

The Editor
World Journal of Diabetes

We would like to submit the revised article entitled “**Reproductive disturbances among Saudi adolescent girls and young women with type 1 diabetes mellitus**” to the World Journal of Diabetes (Manuscript No: 34681). We express our gratitude for the reviewers’ valuable comments. The changes have been made in the article as per the reviewer’s comments. We are looking forward for your consideration to the above-mentioned article for publication at the World Journal of Diabetes.

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Reviewer #1 comments

This descriptive study about: “Type 1 diabetes, Reproductive disturbances, Polycystic ovarian syndrome, Premature ovarian failure, Menarche, Saudi Arabia” that the authors analyze in 102 young women with type 1 diabetes mellitus is an interesting analysis of the menstrual disturbances in this group. More than one fourth of the study population with type 1 diabetes mellitus experience irregular menses and adolescent and young women diagnosed with type 1 diabetes mellitus prior to menarche show higher menstrual irregularity and a delay in the age of menarche. These findings are interesting in the medical practice to assess in this population the abnormalities that they show.

Answers to Reviewer #1 comments

Thank You' for your kind expression of appreciation of our study.

Reviewer #2 comments

Reproductive disturbances among Saudi adolescent girls and young women with type 1 diabetes mellitus. This manuscript is an attempt to identify reproductive disturbances among adolescent girls and young women with type 1 diabetes mellitus (T1DM) in Saudi Arabia. I recommend accepting the manuscript for publishing in the WJD.

Answers to Reviewer #2 comments

Thank You' for your kind expression of appreciation of our study.

Reviewer #3 comments

Needs to discuss more on effect of DM on reproduction. Title needs to be specified more.

Answers to Reviewer #3 comments

Thank You' for your valuable comments. We have written the effect of DM on female reproduction in the second paragraph of introduction (line 1-6) and added a new reference (#7) to support the concept. Regarding the title, as a cross sectional study we simply present the title which is agreed by all the reviewers.

Also, the manuscript has been edited for language by Global Edico Services
<https://www.globaledico.com/>

Reviewer #4 comments

Manuscript Reproductive disturbances among Saudi adolescent girls and young women with type 1 diabetes mellitus by Braham R et al. This is a well-written manuscript on an interesting and important clinical issue namely the frequency of irregular menstruation and amenorrhea in young women and teenagers with type 1 diabetes. The authors have conducted a study with well-recognized methods to investigate and document PCOS, hyperandrogenism and menstrual disturbances. Furthermore this contribution from the Saudi Arabic region is very relevant because most other clinical studies usually concern only the Western population and we need more investigations and knowledge on patients from the Middle East. Major points Regarding “Compared to whose diabetes was diagnosed before menarche 35.4% (17/48), patients diagnosed with diabetes after menarche 18.5% (10/54) showed less irregular menses” This is the main finding and I agree that this is of somewhat interesting, but how does it relate to the normal age of menarche and irregular menses in your country? Which group is more different from the normal population of young women without diabetes? This has been addressed in the Discussion, but a statistical comparison with age and BMI matched controls would improve the study conclusions. How was under- and overweight defined? What reference BMI curves were used? What was the proportion of women using oral contraceptives among the cohort with diabetes in your center, and why were they on oral contraceptives? I.e. if they were on oral contraceptives because of irregular menstruations, hirsutism, and/or PCOS, you underestimate the real proportion of women with these problems in patients with T1DM. This limitation also needs to be recognized and discussed. The manuscript would improve if the authors included much more details on the study population and not only posted the number and proportion of patients with and without a number of variables. I.e. instead of “small ovaries” yes/no I suggest the authors to report mean/median and S.D./C.I of all the variables testosterone, LDL, HDL cholesterol, TGA, thyroid medication doses, age, ovarian size, follicles, DKAs, F-G scale scores just like it has been done for BMI, duration of diabetes, insulin dose etc. Furthermore it would be relevant to describe the population in more details i.e. number of blood glucose measurements per day,

boluses, proportion of insulin pump users. The HbA1c is surprisingly high 8.78 to 9.72%. Is this similar to HbA1c in other countries? What could explain the high values? Minor points None.

Answers to Reviewer #4 comments

Thank You' for your kind expression of appreciation of our study. We would like to bring your kind notice that we did not include patients who under oral contraceptive pills (it is written in criteria for selection of patients under methods section). Also, in Saudi Arabia, the number of female patients on oral contraceptive pills are less than Western countries, because they take only after marriage as contraception or after medical advice. However, there is no local study estimating this especially among female patients with type 1 diabetes.

The present study compared, those diabetes was diagnosed before menarche and patients diagnosed with diabetes after menarche and the influence of diabetes on reproductive disturbance such as delaying the menarche. As the study has no control group with which to compare the study population, this limitation has been added in the limitation section. The under- and overweight defined as per the National Institute of Child Health (2012) Available from: <http://www.ogyei.hu/upload/files/gyermekkoritaplaltsag.pdf>.

All the continuous variables are represented as mean values \pm SD, while categorical variables are expressed as frequencies and percentages. However as per the reviewer suggestion, we have given the mean and SD of all continuous variables. Also The overall mean of the clinical parameters of the study population were as follows: age 18.26 ± 4.05 (range 13-29 years), age at diagnosis of diabetes 11.5 ± 3.96 (range 1-21 years), duration of T1DM 6.8 ± 5.35 years (range 1-28 years), age at menarche 12.56 ± 0.96 (range 9-16 years), BMI 23.54 ± 3.3 kg/m² (range 17.8-34.4) and HbA1c was 9.23 ± 1.92 (range 6-16) are available under the first paragraph of the results. Further, the HbA1c is high 8.78 to 9.72% (all are diabetes) which is similar to other published studies from Saudi Arabia. Regarding the testosterone level, 0.69 to 2.1 nmol/L considered as normal and > 2.1 mmol/L considered as high testosterone level which is added in the manuscript (added under data collection and definitions of methods)

Once again thank you for your valuable comments which helped us to improve the quality of the manuscript lot.