels and normal function of these senses are required. In addition, intact brain function in terms of general intellectual abilities and neuromuscular activity, intact psychological state, stimulating environment, and the desire of the child to communicate with others are important factors for normal language development [15]. Unfortunately, little information is available on language development in children with SCD. Furthermore, the progression of abnormalities of the CNS in SCD and its effect on language development have not been fully delineated. Thus, the present study was designed to determine the effect of SCD on language development in Egyptian children with SCD in order to delineate this group as a possible high-risk group for language disorders. In this way, a further proper assessment of these children will aid the initiation of an early intervention and prevention of these problems.

Participants and methods

Participants

Children were recruited through routine hematological health maintenance visits at the Hematology Clinic, Children's Hospital, Ain Shams University, during the period from June 2009 to August 2010 (after obtaining their parents' consent). They were diagnosed with sickle cell disease (SCD) on the basis of clinical evaluation and Hb electrophoresis. Patients were excluded if they had a history of overt stroke, a recent illness, seizure disorder, or a major developmental disability. Among the 41 consecutive children attending clinic visits, parents of three children refused participation, two children could not complete the assessment, five children had a history of overt stroke, two children had seizure disorders, three showed major developmental delays, and two had a recent illness. The remaining 24 children (G1) were 15 males (62.5%) and nine females (37.5%). Their mean age was 7.05 ± 1.04 years (range, 5 years 2 months to 9 years 7 months). The mean age of onset of the disease was 3.06 ± 1.63 years (range, 1 to 5 years 6 months). Patients of this group belonged to both low and middle socioeconomic classes. Socioeconomic status (SES) was classified into low, middle, and high levels according to the education, occupation, and income of the studied families [16].

This group of SCD (G1) was compared with a group of normal children (G2) that was selected randomly from individuals without any language and speech disorders. They were recruited from the general Pediatric Outpatient Clinic, Ain Shams University Hospitals, during the same period after obtaining their parents' consent and they were used as a reference for their language development. This group included 17 normal children; there were 11 males (64.7%) and six females (35.3%). Their mean age was 6.85 ± 2.96 years (range, 5 years 1 month to 8 years 9 months). Children of this group were of the same SES as the study group.

Procedures and clinical tools

Each individual of both groups was subjected to the following assessment:

Thorough assessment of history according to the protocol of language assessment of Kotby *et al.* [17]: assessment of a full personal, family, medical, and developmental history, with a special focus on age of acquisition of the first word and the first sentence, was carried out. For children with SCD, the following data were collected: the age of onset of the disease, the frequency of vaso-occlusive crises, line of treatment of the disease, duration of blood transfusion, and dose of blood transfusion per year.

Patients' examination: general examination, neurological examination, vocal tract, and ENT examination to exclude cases with any disorders.

Assessment of mental ability using the Stanford Binet Intelligence Test [18]: the IQ is determined as a percent ratio of the mental age to the chronological age.

Vinland Social Maturity Scale [19]: used to assess the social ability and behavior.

Detailed language assessment using the Standardized Arabic Language Test [17]: this was carried out to determine the percentage of receptive language, expressive language, semantics, pragmatics, and total language scores, yielding a total language age and language age deficit in years. The language age deficit was calculated as the difference between the chronological age at the time of evaluation and the corresponding language age scores obtained at that time.

Laboratory investigations: it included measurement of blood Hb (gm/dl) and serum ferritin level (μg/dl) just

before the time of audiological evaluation, language, and IQ assessments.

The baseline audiological evaluation was carried out to detect hearing impairment, including:
Tympanometry using Grasson Staddler audiometer model GSI33 (Georgia, USA).

Audiometry: hearing threshold levels were assessed separately in each ear at octave frequencies from 250 to 8000 Hz. All patients were tested by conventional audiometry, except for some younger children, who could not perform conventional audiometry, and were evaluated by play audiometry. Measurements were made on an Orbiter 922 audiometer (Georgia, USA).

Transient evoked otoacoustic emissions (TEOAEs) testing was carried out to detect early or subclinical cochlear dysfunction. TEOAEs were measured using Smart Intelligent OAEs, TEOAEs version 3.02. Patients were allowed to sit in a sound-treated room and the otoacoustic emission probe was well fitted in the tested ear. For TEOAEs recording, an acoustic stimulus was delivered to the ear with an average intensity of 85 dB SPL. Emission was recorded at five frequency bands over a frequency range of 0.7–4.0 kHz. Recorded measures were echo levels for TEOAEs. A response was considered positive at a given frequency band if it measured 3 dB or above. According to the number of bands showing a pass response, the overall responses were classified into pass, partial pass, and fail responses [20].

Statistical methods

Quantitative variables were presented as mean and SD. Qualitative variables were presented as frequency and percentage. The Kolmogorov test was carried out to test normality. Parametric variables were compared between two groups using an independent-sample *t*-test. The correlation between parametric variables was assessed using the Pearson correlation coefficient.

Nonparametric variables were compared between two groups using the Mann–Whitney test. The correlation between nonparametric variables was assessed using the Spearman rank correlation coefficient.

The significance level used was 0.05. SPSS statistical package version 18 was used in the data analysis (IBM Corporation, Chicago, Illinois, USA).

Results

The results of comparison between children with SCD and normal children in the clinical characteristics are shown in Table 1.

Psychometric evaluation

Although both groups were matched in terms of their chronological age, there was a significant difference between them in the mental age, social age, and scores of IQ, which were significantly lower in the group of children with SCD (Table 2).

Results of language evaluation

There was a significant difference between both groups in the age of acquisition of the first word and the first sentence, which were delayed in SCD children in comparison with normal children (Table 3).

Language evaluation using the Arabic Language Test

The results of the Arabic Language Test indicated a significant difference between both groups in all the measured parameters. Scores of the language test were significantly lower in the group of children with SCD than those of the normal children. Language age deficit

Table 1 Comparison of both groups in the clinical characteristics

The clinical characteristics	Children with SCD, G1 ($n=24$)	Normal children, G2 ($n=17$)	*P* value	Significance
Chronological age (year)	7.05 ± 1.04	6.85 ± 2.96	0.516	NS
Sex				
Male	15 (62.5%)	11 (64.7%)	0.885	NS
Female	9 (37.5%)	6 (35.3%)		
Socioeconomic status				
Low	10 (41.7%)	11 (64.7%)	0.146	NS
Middle	14 (58.3%)	6 (35.3%)		
Sitting (month)	9.96 ± 0.95	5.29 ± 0.85	0.026	S
Walking (month)	19.21 ± 2.43	13.0 ± 1.84	0.007	S
Height (cm)	116.46 ± 6.36	132.82 ± 6.89	0.012	S
Weight (kg)	19.38 ± 2.63	26.29 ± 3.41	<0.001	S
Mean Hb (gm/dl)	7.79 ± 1.1	12.24 ± 0.73	<0.001	S

S, significant, SCD, sickle cell disease.

Table 2 Comparison of both groups in psychometric evaluation

Psychometric evaluations	Children with SCD, G1 ($n=24$)	Normal children, G2 ($n=17$)	*P* value	Significance
Chronological age (year)	7.05 ± 1.04	6.85 ± 2.96	0.516	NS
IQ scores	79.04 ± 4.69	94.29 ± 5.19	<0.001	S
Mental age (year)	5.13 ± 0.93	6.96 ± 1.82	<0.001	S
Social age (year)	5.17 ± 0.47	6.97 ± 2.51	<0.001	S

IQ, intelligence quotient; S, significant; SCD, sickle cell disease.

Table 3 Comparison of both groups in the age of acquisition both first word and first sentence

Parameters	Children with SCD, G1 ($n=24$)	Normal children, G2 ($n=17$)	*P* value	Significance
First word (month)	16.71 ± 4.05	12.53 ± 3.73	0.002	S
First sentence (month)	29.71 ± 5.73	21.47 ± 3.81	0.004	S

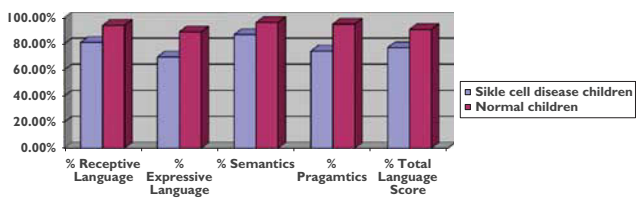
S, significant; SCD, sickle cell disease.

Table 4 Comparison of both groups in the results of the Arabic Language Test

Results of the Arabic Language Test	Children with SCD, G1 ($n=24$)	Normal children G2 ($n=17$)	*P* value	Significance
Receptive language (%)	81.07 ± 9.55	94.12 ± 3.97	0.030	S
Expressive language (%)	69.85 ± 13.67	89.10 ± 9.63	0.003	S
Semantics (%)	87.01 ± 4.27	96.24 ± 3.71	0.016	S
Pragmatics (%)	74.37 ± 19.55	95.11 ± 4.67	0.020	S
Total language (%)	76.93 ± 19.22	90.92 ± 8.67	0.018	S
Total language age (year)	4.29 ± 1.01	6.15 ± 2.88	0.015	S
Language age deficit (year)	2.76 ± 0.03	0.7 ± 0.08	<0.001	S

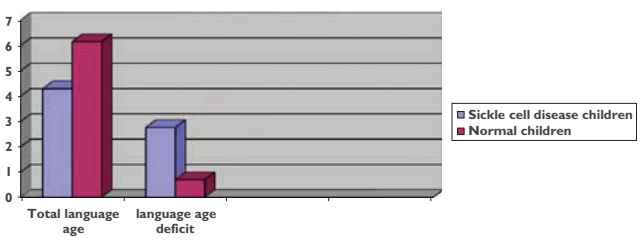
S, significant; SCD, sickle cell disease.

Figure 1



Comparison between both groups in the results of the language test.

Figure 2



Comparison between both groups in the total language and language age deficit.

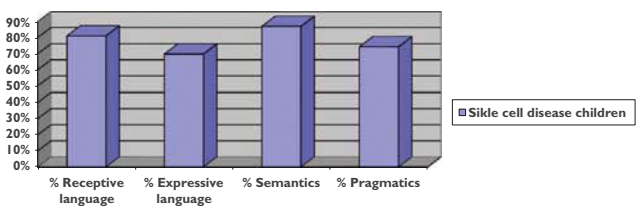
was significantly higher in the group of children with SCD than the normal group. Children with SCD had significantly lower expressive language abilities and pragmatics than semantics and receptive language abilities (Table 4).

The results of the language test were significantly lower in children with SCD than the normal children (Fig. 1).

The total language age was significantly lower and language age deficit was significantly higher in the SCD group than that in normal children (Fig. 2).

Percentages of expressive language and pragmatics were lower than the percentage of semantics and receptive language abilities in the group of children with SCD (Fig. 3).

Figure 3



Comparison between different language parameters in children with sickle cell disease.

Results of audiological assessment

The results of tympanometry showed that all children of both groups had normal tympanograms, indicating normal middle ear functions.

All children of both groups had normal audiograms, with no statistically significant differences between the two groups (Fig. 4).

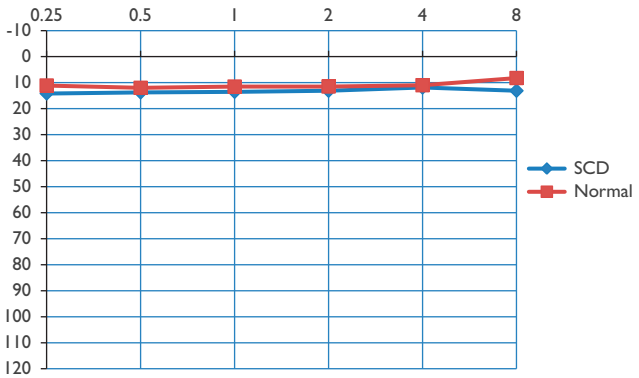
Qualitatively, TEOAEs showed a bilateral partial pass response in one patient and a unilateral partial pass response in three patients. Quantitatively, there were reduced echo levels in children with SCD more than the control group at different frequencies and the differences were highly significant at 1, 1.5, and 4 kHz (Table 5).

Results of correlation between language parameters and intelligence quotient score with different variables in the group of children with sickle cell disease

The age of onset of the disease showed a negative significant association with the age of acquisition of both the first word and sentence and language age deficit. A positive significant association was found with IQ scores and all language parameters. The mean number of vaso-occlusive crisis/year showed a positive significant association with age of acquisition of both the first word and sentence and language age deficit, whereas a negative significant association was found with all language parameters and IQ scores. The mean Hb showed a positive significant correlation with the IQ

score, total language %, and total language age. Also, the mean Hb showed a negative significant association with language age deficit (Table 6).

Figure 4



Pure tone audiometry of the study and the control groups. SCD, sickle cell disease.

Results of correlation between language parameters and intelligence quotient score with transient evoked otoacoustic emission in the group of children with sickle cell disease

TEOAEs in patients with SCD showed a positive significant correlation with % receptive language at 1.5, 2 3, and 4 kHz frequencies. Also, a positive significant correlation was found between % expressive language and TEOAEs at 4 kHz frequency. Moreover, % total language score and total language age showed a positive significant correlation with TEOAEs at 2, 3, and 4 kHz frequencies. A negative significant correlation was found between language age deficit and TEOAEs at 1.5 and 4 kHz (Table 7).

Discussion

Understanding of the cognitive function in children with SCD has increased markedly over the last decade [4–10]. Schatz and McClellan [7] have reported that greater public awareness of the neurocognitive effects of SCD and their

Table 5 Transient evoked otoacoustic emissions in the patient and the control group

TEOAEs frequency (kHz)	Children with SCD, G1 ($n=24$)	Normal children, G2 ($n=17$)	*P* value	Significance
1	9.12 ± 5.14	13.64 ± 6.09	0.011	S
1.5	8.87 ± 4.99	13.57 ± 5.58	0.007	S
2	12.39 ± 7.47	17.33 ± 6.92	0.341	NS
3	15.22 ± 7.36	15.90 ± 5.65	0.721	NS
4	9.65 ± 7.73	16.17 ± 5.76	0.005	S

S, significant; SCD, sickle cell disease; TEOAE, transient evoked otoacoustic emission.

Table 6 Correlation between language parameters and intelligence quotient score with different variables in the group of children with sickle cell disease

	Age of onset of the disease (year)	Mean number of vaso-occlusive crisis (year)	Mean Hb % (gm/dl)	Mean duration of blood transfusion (year)	Mean transfusion index (cm^3/kg/year)	Mean serum Ferrettin (µg/l)	Mean dose of dexofeosamine/kg/day
Age of acquisition first word (month)							
r	−0.056	0.628	−0.240	0.182	−0.011	−0.097	−0.003
P	0.008*	0.001*	0.258	0.394	0.961	0.653	0.990
Age of acquisition first sentence (month)							
r	−0.018	0.671	−0.526	0.080	0.068	−0.213	−0.233
P	0.001*	0.000*	0.793	0.709	0.751	0.318	0.272
Receptive language (%)							
r	0.346	−0.729	0.380	−0.171	−0.121	0.238	−0.056
P	0.002*	0.000*	0.067	0.423	0.572	0.262	0.794
Expressive language (%)							
r	0.179	−0.598	0.358	−0.255	−0.110	0.051	0.123
P	0.000*	0.002*	0.086	0.229	0.609	0.812	0.568
Semantics (%)							
r	0.360	−0.453	0.373	0.587	0.020	0.179	0.066
P	0.003*	0.026*	0.073	0.083	0.925	0.402	0.759
Pragmatics (%)							
r	0.336	−0.514	0.395	0.517	0.050	0.163	0.052
P	0.009*	0.010*	0.056	0.081	0.815	0.447	0.809
Total language (%)							
r	0.273	−0.715	0.406	−0.215	−0.115	0.224	0.067
P	0.196	0.000*	0.049*	0.313	0.591	0.293	0.757
Total language age (year)							
r	0.244	−0.519	0.429	0.544	0.071	0.206	0.025
P	0.010*	0.009*	0.036*	0.085	0.740	0.335	0.909
Language age deficit (year)							
r	−0.033	0.676	−0.344	0.364	0.127	−0.181	−0.007
P	0.000*	0.000*	0.000*	0.810	0.555	0.397	0.973
Intelligence quotient							
r	0.280	−0.703	0.296	−0.359	−0.092	0.056	0.187
P	0.002*	0.000*	0.046*	0.906	0.669	0.795	0.381

*Significant.

Table 7 Correlation coefficient between language parameters and intelligence quotient score with transient evoked otoacoustic emissions in the group of children with sickle cell disease

TEOAEs frequency (kHz)	Receptive language (%)	Expressive language (%)	Semantics (%)	Pragmatics (%)	Total language score (%)	Total language age (year)	Language age deficit	IQ
1.0								
r	0.244	0.171	−0.016	−0.057	0.240	0.011	−0.336	0.167
P	0.250	0.424	0.940	0.791	0.259	0.960	0.108	0.434
1.5								
r	0.429	0.343	0.142	0.227	0.386	0.322	−0.466	0.048
P	0.037*	0.101	0.509	0.287	0.062	0.125	0.022*	0.823
2								
r	0.499	0.344	0.067	0.041	0.423	0.095	−0.217	0.244
P	0.013*	0.100	0.757	0.851	0.039*	0.060*	0.307	0.250
3								
r	0.464	0.394	0.273	0.299	0.426	0.356	−0.338	0.038
P	0.022*	0.057	0.196	0.156	0.038*	0.028*	0.106	0.860
4								
r	0.567	0.474	0.060	0.122	0.504	0.232	−0.485	0.190
P	0.004*	0.019*	0.779	0.571	0.012*	0.026*	0.016*	0.373

IQ, intelligence quotient; TEOAE, transient evoked otoacoustic emission
*Significant.

impact on children's developmental outcomes is a critical step toward improved treatment, adaptation to illness, and quality of life. Unfortunately, most previous studies have reported the impact of the illness on certain cognitive domains. Yet, the profile of language development in children with SCD is still unclear. To the best of our knowledge, no previous study has been carried out to assess the language function in Arabic-speaking children with SCD in comparison with normal children of the same age, sex, and same social class. Therefore, the present study examined the language function in Egyptian children with SCD to assess how a chronic disease such as SCD could affect this ability.

Previous research has shown a significant association between SES and language skills. Parents of low SES have less positive parent–child interactions, which in turn affect children's cognitive and language development. These children have a slower rate of growth for expressive language skills compared with children in higher SES families [21,22]. In the present study, children of both groups were from the same SES in order to exclude the role of SES on language development.

In the current study, the developmental milestones were significantly delayed in the children with SCD in comparison with their normal peers. This finding is in agreement with that of Whitten [23], who reported that children with SCD often experience delays in achieving developmental milestones. Moreover, these children showed significantly lower weight and height associated with decreased hemoglobin level than the controls. These results were in agreement with El-Henidy [24] and Farid and Said [25], who found growth retardation in terms of weight and height and lower hemoglobin level in patients with SCD. Also, Silva and Viana [26], in their study, found growth deficit in children with SCD and they considered fast red blood cell turnover to be partially responsible for this defect.

In the present study, the significant decrease in mental ability as well as lower IQ scores that were found in the group of children with SCD are in agreement with the findings of Hijmans *et al.* [27], who reported that children with SCD are at an increased risk of lower intelligence relative to their controls. Similar results have been reported by Schatz *et al.* [6], who detected approximately four-point to five-point decrease in children with SCD on IQ measures compared with the normal control group. Moreover, previous studies have reported that children with SCD are more likely to have impairments in their mental abilities and cognitive function [8–28]. Cognitive function is an intellectual process by which one becomes aware of, perceives, or comprehends ideas. It involves all aspects of perception, thinking, reasoning, remembering, speaking, and reading comprehension. It is generally measured using tests such as the IQ tests and more sensitive tests to measure specific cognitive abilities. The cause of this cognitive decline may include the direct effects of SCD on brain function or the indirect effects of chronic illness related to social or environmental disadvantages [6]. Brown *et al.* [29] have suggested that cognitive and mental abilities impairments in children with SCD may be a function of chronic hypoxia of the brain. In addition, Steen *et al.* [30] have reported that low hematocrit level is a significant predictor of cognitive impairment in children with SCD, which indicates that cognitive impairment is associated with chronic hypoxia. Furthermore, both Steen *et al.* [10] and Wang *et al.* [28] found that cognitive ability tends to decrease with age, which is not observed in healthy children and which is presumably an indication of the cumulative effect of disease on the brain. The findings of Steen *et al.* [11] have indicated that there is diffuse brain injury in these patients and that deficits increase with age.

The results of the present study show a significant delay in social abilities in the children with SCD in comparison with the normal group. This finding are in agreement with the finding of Taylor *et al.* [31], who reported that the developmental outcomes for children with SCD have been shown to be more dependent on the quality of the social environment than for normal children. Thus, both the social context of a child with SCD and the interaction of that context with the disease may be critical to developmental outcomes. In the current study, the significant delay in the acquisition of the first word and sentence in addition to the significant decrease in their

social ability in the group of children with SCD may point to the fact that these children with chronic disease are exposed to iatrogenic factors such as a long duration of isolation in the hospital, side effects of medications, and the sequelae of complications of the disease in conjunction with overprotection of their parents. These factors may affect negatively the language stimulation and normal acquisition. This delay in language acquisition in SCD children was similar to the results reported by Schatz *et al.* [32], which indicated specific language delay in pediatric SCD that appeared to be related to the direct neurological effects of the disease and indirect effects related to the social and environmental disadvantages associated with the SCD.

In addition, the present study found significant disabilities in all language parameters that were prominently affected in the children with SCD relative to their controls. Total language age was significantly lower, whereas language age deficit was higher in the group of children with SCD in comparison with normal children. Moreover, our results showed that the most frequently affected language ability in the SCD group was expressive language, followed by pragmatics, and the least affected was semantics and receptive language. Meanwhile, these findings were similar to the results of Schatz *et al.* [32], which showed significant deficits in all three language domains (semantic, syntactic, and phonological processing), with a high prevalence of alteration in the expressive language acquisition process that appeared to be related to the neurological effects of the disease. These children used less complex expressive language and showed low receptive comprehension with affection of listening memory and verbal reasoning. In addition, the findings of Sanchez *et al.* [1] indicated that the decreased syntactical ability may contribute to a lower verbal IQ or that syntactical impairment may precede declines in semantic knowledge, with declines in semantic ability emerging with age. Moreover, difficulties in both syntactical and phonological processing in SCD may also be related, in part, to altered short-term memory functions [33]. Impairments in expressive language ability could also result from a complex working memory or executive functioning deficit [34]. This deficit could affect normal language development in children with SCD. Therefore, better knowledge of the nature of language deficits in these children may help in understanding the exact language problems, and the proper management and design of a therapeutic program for these children.

Another factor that may be related to language development in SCD patients is hearing involvement. There is a consensus in the various audiological studies that patients with SCD have a much higher incidence of sensorineural hearing loss (SNHL) than the rest of the population [13,14], and the frequency of this complication is variable, ranging from 12 to 29% [13–35]. In the present study, all patients with SCD had normal pure tone thresholds and no significant differences were observed between the study and the control group. However, there were reduced echo levels of TEOAEs in SCD patients relative to the control group and this indicates outer hair cell dysfunction that can be detected by TEOAEs before pure tone thresholds are affected. Similar audiological findings have been reported by Farid and Sayed [25], who recommended implementing otoacoustic emission testing in the evaluation of SCD patients even if they have no hearing complaints. In addition, there was a significant correlation between cochlear dysfunction indicated by TEOAEs in patients with SCD and most of the language parameters.

This study showed that the age of onset of the disease was significantly correlated with IQ measures, the age of acquisition of the first word and sentence, and all the measured language parameters. Generally, our results indicated that children with early onset of the disease were found to have lower IQ scores, late acquisition of the first word and sentence, and lower language abilities in addition to higher language age deficit. These findings are reasonable because children with early onset of the SCD were more likely to suffer from the sequelae of complications of the disease and frequent isolation in the hospital. These problems may impact the amount, type, and quality of communication between the parents and the child. This may limit a child's opportunities for language exposure and acquisition or alter the type of language models provided by the parents. These findings raise the possibility of a relationship between age of onset of the disease and the language abilities in children with SCD.

In addition to the previous findings, the present study showed that children who more frequently had vaso-occlusive crisis were found to have a delay in first word and sentence acquisition, lower IQ scores, lower language abilities, and higher language age deficit compared with children who less frequently had vaso-occlusive crisis. Also, Farid and Sayed [25] reported that the increased frequency of vaso-occlusive crises and noncompliance to hydroxyurea treatment were the main predictive factors for hearing impairment. These findings are supported by Jacob *et al.* [36], who reported that the most common SCD complication and the most common reason for hospitalization is the vaso-occlusive crisis. These crises vary in intensity, location, and quality. The typical vaso-occlusive crisis requiring hospitalization lasts approximately 10 days. This hospitalization and environmental isolation may have a major impact on the normal cognitive development, daily life, and academic attainment of the children with SCD.

Previous studies have found relationships between neurological risk and language ability [6–28]. Decreased verbal ability may be related to the direct effects of the accumulation of micro infarcts, chronic brain hypoxia related to severe anemia, acute hypoxia related to physical complications such as acute chest syndrome, and nutritional deficiencies related to high metabolic demands [29,30]. As an alternative to the more direct effects of SCD on brain functioning, indirect effects related to social or environmental disadvantages (e.g. decreased learning opportunities, increased physical limitations from chronic illness) have been cited as potential causes [28,29].

Our results indicated a positive significant association between IQ score, total language %, and total language age and Hb level, whereas a negative significant association was found between Hb level and language age deficit. These results may point to the fact that the increase in Hb level was related to improvement in language abilities and IQ scores. Similar results have been found by Sanchez *et al.* [1], who reported that hematocrit levels were related to language testing. These findings are consistent with previous literature linking anemia with low cognitive scores in school-age children [9–37].

Conclusion and recommendations

Our findings show evidence that SCD is associated with significant deficits in language development, IQ measurements, and hearing abilities. The influence of SCD on language development is complex and multifactorial. Therefore, proper assessment of these abilities in children with SCD from early infancy onwards may be important for understanding early disease-related effects and may be essential for identifying the specific causes of these effects. This may help in applying the most appropriate screening tools to identify at-risk children in order to detect deficits early in life and prevent delayed language development, hearing impairment, and poor academic achievement as much as possible. Moreover, the cognitive abilities of SCD children as well as their language abilities are highly correlated with the age of onset of the disease and number of vaso-occlusive crises, which indicates that controlling the vaso-occlusive crisis and targeting the cognitive and language abilities in the therapy will ultimately result in an improvement in these abilities in children with SCD.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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