
Socioeconomic Determinants Affecting Compliance to therapy in Patients with Congenital Hypothyroidism in Sharkia Governorate

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Abstract

Background: Congenital hypothyroidism (CH) is the most common preventable causes of mental retardation in children thus compliance to medication is known to improve the neurodevelopmental outcomes. Compliance to therapy can be affected by multiple factors.

Objective: The study aimed to explore compliance of the patients' guardian to medical therapy and to explore the socioeconomic factors affecting compliance to medication in patients with CH.

Methods: A cohort follow-up study was conducted in Endocrinology and Pediatric Out-patient Clinics in Sharkia Governorate health insurance center. The study participants were 120 newborn and infant with CH. Data were collected using multi-structured questionnaires for determining socioeconomic state and Morisky Medication Adherence Scale (MMAS 8) to assess patient compliance. The results of investigations at diagnosis (initial TSH and T4) and during the follow-up visits were reviewed.

Results: About two third of patient families were highly compliant to therapy. Compliance to therapy was affected by the occupational and educational levels of the parents as well as residence, income, social class of the parents and presence of symptoms and associated congenital anomalies. But the most significant factors affecting compliance to therapy were mother's education, social class, and the presence of symptoms at presentation.

Conclusion: Compliance with L-thyroxin therapy in our patients and/or their family was found to be reasonable. The most significant factors affecting the compliance were mother's education, social class, and the presence of symptoms at presentation.

Key words: congenital, hypothyroidism, compliance, adherence, TSH

Introduction:

Congenital hypothyroidism (CH) had gained its recognition among the endocrinological disorders owing the fact that it's the most common preventable cause of mental retardation in children.(1) Congenital hypothyroidism is defined as thyroid hormone deficiency that exist at birth. It is mainly due to problem in the thyroid gland development (dysgenesis) or due to disruptions in thyroid hormone biosynthesis (dysharmonogenesis).(2)

It was estimated that the incidence of CH was 1/3000 to 1/4000 live births in iodine sufficient countries.(3) In Egypt, a study conducted in Fayoum revealed that the incidence of CH during the period from January 2003 to December 2011 was 1/2941 live births.(4) The clinical features of congenital hypothyroidism are frequently subtle and the newborns with CH are asymptomatic. Thus, without newborn screening, many newborns remain undiagnosed at birth.(5)

The delay in the diagnosis and treatment of CH subsequently leads to neurological consequences including mental retardation, poor motor coordination, learning disorders, and attention deficiency. Therefore early diagnosis and treatment is critical in CH. (6) Neonatal screening programs permit the early detection and treatment of CH preventing the undesired consequences. (7) The mainstay of the treatment of CH lies in the early diagnosis and thyroid hormone replacement. The optimal care comprises the diagnosis before the age of 10 to 13 days and normalization of thyroid hormone blood levels by 3 weeks age. The goal of therapy is to achieve a growth and mental development close to the normal.(8)

However, poor medication compliance is a persistent problem across many diseases,

especially chronic conditions like CH. Research had suggested that about three-quarters of patients with CH were compliance therapy.(9) Poor medication compliance has a substantial impact on disease progression, disease complications, functional outcomes, and quality of life leading to significant growth failure and psychomotor delay during childhood and a possible cause of permanent neurological deficits.(10,11) Poor compliance to treatment was multifaceted and complex including; Patient-centered factors (such as age, gender, education, and forgetfulness, socioeconomic), therapy-related factors (such as treatment complexity and side effects) and healthcare system factors.(12)

The study aimed to assess the compliance of the patients and/ or their target families to L thyroxin therapy, and to explore the socioeconomic factors affecting compliance to medication in patients with CH.

Methods:

This study protocol was approved by the Ethical Committee of Menoufia Faculty of Medicine, and enrollment of the individuals to the study was conditioned with written informed consent obtained from patient's guardians. A Cohort follow-up study was conducted from the 1st of January, 2015 till the end of December of 2015 in the Endocrinology and Pediatric Outpatient Clinics in Sharkia Governorate health insurance center. All newborn diagnosed with congenital hypothyroidism and infants and / or children who come for treatment and follow up in the center during 6 month of the study period were enrolled in the study. It included 120 patients (57 males and 63 females). All the parents of the participants were interviewed using 4 predesigned questionnaires. These questionnaires aimed at determining Socioeconomic state, clinical

picture of congenital hypothyroidism at presentation, personal history and family history and Morisky Medication Adherence Scale (MMAS 8) that is assessing patient compliance.(13) Patients with MMAS 8 score =8 were considered highly compliant, patients with score 6 or 7 were considered medium compliant and those with score less than 6 were considered of low compliance. The patient's investigation results (Thyroid-stimulating hormone (TSH)) were reviewed in the child health record in the initial diagnosis and during the follow up visits.

Statistical analysis:

Data were checked, entered and analyzed using Statistical Package for Social Science (SPSS) version 13 (SPSS Inc., Chicago, Illinois, USA).Data were expressed as mean \pm SD for quantitative variables, number and percentage for categorical variables. Analysis of variance (ANOVA) was used to compare the means of more than 2 samples. Chi-square (X²) and Fisher exact test were used to test the association between qualitative variables. Binary logistic regression test was used to assess the effect of several potential risk factors and to adjust for underlying confounding effect of other variables. A P value of <0.05 was considered statistically significant.

Results:

The children with confirmed CH and on treatment were 120 during the year of 2015 Sharkia governorate. Nearly 60% of the children were highly compliant to therapy while less than one third of the patients were low compliant to therapy and only 11.7% of patients were medium compliant (Figure 1). There are highly statistical significant differences between high, medium and low compliant grades regarding the mean \pm SD of the TSH levels during the follow up visits

(P value < 0.001). The higher the TSH level, the lower the compliance grades (Table 1). There is a significant negative correlation between compliance score and TSH level at the start of the study and after one month. Also, there is highly significant negative correlation between the compliance score and the follow up TSH level at three and six months follow up (Table 2).

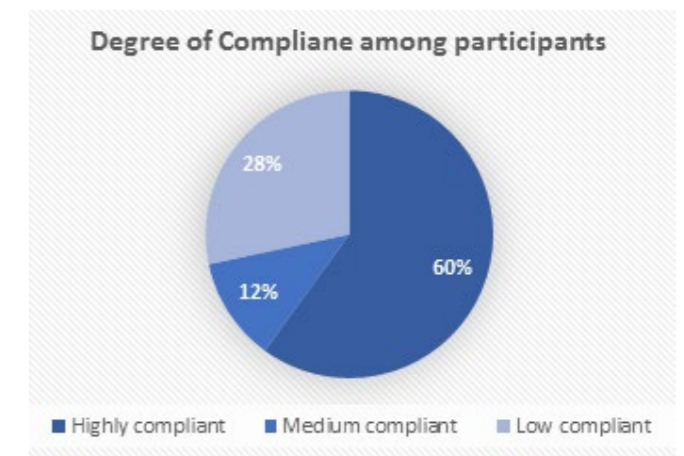


Figure (1): Degree of compliance among participants

The compliance of the participants to therapy is affected by: the occupational and educational levels of the parents; the higher the level of occupation and/or education of the parents, the higher the compliance. Also the compliance is affected by the residence, income, and the social class of the parents; all the individuals living in urban areas were highly compliant to therapy and most of the individuals living in urban slum were low compliant, and the higher the income and the higher the social class the higher the grade of compliance (Table 3). By the use of binary logistic regression for factors affecting compliance there is only statistical significant difference between compliance and mothers' education and social. On the other hand, there is no statistically significant difference as regard other factors (Table 4).

Table (1): Comparison between different compliant grades as regard the TSH level

| TSH* (X ± SD)** | Highly compliant (n. 72) | Medium compliant (n. 14) | Low compliant (n. 34) | ANOVA*** | P |
|--------------------|-----------------------------|-----------------------------|--------------------------|----------|---------|
| At one month | 7.238±5.022 | 19.75± 9.90 | 38.11±23.7 | 17.676 | < 0.001 |
| At 3 months | 3.16±2.19 | 7.193±5.194 | 16.18±13.88 | 30.85 | < 0.001 |
| At 6 Months | 2.85±2.16 | 6.591±5.749 | 11.87±7.71 | 40.646 | < 0.001 |

*TSH: Thyroid-Stimulating Hormone

**X ± SD: Mean ± Standard Deviation

*** ANOVA: Analysis of Variance

Table (2): Correlation between compliance score and TSH level

| TSH Level | Compliance score | |
|-------------------------------|------------------|---------|
| | r | p |
| TSH at the start of the study | - 0.179 | 0.05 |
| TSH after one month | - 0.421 | 0.013 |
| TSH after 3 month | - 0.343 | < 0.001 |
| TSH after 6 month | - 0.324 | < 0.001 |

*TSH: Thyroid-Stimulating Hormone

Table (3): Socio-economic determinants affecting the degree of compliance

| Compliance degree Variable | High (72) | | Med. (14) | | Low (34) | | Total | | F | P |
|-----------------------------------------|-----------|------|-----------|------|----------|------|-------|------|------|---------|
| Mother's Education | | | | | | | | | | |
| ▪ Illiterate. | 2 | 2.8 | 2 | 14.3 | 10 | 29.4 | 14 | 11.7 | 44.7 | < 0.001 |
| ▪ Read and write | 2 | 2.8 | 3 | 21.4 | 6 | 17.6 | 11 | 9.2 | | |
| ▪ Primary | 9 | 12.5 | 0 | 0 | 7 | 20.6 | 16 | 13.3 | | |
| ▪ Preparatory | 8 | 11.1 | 3 | 21.4 | 3 | 8.8 | 14 | 11.7 | | |
| ▪ Secondary | 15 | 20.8 | 5 | 35.7 | 5 | 14.7 | 25 | 20.8 | | |
| ▪ University graduate | 36 | 50 | 1 | 7.1 | 3 | 8.8 | 40 | 33.3 | | |
| Father's education | | | | | | | | | | |
| ▪ Illiterate | 1 | 1.4 | 0 | 0 | 8 | 23.6 | 9 | 7.5 | 32.6 | < 0.001 |
| ▪ Read and write | 5 | 6.9 | 5 | 35.7 | 11 | 32.4 | 21 | 17.5 | | |
| ▪ Primary | 5 | 6.9 | 0 | 0 | 7 | 20.6 | 12 | 10 | | |
| ▪ Preparatory | 10 | 13.9 | 4 | 28.6 | 2 | 5.9 | 16 | 13.3 | | |
| ▪ Secondary | 24 | 33.3 | 4 | 28.6 | 4 | 11.8 | 32 | 27.8 | | |
| ▪ University graduate | 27 | 37.5 | 1 | 7.1 | 2 | 5.9 | 30 | 25 | | |
| Mother's Occupation | | | | | | | | | | |
| ▪ House wife | 40 | 55.6 | 9 | 94.3 | 34 | 100 | 83 | 69.2 | 31.9 | < 0.001 |
| ▪ Unskilled worker | 4 | 5.6 | 3 | 21.4 | 0 | 0 | 7 | 5.8 | | |
| ▪ Skilled worker | 3 | 4.2 | 0 | 0 | 0 | 0 | 3 | 2.5 | | |
| ▪ Trades business | 8 | 11.1 | 2 | 14.3 | 0 | 0 | 10 | 8.3 | | |
| ▪ Semiprofessional | 11 | 15.3 | 0 | 0 | 0 | 0 | 11 | 9.2 | | |
| ▪ Professional | 6 | 8.3 | 0 | 0 | 0 | 0 | 6 | 5 | | |
| Father's Occupation | | | | | | | | | | |
| ▪ Non-working | 1 | 1.4 | 0 | 0 | 3 | 8.8 | 4 | 3.3 | 20.9 | 0.02 |
| ▪ Unskilled worker | 11 | 15.3 | 5 | 35.7 | 12 | 35.3 | 28 | 23.3 | | |
| ▪ Skilled worker | 15 | 20.8 | 2 | 14.3 | 8 | 23.5 | 25 | 20.8 | | |
| ▪ Trades business | 23 | 31.9 | 6 | 42.9 | 10 | 29.4 | 39 | 32.5 | | |
| ▪ Semiprofessional | 15 | 20.8 | 1 | 7.1 | 0 | 0 | 16 | 13.3 | | |
| ▪ Professional | 7 | 9.7 | 0 | 0 | 1 | 2.9 | 8 | 6.6 | | |
| Residence: | | | | | | | | | | |
| ▪ Urban slum | 2 | 2.8 | 0 | 0 | 12 | 35.3 | 14 | 11.7 | 40.3 | < 0.001 |
| ▪ Rural | 47 | 65.3 | 14 | 100 | 22 | 64.7 | 83 | 69.2 | | |
| ▪ Urban | 23 | 31.9 | 0 | 0 | 0 | 0 | 23 | 19.2 | | |
| Income : | | | | | | | | | | |
| ▪ Not sufficient | 12 | 16.7 | 5 | 35.7 | 14 | 41.2 | 31 | 25.8 | 15.8 | o.015 |
| ▪ In debt | 42 | 52.3 | 9 | 64.3 | 19 | 55.9 | 70 | 58.3 | | |
| ▪ just meet routine expenses | 12 | 16.7 | 0 | 0 | 1 | 2.9 | 13 | 10.8 | | |
| ▪ Meet routine expenses and emergencies | 6 | 8.3 | 0 | 0 | 0 | 0 | 6 | 5 | | |
| Social class: | | | | | | | | | | |
| ▪ Very low | 0 | 0 | 0 | 0 | 11 | 32.4 | 11 | 9.2 | 48.4 | < 0.001 |
| ▪ Low | 20 | 27.8 | 9 | 64.3 | 16 | 47.1 | 45 | 37.5 | | |
| ▪ Medium | 38 | 52.8 | 5 | 35.7 | 7 | 20.6 | 50 | 41.7 | | |
| ▪ High | 14 | 19.4 | 0 | 0 | 0 | 0 | 14 | 11.7 | | |

Table (4): Binary logistic regression of socioeconomic determinant affecting patient's compliance

| | Beta | S.E. | Wald | P | Odds ratio |
|---------------------|---------|----------|-------|--------|-----------------------|
| Father's occupation | 17.48 | 9918.27 | 0.000 | 0.999 | 0.001 (0.007- 5.892) |
| Mother's occupation | 0.283 | 0.670 | 0.178 | 0.673 | 1.327 (0.357- 4.937) |
| Father's education | 12141.4 | 0.000 | 8.043 | 0.999 | 0.009 (0.004-11.860) |
| Mother's education | 1.085 | 4.131 | 1.835 | 0.042* | 9.065 (1.082 -75.947) |
| Residence | 18.921 | 7009.998 | 0.000 | 0.998 | 0.226 (1.417 -14.283) |
| Income | 0.457 | 0.654 | 0.489 | 0.484 | 0.002 (0.081- 0.063) |
| Social class | 1.049 | 0.321 | 5.291 | 0.015* | 0.454 (0.021 - 0.282) |

* Statistically Significant

Discussion:

The mainstay in the treatment of CH is early diagnosis and thyroid hormone replacement to prevent the negative impact on the physical and mental development.(8) In the current study, the incidence of CH in Sharkia governorate was 1/3195 live births during the year of 2015. This result is similar to the reported results by Dabbous and his collage (1:2567 and 1/3306 live births in the year 2001 and 2002 in Alexandria, Egypt) (9); Abdel-Rasoul et al (1/ 3000 live births in Menoufiya governorate from year 2003 till 2008) (14), and Corbetta et al (1/3000 to 1/4000 live births in iodine sufficient countries in 2009).(3)

Compliance to thyroid hormone therapy, nearly 60% of the patients were highly compliant to therapy. While less than one third of the patients were low compliant. This is consistent with data recorded by Dabbous et al. who documented that nearly quarter of cases (26.7%) were not always compliant to thyroid hormone therapy, and they

concluded that the day of starting treatment with thyroid hormone and compliance to treatment are the main prognostic factors for normal child development and adult height.(9) This is supported by our results of highly significant negative correlation between the compliance score and the TSH level.

In the present study the compliance to therapy was affected by multiple socioeconomic factors; education and occupation, social class, residence and income of the parents. This is consistent with that reported results by EI-Hadiyah et al who demonstrated that the reasons for poor adherence to treatment are multifaceted and complex, and include, Patient-centered factors (such as age, sex, education, and forgetfulness), therapy-related factors (such as treatment complexity and side effects), healthcare system factors (such as drug availability and accessibility to healthcare), social and economic factors (such as cost of therapy, income and social support).(12)

By the use of binary logistic regression for factors affecting compliance there is only statistically significant difference between compliance grades and education of mothers, social class and presence of symptoms. But no statistically significant difference was found as regard other factors. This is consistent with review by Peltzer and Pengpid who performed a systematic review of the association of socioeconomic status with adherence to treatment of patients with HIV/AIDS in low- and middle income countries and they concluded that Income, level of education, and employment/occupational status were significantly and positively associated with the level of adherence.(15)

Also the current results are in agreement with Cho and Kim who on studying adherence of patient to antihypertensive medications. They demonstrated that a lower education attainment level was associated with higher rates of non-adherence to antihypertensive medication in Korea. Furthermore, those with higher levels of educational attainment were more likely to be adherent than those with lower levels.(16) Also they demonstrated that age, gender, income and residence were associated with non-adherence in the first model. However, the statistical significance of gender, residence and income disappeared after adjusting for the socioeconomic variables.(17)

Moreover a study by Braverman and Dedier found that the effects of education on medication adherence varied by sex, showing that lower educational attainment was associated with lower adherence in women but not in men.(17) Correspondingly a study by Farahat et al., showed that there was statistically significant difference between the two studied groups as regards gender, education, social class and presence

of family members helpful in reminding about medication.(18)

Conclusion:

High compliance to treatment of CH was an important prognostic factor for normal mental and physical development in infant and children with CH. It is recommended to emphasize the importance of early screening for and treatment of CH during the 1st week of life, to emphasize the importance of compliance of patients and/or their family to therapy of congenital hypothyroidism. Also, to improve the compliance to therapy through health education of both patients and their families and the health care providers.

References:

1. Léger J. Endocrinology and adolescence: congenital hypothyroidism: a clinical update of long-term outcome in young adults. *European Journal of Endocrinology*. 2015; 172(2):R67-77.
2. Rastogi M, LaFranchi S. Congenital hypothyroidism. *Orphanet journal of rare diseases*. 2010; 5(1):17.
3. Corbetta C, Weber G, Cortinovic F, et al. A 7-year experience with low blood TSH cutoff levels for neonatal screening reveals an unsuspected frequency of congenital hypothyroidism (CH). *Clinical endocrinology*. 2009 ;71(5):739-45.
4. Bekhit O, Yousef R. Permanent and transient congenital hypothyroidism in Fayoum, Egypt: a descriptive retrospective study. *PloS one*. 2013; 8(6):e68048. www.plosone.org last accessed Febryry,2017
5. Agrawal P, Philip R, Saran S, et al. Congenital hypothyroidism. *Indian journal of endocrinology and metabolism*. 2015 ;19(2):221-227
6. Ünüvar T, Demir K, Abaci A, et al. Monitoring and prognostic evaluation of patients with congenital hypothyroidism

- treated in a pediatric endocrinology unit. The Turkish journal of pediatrics. 2013; 55(4):384-390.
7. Dayal D, Prasad R. Congenital hypothyroidism: Current perspectives. Res Rep Endocr Disord. 2015; 5:91-102.
8. Grosse S, Van Vliet G. Prevention of intellectual disability through screening for congenital hypothyroidism: how much and at what level? Archives of disease in childhood. 2011; 96(4):374–379.
9. Dabbous NI, Abdel-Aziz HM, Abou El-Enein, et al. Indicators of the screening program for congenital hypothyroidism in Alexandria. J Egypt Public Health Assoc. 2008; 83(3):307-327.
10. American Pharmacists Association. Improving medication adherence in patients with severe mental illness. Pharmacy Today. 2013; 19(6):69-80.
11. Kubicky R, Weiner E, Carlson B, et al. Effect of prolonged discontinuation of L-thyroxine replacement in a child with congenital hypothyroidism. Case reports in endocrinology. 2012.
12. El-Hadiyah T, Madani A, Abdelrahim H, et al. Factors Affecting Medication Non Adherence in Type 2 Sudanese Diabetic Patients. Pharmacology & Pharmacy. 2016 ;7(04):141-146
13. Morisky Dm, DiMatteo M. Improving the measurement of self-reported medication nonadherence: response to authors. Journal of clinical epidemiology. 2011 ; 64(3): 255-257
14. Abdel-Rasoul G, Hathout H, Abu Salem M, et al. Epidemiological Features of Neonatal hypothyroidism in Menoufiya Governorate - Egypt. (A case- control study). Menoufiya Medical Journal Vol. 24 No. 1 Jan 2011.
15. Peltzer K, Pengpid S. Socioeconomic Factors in Adherence to HIV Therapy

- in Low- and Middle-income Countries. J Health Popul Nutr. 2013; 31(2):150-170.
16. Cho S, Kim J. Factors associated with nonadherence to antihypertensive medication. Nursing and Health Sciences.2014; 16: 461–467.
17. Braverman J, Dedier J. Predictors of medication adherence for African American patients diagnosed with hypertension. Ethnicity & disease. 2009; 19(4):396–400.
18. Farahat T, Shaheen H, Khalil N et al. Comparative study between adult and elderly patients as regards adherence to antihypertensive medication. Menoufia Medical Journal. 2016;29(1):121-5.

المخلص العربي

المحددات الاجتماعية والاقتصادية التي تؤثر على الامتثال للعلاج لدى مرضى قصور الغدة الدرقية الخلقية بمحافظة الشرقية

يعتبر قصور الغدة الدرقية الخلقية من الأسباب الأكثر شيوعاً للتخلف العقلي لدى الأطفال والتي يمكن الوقاية منها وبالتالي ومما لا شك فيه ان الامتثال للعلاج الدوائي يؤدي الى تحسين في الوظائف النمائية العصبية لدى الاطفال المصابين وجدير بالذكر ان الامتثال للعلاج الدوائي يمكن أن يتأثر بعوامل متعددة. وهدفت هذه الدراسة الى تحديد مدى الامتثال للعلاج الطبي من قبل الوصي على الطفل ، واستكشاف العوامل الاجتماعية والاقتصادية التي تؤثر على الامتثال للدواء في المرضى. وقد تم اجراء هذه الدراسة المقطعية في عيادات الأطفال و الغدد الصماء الخارجية بمركز التأمين الصحي في محافظة الشرقية وكان عدد المشاركين في الدراسة ١٢٠ من حديثي الولادة والرضع، تم تجميع البيانات باستخدام استبيانات متعددة لتحديد الحالة الاجتماعية والاقتصادية، و”مقياس موريسكي للالتزام الدوائي” لتقييم درجة امتثال المريض للدواء وتم مراجعة نتائج الفحوصات عند التشخيص الأولى وأثناء متابعة الزيارات. وانتهت الدراسة الى ان ثلثي أسر المرضى على درجة عالية من الامتثال للعلاج. وتأثر الامتثال للعلاج بالمستويات المهنية والتعليمية للأباء والأمهات وكذلك الإقامة، الدخل، الطبقة الاجتماعية للوالدين. ولكن أهم العوامل التي تؤثر على الامتثال للعلاج كان تعليم الأم والطبقة الاجتماعية التي تنتمي لها، ووجود أعراض للمرض عند اكتشافه. وخلصت الدراية الى ان الامتثال للعلاج الدوائي بهرمون الغدة الدرقية في المرضى متحقق بشكل كبير وكانت أهم العوامل التي تؤثر على الامتثال هي تعليم الأم، والطبقة الاجتماعية، ووجود أعراض عند الاكتشاف