Review Form 1.6

Journal Name:	**Journal of Pharmaceutical Research International**
Manuscript Number:	**Ms_JPRI_76969**
Title of the Manuscript:	**Glucokinase Gene Mutations in Subjects with Gestational Diabetes Mellitus from Gaza Strip**
Type of the Article	**Original Research Article**

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty'**, provided the manuscript is scientifically robust and technically sound.
To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(http://peerreviewcentral.com/page/manuscript-withdrawal-policy)

Review Form 1.6

PART 1: Review Comments

<table>
<tr><th></th><th>Reviewer's comment</th><th>Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</th></tr>
<tr><td><u>Compulsory</u> REVISION comments</td><td>Reviewer 1: In this study the authors performed a case-control study including 54 women with Gestational Diabetes Mellitus (GDM) and 42 controls across Gaza strip to evaluate the frequency of glucokinase (GCK) gene mutations for exons 7, 8 & 9 mutations at positions C.682A>G (p.Thr228Ala); C.895G>C (p.Gly299Arg) and C.1148C>A (p.Ser383X), respectively.of using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) methodology. The results showed that 20% GDM subjects harboured the exon 8 (895G>C) mutation and the genotype GC was significantly more frequent in case than in the controls (20% vs. 0.0%, P= 0.002*) and that the genotype (GG) was significantly more frequent in controls than in the case (100% vs. 80%, P= 0.002*). And the results showed that relationship between exon 8 p.Gly299Arg mutation and the biochemical parameters among the study population.</td><td></td></tr>
<tr><td><u>Minor</u> REVISION comments</td><td>Comment1:

Abstract Objective Added abbreviation of
Gestational Diabetes Mellitus (GDM)

Introduction complete the abbreviations

Maturity-onset diabetes of the young (MODY)

Study population
Our study included forty-five (45) pregnant..

Molecular analysis
Genomic DNA was extracted from blood...
Program of PCR-RFLP for the exons 7. 8 and 9

The methods are clear. The results are presented in tables and the statistical study is well done. Overall, the study is well conducted. However, there some errors in the presentation of the tables. For example, in table 3, 4 the N. Odd ration OR

Comment 3:

It is necessary to calculate the OR for the polymorphism; correct the p for the exon 8

<table>
<tr><th>Mutation</th><th>Genotype</th><th>Controls (N=42) n (%)</th><th>Cases (N=45) n (%)</th><th>P-value</th><th>OR (IC 95%)</th></tr>
<tr><td rowspan="2">p.Thr228Ala (Exon 7)</td><td>AA</td><td>42 (100.0)</td><td>45 (100.0)</td><td rowspan="2">1.000</td><td rowspan="2"></td></tr>
<tr><td>AG</td><td>0 (0.0)</td><td>0 (0.0)</td></tr>
<tr><td rowspan="2">p.Gly299Arg (Exon 8)</td><td>GG</td><td>42 (100.0)</td><td>36 (80.0)</td><td rowspan="2">0.002*
1.3 10⁻⁷</td><td rowspan="2">0.8 (0.69-0.93)
1.45(7.6-∞)</td></tr>
<tr><td>GC</td><td>0 (0.0)</td><td>9 (20.0)</td></tr>
</table></td><td>Corrected as required

I have contacted a statistician and he told me that we do not calculate OD if one of the values is zero. This is also supported by published research papers. As aforementioned, rare events caused difficulty in estimation of odds ratio due to the occurrence of zeros or small observed counts in numerator or in denominator or in both, resulting in the large standard error and therefore less precise confidence interval. [1]

one or two cells of 2x2 tables may have zero (0) counts or a count very close to zero. This issue makes the estimation of Odds Ratio (OR) impossible or leads to unstable OR estimates due to complete or quasi-complete separation. [2]

[1] Raweesawat, K., Areepong, Y., Jampachaisri, K., & Sukparungsee, S. (2016). Odds ratios estimation of rare event in binomial distribution. Journal of Probability and Statistics, 2016.

[2] Koçak, M. (2017). An Empirical Bayesian Approach in Estimating Odds Ratios for Rare or Zero Events. Turkiye Klinikleri Journal of Biostatistics, 9(1).</td></tr>
</table>

p.Ser383Ter (Exon 9)	CC	42 (100.0)	45 (100.0)	1.000		
	CA	0 (0.0)	0 (0.0)			

Comment4:

The relationship between exon 8 p.Gly299Arg mutation and the studied parameters among the study population; this results are not sufficient exploit between the polymorphism and biochemical parameters

Comment5:

In your results you reported that the concentration of glucose in mutation-positive (GC) cases was lower as compared to mutation-negative (GG) ones but there was no statistically significant difference
Between mutation-negative (GG) cases and mutation-positive (GC) for all parameters (P> 0.05) except for OGTT

Discussion

The discussion is very rich and well justified.

Table 6 represents the relationship between p.Gly299Arg (Exon 8) mutations and the different studied parameters among the study population.

The results of FBG is correlated to that of OGTT. Research has indicated that the OGTT offers a more reliable test for diagnosis of diabetes.

Optional/General comments		

PART 2:

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Are there ethical issues in this manuscript?	*(If yes, Kindly please write down the ethical issues here in details)*	