Factors Associated with Type-1 Diabetes Mellitus in Children Aged 2-15 Years: A Case-Control Study from southern Iran

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Research

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Abstract

Background

This study aimed to investigate the association between Type-1 Diabetes Mellitus and diet in the first two years of life as well as a select group of demographic variables.

Methods

This case-control study was conducted on 76 children with T1DM and 209 non-diabetic children selected through convenience sampling from the population of people visiting the community health centers of the city of Jahrom, Iran. The required data were collected by a questionnaire of diet and demographic information that was completed by the mothers of the children. The data were analyzed using logistic regression and adjusted odds ratio.

Results

Finally, the results of multiple backward logistic regression showed that Body Mass Index (BMI) of the mother being less than 18.5 before pregnancy (OR: 4.4, 95% CI: 1.61 to 11.97), mothers without a history of diabetes (OR: 0.02, 95% CI: 0.001 to 0.60), mother's weight before pregnancy (OR: 0.88, 95% CI: 0.84 to 0.91), mother's excess weight during pregnancy (OR: 0.83, 95% CI: 0.75 to 0.93), exclusive breastfeeding for more than six months (OR: 0.19, 95% CI: 0.03 to 0.96), low weight gain in the first two years of life (OR: 6.98, 95% CI: 2.16 to 22.5), and the breastfeeding less than 12 months (OR: 10.52, 95% CI: 1.62 to 66.64) have association with Type 1 diabetes (p < 0.05).

Conclusion

Body mass index less than 18 mothers before pregnancy, Low weight gain in the first two years of life and breastfeeding less than 12 months increases the risk of developing Type-1 Diabetes in children.

Background

Type 1 diabetes mellitus (T1DM) is a chronic autoimmune disease associated with the destruction of pancreatic β cells, which leads to extreme or absolute insulin deficiency. People with T1DM require lifelong insulin therapy. T1DM is a major public health problem with increasing prevalence worldwide (1, 2).

The increase in knowledge of type 1 diabetes over the past 25 years has led to a broad understanding of many aspects of the disease, including genetics, epidemiology, the phenotype of immune cells, and beta
cells and the burden of disease. Globally, type 1 diabetes is increasing in both prevalence and incidence, with an overall annual increase in occurrence of about 2–3% per year (3).

However, the incidence of type 1 diabetes varies by country and by region within countries (4). For example, at northern latitudes, people born in the spring are more likely to develop the disease than those born in the other seasons (5).

Type 1 diabetes mellitus is one of the most common chronic diseases that develops in childhood. For unknown reasons, its incidence in children increases from 3 to 5% every year worldwide (6). The peak incidence of diagnosis is seen in children aged 10–14 years (3, 4).

On the other hand, diabetes is the most common chronic metabolic disease diagnosed in children and adolescents. Although diabetes is not contagious, it is the first and only disease that the United Nations has designated as a 21st century epidemic (6). However, no reliable data are available on the prevalence of diabetes in many countries (7). The results of international research (DIAMOND and EURODIAB) reveal an increasing trend in Diabetes prevalence in most regions of the world, with the highest growth dynamics in the youngest age group (6, 7).

The global increase in T1DM prevalence is a well-known fact; with the highest rate reported from fast developing countries (8, 9).

Infants experience many changes in their diet in the first year of life. In many cases, their diet initially consists exclusively of breast milk, but gradually shifts from being entirely liquid (breast milk, cow milk, and formula) to also a variety of solid foods (10, 11). Research has shown that using cow milk in infancy increases the risk of β-cell autoimmunity, probably because of the similarity of the molecular sequence of cow milk proteins with the body’s own antigens (12, 13). According to several studies, introducing gluten or cereals, fruits, roots, and seeds to the food before 3 months of age is a risk factor for the autoimmunity to the islets of Langerhans (14, 15). Solid foods can also play a pathogenic role in the development of T1DM in the same way as hypothesized for cow milk (12). Some have recommended that to reduce the risk of immunodeficiency disorders, complementary foods should be added to breast milk starting from the age of 4 to 6 months (14).

However, numerous epidemiological reports have linked the increased risk of T1DM to short breastfeeding period and early introduction of cow milk, formula, or complementary foods to the baby’s diet (14, 16, 17).

It is widely recommended to continue exclusively breastfeeding for the first 4 to 6 months of the infant’s life. Research has confirmed the health benefits of this breastfeeding and also continued breastfeeding during the first year of life. In any case, it is not recommended to start complementary feeding before 4 months of age (10, 14, 16, 17).
With the increasing prevalence of T1DM worldwide, the management and treatment of this disease and its acute and chronic complications are imposing significant burdens on patients as well as health care systems (18, 19). In this study, the objective was to investigate the potential relationships between T1DM and infant's diet in the first two years of life as well as some demographic variables.

**Methods**

**Design**

The present case-control study was conducted on a sample of children (aged 2–15 years old) in Jahrom, Fars Province, southern Iran in 2018. The study was approved by the Ethics Committee of Jahrom University of Medical Sciences (IR.JUMS.REC.2017.173).

**Sample size and sampling**

The required sample sizes were calculated using a similar study (20) with, 95% confidence level, and the required size was estimated at 285.

In this study, the cluster sampling method was used, in which each health center was considered as a cluster. At first, at each center a sequential number was assigned to all children with Type 1 diabetes. Then, regarding the proportion of participants, cases were selected randomly using the random number table. Next, controls were selected from healthy children referred to centers and matched with cases in terms of age and gender.

Case and control groups were selected considering the inclusion and exclusion criteria.

The inclusion criteria for the case group were as follows: being 2 to 15 years of age and having T1DM as reported by the mother or according to the child's health record. The inclusion criteria for the control group were as follows: being in the same age range as the case group and not having type 1 or type 2 diabetes or impaired glucose tolerance (IGT) at the time of the study. The exclusion criteria for the case group were as follows: not being in the age range of 2–15 years or not having T1DM and refusal to give informed consent.

The exclusion criteria for the control group were as follows: not being in the same age range as the case group and being diagnosed with type 1 or 2 diabetes or IGT and refusal to give informed consent.

**Data collection**

The data collection method was upon visiting the community health centers, the mothers of the eligible children were asked to complete a self-administered questionnaire of diet and demographic information, which consisted of two groups of questions

**Instruments**

1- Demographic and child nutrition status information questionnaire:
It was specifically developed based on the study objectives and contained 11 items including

Questions about the child (gender, age, duration of exclusive breastfeeding, age of onset of complementary feeding, age of complete weaning, use of formula or similar products in the first six months of life, use of pasteurized milk in the first year of life, birth weight, weight at 1 year of age, fetal age at birth, and birth order).

2- Demographic and mother pregnancy status information questionnaire:

Questions about the mother contained 5 items including age at delivery, excess weight during pregnancy, method of delivery, history of diabetes, history of diabetes among the child's other first-degree relatives.

**Data analysis**

After collecting the questionnaires, the obtained data were entered into SPSS Version 16.0. (Chicago, SPSS Inc.).

Normality of all data were checked by Kolmogorov-Smirnov test. For normally distributed data, the chi-square test and the t-test, and for non-normally distributed data, the Mann-Whitney test were used to compare qualitative and quantitative variables of the case and control groups. Finally, logistic regression with the backward technique was used to compute the odds ratio and the 95% confidence interval and investigate the association between T1DM and the variables.

**Results**

This study comprised of 285 children, including 165 (57.89%) males and 120 (42.11%) females, with 76 case and 209 as of control.

The results obtained did not reveal any significant association between child age, maternal age during pregnancy, gestational age, sex, birth weight, one-year weight, birth rank, history of diabetes in relatives, age of starting complementary feeding, consumption of cow milk under one year and use of artificial milk (p > 0.05) (Table 1, 2).
Table 1
Mean and standard deviation of the child's age and mother's age at delivery, weight before pregnancy, and excess weight during pregnancy in the case and control groups (univariate analysis)

| Quantitative variables                              | Control group | Case group | p-value * |
|-----------------------------------------------------|---------------|------------|-----------|
| Mean ± standard deviation                           |               |            |           |
| Child's age (years)                                 | 11.94 ± 3.3   | 12.14 ± 4.13 | 0.69      |
| Mother's age at delivery (years) ¥                   | 25.58 ± 6.87  | 25.71 ± 5.31 | 0.88      |
| Mother's weight before pregnancy (kg) ●              | 64.81 ± 8.81  | 56.62 ± 10.72 | 0.0001    |
| Mother's excess weight during pregnancy (kg) ●       | 10.72 ± 2.91  | 8.92 ± 4.51 | 0.0001    |

* p < 0.5 is considered statistically significant.

¥ Mean and standard deviation are obtained using the Mann-Whitney test.

● Mean and standard deviation are obtained using the t-test.
Table 2
Absolute frequency and distribution (percentage) of study variables in the case and control groups (univariate analysis)

| Qualitative variables | Control: frequency No. (%) | Case: frequency No. (%) | p-value  |
|-----------------------|-----------------------------|-------------------------|----------|
| **Child’s non-diet variables** |                             |                         |          |
| Fetal age at birth    |                             |                         |          |
| Less than 37 weeks    | 22 (10.5)                  | 10 (13.1)               | 0.53     |
| More than 37 weeks    | 187 (89.5)                 | 66 (86.9)               |          |
| Gender                |                             |                         |          |
| Female                | 90 (43.1)                  | 30 (39.5)               | 0.58     |
| Male                  | 119 (56.9)                 | 46 (60.5)               |          |
| Birth weight          |                             |                         |          |
| Less than 2500 gr     | 20 (9.6)                   | 8 (10.5)                | 0.81     |
| More than 2500 gr     | 189 (90.4)                 | 68 (89.5)               |          |
| Weight at 1 year of age |                         |                         |          |
| Less than 9500 gr     | 49 (23.4)                  | 21 (27.6)               | 0.47     |
| More than 9500 gr     | 160 (76.6)                 | 55 (72.4)               |          |
| Birth order           |                             |                         |          |
| First or second       | 143 (68.4)                 | 57 (75)                 | 0.28     |
| Third or fourth       | 66 (31.6)                  | 19 (25)                 |          |
| **Mother’s variables** |                             |                         |          |
| History of diabetes   |                             |                         |          |
| Yes (before pregnancy/pre-gestational) | 1 (0.5) | 3 (3.9) | 0.07    |
| Yes (during pregnancy/gestational) | 13 (6.2) | 6 (7.9) |          |
| No                    | 195 (93.3)                 | 67 (88.2)               |          |
| Method of delivery    |                             |                         |          |
| Vaginal               | 119 (56.9)                 | 57 (75)                 | 0.02     |
| C-section             | 90 (43.1)                  | 19 (25)                 |          |
| Mother’s BMI          |                             |                         |          |
| Normal                | 119 (56.9)                 | 49 (64.5)               | 0.0001   |
| Underweight           | 16 (7.7)                   | 18 (23.7)               |          |
| Overweight            | 62 (29.7)                  | 8 (10.5)                |          |
| Qualitative variables                                                                 | Control: frequency | Case: frequency | p-value |
|---------------------------------------------------------------------------------------|--------------------|----------------|---------|
| Obese                                                                                 | 12 (5.7)           | 1 (1.3)        |         |
| History of diabetes in first-degree family members                                     |                    |                |         |
| Yes                                                                                    | 112 (53.6)         | 33 (43.4)      | 0.12    |
| No                                                                                    | 97 (46.4)          | 43 (56.6)      |         |
| Child's diet and growth variables (in the first two years of life)                     |                    |                |         |
| Exclusive breastfeeding                                                                |                    |                |         |
| Less than 4 months                                                                     | 19 (9.1)           | 13 (17.1)      | 0.04    |
| 5 months                                                                               | 17 (8.1)           | 2 (2.6)        |         |
| 6 months                                                                               | 65 (31.1)          | 30 (39.5)      |         |
| More than 6 months                                                                     | 108 (51.7)         | 31 (40.8)      |         |
| Status of the baby's weight gain chart during the first two years of life              |                    |                |         |
| Below the normal line                                                                  | 49 (23.4)          | 10 (13.2)      | 0.08    |
| Normal                                                                                 | 146 (69.9)         | 63 (82.9)      |         |
| Above the normal line                                                                  | 14 (6.7)           | 3 (3.9)        |         |
| Age of onset of complementary feeding                                                 |                    |                |         |
| Less than 4 months                                                                     | 7 (3.3)            | 4 (5.3)        | 0.18    |
| 5 months                                                                               | 16 (7.7)           | 8 (10.5)       |         |
| 6 months                                                                               | 118 (56.5)         | 49 (64.5)      |         |
| More than 6 months                                                                     | 68 (32.5)          | 15 (19.7)      |         |
| Use of cow milk in the first year of life                                              |                    |                |         |
| Yes                                                                                    | 20 (9.6)           | 12 (15.8)      | 0.14    |
| No                                                                                    | 189 (90.4)         | 64 (84.2)      |         |
| Use of artificial milk                                                                 |                    |                |         |
| Yes - along with breast milk                                                           | 33 (15.8)          | 12 (15.8)      | 0.64    |
| Yes - without breast milk                                                               | 34 (16.3)          | 9 (11.8)       |         |
| No                                                                                    | 142 (67.9)         | 55 (72.4)      |         |
| Breastfeeding period                                                                  |                    |                |         |
| 12 months or less                                                                      | 21 (10)            | 11 (14.5)      | 0.0001  |
| 12–24 months                                                                          | 174 (83.3)         | 39 (51.3)      |         |
Table 3 indicates the univariate and adjusted association of independent variables with the Type 1 diabetes. The unadjusted results showed a significant association between Type 1 diabetes in children and the mothers without a history of diabetes (OR: 0.12, 95% CI: 0.01 to 0.12), maternal weight before pregnancy (OR: 0.94, 95% CI: 0.88 to 0.97), maternal overweight during pregnancy (OR: 0.84, 95% CI: 0.76 to 0.92), cesarean delivery (OR: 0.45, 95% CI: 0.25 to 0.81), Body Mass Index (BMI) of the mother being less than 18.5 (OR: 2.73, 95% CI: 1.28 to 5.79) before pregnancy, exclusive breastfeeding for more than six months [compared to less than 4 months] (OR: 0.42, 95% CI: 0.18 to 0.94) and the breastfeeding less than 12 months [compared to over 24 months] (OR: 3.54, 95% CI: 1.33 to 9.41).
| Quantitative-qualitative variables | Unadjusted OR [95% CI] | p-value | Adjusted OR [95% CI] | p-value |
|------------------------------------|------------------------|---------|----------------------|---------|
| **Child's non-diet variables**     |                        |         |                      |         |
| Age                                | 1.01 [0.94–1.09]       | 0.66    | 1.002[0.88–1.13]     | 0.97    |
| Fetal age at birth                 | 0.77 [0.34–1.72]       | 0.53    | 1.43[0.27–7.59]      | 0.66    |
| Gender                             | 0.86 [0.50–1.47]       | 0.58    | 0.6[0.26–1.38]       | 0.23    |
| Birth weight                       | 2.13 [0.37–2.14]       | 0.81    | 0.47[0.11–1.92]      | 0.29    |
| Weight at 1 year of age            | 1.25 [0.42–3.66]       | 0.68    | 1.21[0.04–3.62]      | 0.72    |
| Birth order                        | 0.72 [0.39–1.31]       | 0.28    | 0.5[0.2–1.23]        | 0.13    |
| **Mother's variables**             |                        |         |                      |         |
| Mother's age at delivery [years]   | 1.006[0.95–1.05]       | 0.81    | 1.02[0.94–1.14]      | 0.49    |
| History of diabetes                | 0.15[0.01–1.81]        | 0.13    | 0.04[0.001–1.15]     | 0.06    |
| Gestational diabetes               | 0.12 [0.01–0.12]       | 0.06    | 0.02[0.001–0.60]     | 0.02    |
| No diabetes [compared to pre-      |                        |         |                      |         |
| gestational diabetes]              |                       |         |                      |         |
| Mother's weight before pregnancy   | 0.94[0.88–0.97]        | 0.0001  | 0.88[0.84–0.91]      | 0.0001  |
| Mother's excess weight during      | 0.84[0.76–0.92]        | 0.0001  | 0.83[0.75–0.93]      | 0.001   |
| Quantitative-qualitative variables | **Unadjusted OR [95% CI]** | **p-value** | **Adjusted OR [95% CI]** | **p-value** |
|-----------------------------------|-----------------------------|-------------|---------------------------|-------------|
| **Method of delivery**            |                             |             |                           |             |
| C-section                         | 0.45[0.25–0.81]             | 0.007       | 0.56[0.24–1.3]             | 0.18        |
| **Mother's BMI**                  |                             |             |                           |             |
| Underweight                       | 2.73[1.28–5.79]             | 0.009       | 4.4[1.61–11.97]            | 0.004       |
| Overweight                        | 0.31[0.14–0.70]             | 0.005       | 0.18[0.06–0.53]            | 0.002       |
| Obese                             | 0.20[0.02–1.59]             | 0.13        | 0.03[0.002–0.45]           | 0.011       |
| **History of diabetes in first-degree family members** |                             |             |                           |             |
| No [compared to Yes]              | 1.5[0.88–2.55]              | 0.13        | 1.76[0.79–3.87]            | 0.16        |
| **Child's diet and growth variables (in the first two years of life)** |                             |             |                           |             |
| Exclusive breastfeeding           |                             |             |                           |             |
| 5 months                          | 0.17[0.034–0.87]            | 0.03        | 0.08[0.006–1.06]           | 0.05        |
| 6 months                          | 0.67[0.29–1.54]             | 0.35        | 0.35[0.07–1.68]            | 0.19        |
| More than 6 months                | 0.42[0.18–0.94]             | 0.03        | 0.19[0.03–0.96]            | 0.04        |
| **Status of the baby's weight gain chart during the first two years of life** |                             |             |                           |             |
| Abnormal                          | 2.11[1.007–4.43]            | 0.049       | 6.98[2.16–22.5]            | 0.001       |
| Above the normal line             | 1.05[0.25–4.35]             | 0.94        | 1.31[0.19–8.93]            | 0.78        |
| **Age of onset of complementary feeding** |                             |             |                           |             |
| 5 months                          | 0.87[0.19–3.89]             | 0.86        | 15.25[0.88–262.01]         | 0.06        |
| Quantitative-qualitative variables | Unadjusted OR [95% CI] | p-value | Adjusted OR [95% CI] | p-value |
|-----------------------------------|------------------------|---------|----------------------|---------|
| 6 months [compared to less than 4 months] | 0.72 [0.20–2.59] | 0.62 | 0.86 [0.08–7.56] | 0.86 |
| More than 6 months [compared to less than 4 months] | 0.36 [0.10–1.48] | 0.17 | 0.54 [0.05–5.65] | 0.61 |
| Use of cow milk in the first year of life | No [compared to Yes] | 0.56 [0.26–1.21] | 0.14 | 0.34 [0.08–1.45] | 0.14 |
| Use of artificial milk | Yes - along with breast milk [compared to No] | 0.68 [0.30–1.51] | 0.35 | 0.54 [0.24–1.32] | 0.30 |
|  | Yes -without breast milk [compared to No] | 0.93 [0.45–1.94] | 0.86 | 1.38 [0.45–4.24] | 0.56 |
| Breastfeeding period | 12–24 months [compared to over 24 months] | 0.43 [0.19–0.96] | 0.04 | 0.89 [0.17–4.62] | 0.88 |
|  | Less than 12 months [compared to over 24 months] | 3.54 [1.33–9.41] | 0.01 | 10.52 [1.62–66.64] | 0.01 |

Finally, the results of multiple backward logistic regression showed that Body Mass Index (BMI) of the mother being less than 18.5 before pregnancy (OR: 4.4, 95% CI: 1.61 to 11.97), mothers without a history of diabetes (OR: 0.02, 95% CI: 0.001 to 0.60), mother’s weight before pregnancy (OR: 0.88, 95% CI: 0.84 to 0.91), mother’s excess weight during pregnancy (OR: 0.83, 95% CI: 0.75 to 0.93), exclusive breastfeeding for more than six months (OR: 0.19, 95% CI: 0.03 to 0.96), low weight gain in the first two years of life (OR: 6.98, 95% CI: 2.16 to 22.5), and the breastfeeding less than 12 months (OR: 10.52, 95% CI: 1.62 to 66.64) have association with Type 1 diabetes (p < 0.05) (Table 3).

**Discussion**

The results of this study showed that exclusive breastfeeding for six months and more can be effective in preventing the development of T1DM in children (OR = 0.19). While several other studies have also
reported that exclusive breastfeeding can prevent T1DM (17, 21–24), there are also reports to the contrary (25).

Over the last three decades, the prevalence of obesity has more than doubled in children and tripled in adolescents (26). Short-term breastfeeding and early introduction of complementary foods may be associated with respiratory and gastrointestinal infections and obesity in children (14). Also, the consumption of excess protein in childhood is associated with an increase in BMI at older ages. The protein contained in artificial milk can also lead to the secretion of insulin and insulin-like growth factor, which may explain why formula-fed babies have higher plasma insulin levels than breastfed children (21). The results of this study showed higher odds of developing T1DM in children whose weight gain was below the normal growth line (OR: 6.98) and also those whose weight gain was above the normal growth line (OR: 1.31). It was also found that exclusively breastfed babies had lower odds of developing T1DM at an older age than exclusively formula-fed ones (OR: 0.19). This suggests that exclusive formula feeding is associated with a higher risk of T1DM, and is consistent with the findings of Rabiei et al. (21), which showed a higher risk of T1DM at an older age in babies breastfed for less than 12 months compared to those breastfed for more than 24 months (OR: 10.52).

This study found no association between T1DM and cow milk consumption in the first year of life, which is consistent with the results of Rabiei et al. (21) and Savilahti & Saarinen (27). It appears that the early introduction of complementary foods may also stimulate the development of T1DM by disrupting the autoimmune responses. This is especially true for children who are genetically predisposed to diabetes (27, 28).

In this study, children whose complementary feeding had started before the age of fourth months were 46% more likely to develop T1DM than those whose complementary feeding had started after the age of six months. However, this relationship was not statistically significant.

The results show that mother’s excess weight during pregnancy decreases the odds of the development of T1DM in the baby. Rasmussen et al in a study showed that, having less than 10.75kg excess weight during pregnancy decreases the risk of T1DM in the child by approximately 17% (29).

As of this writing, only a handful of studies have investigated the effect of having diabetes before or during pregnancy (gestational or pregestational) on the risk of diabetes in the delivered child, and it is still not clear whether the breast milk of diabetic mothers has the same ingredients as the breast milk of healthy mothers. Some researchers believe that breastfeeding from diabetic mothers is also effective in preventing diabetes in children (17, 22). However, others have suggested that the breast milk of diabetic mothers should be considered a risk factor for the development of diabetes in children (21). In the present study, the incidence of T1DM in children had a direct relationship with the mothers having diabetes during pregnancy (gestational diabetes), but had no relationship with diabetes in the child’s other first-degree family members, which is consistent with other reports (21, 29).
Breastfeeding has nutritional, immunological, and physiological benefits. It also plays an important role in the formation of a healthy maternal attachment and the healthy development of the baby (30). Some researchers believe that the method of delivery affects the success of breastfeeding, as mothers who give birth naturally tend to breastfeed their baby for longer than those who give birth by C-section (30, 31). In the present study, there was no significant difference in terms of incidence of T1DM between the children born vaginally and those born by C-section. Therefore, there seems to be no relationship between the incidence of diabetes and the type of delivery. While this conclusion is consistent with the findings of Rabiei et al. (21), it should be noted that not many studies have been conducted on this relationship.

One of the limitations of this study was that some respondents in both case and control groups had difficulty recalling the information of interest. This problem had two dimensions. The first was the general differences among the respondents in terms of their capacity to recall events. To resolve the issue, researchers tried to compare the respondents’ inputs with their medical records and detect and correct inconsistencies as much as possible. The second dimension was the difference (bias) between the mothers in the case group and those in the control group in terms of accuracy in remembering the event related to their child. This is because mothers in the case group often wonder why their children has this condition and whether they have done something wrong that has contributed to their child becoming diabetic. Therefore, these mothers are often more accurate in recalling past events and information related to their child, and this creates a bias, which is one of the inherent problems of case-control studies.

Conclusion

Body mass index less than 18 mothers before pregnancy, Low weight gain in the first two years of life and breastfeeding less than 12 months increases the risk of developing Type-1 Diabetes in children. However, the findings did not confirm the role of the early introduction of complementary food and the use of cow milk in the development of T1DM. Considering the findings of this study and the proven health benefits of breastfeeding, it is recommended to commit to exclusive breastfeeding for at least six months after birth.

Abbreviations

T1DM
Type 1 Diabetes Mellitus
IGT
Impaired Glucose Tolerance

Declarations

Ethics approval and consent to participate
The ethics committee of Jahrom University of Medical Sciences (Code: IR.JUMS.REC.2017.173) approved this study. All participant gave written consent to take part in the study.

Consent to publish

Not applicable.

Availability of data and materials

The data are available from the corresponding authors.

Competing interests

The authors declare that they have no conflict of interests.

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Authors’ Contributions

The idea of this study was initiated by MZ. MZ and AN and VR contributed to design, management of the study and writing of the manuscript. SA contributed to data collection. VR participated in performed the statistical analysis and writing of the manuscript. HK contributed in writing of the manuscript. All authors read and approved the final manuscript.

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