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Geographical Determinants of the Prevalence of Gestational Diabetes in North and South Kivu in the Democratic Republic of Congo

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ABSTRACT

Objectives: To explore the geographic determinants of gestational diabetes in eastern DRC and to seek confounding factors.

Methods: Cross-sectional descriptive study with a multicenter analytical aim conducted in the hot and cold season from April 2019 to February 2021. Included were 392 pregnant women at 24-28 weeks of amenorrhea. Blood glucose, cortisol, SO2, anthropometric measurements, 30 previous day's temperature, altitude and atmospheric pressure (atm) were examined. The glycaemia ≥92mg/dL was pathological, in which case cortisolaemia was measured after matching with normal glycaemia.

Data were analyzed using SPSS version 23 by calculating median, proportion, ANOVA, Pearson's Chi2 or Fisher's exact test, Wilcoxon -Mann–Whitney test.

Results: The proportion of 23.8%, 37.4%, 13.8% and 25.0% of 392 pregnant women lived respectively at the altitude of 1400 m, 1500m, 1700m and 2419m. Pathological glycaemia was twice higher at < 1700 m = atm > 82% [32.9% (n = 295)] Vs ≥ 1700 m [15.0% (n = 295)] [OR 2.2 95% CI (1.5- 3.2)] (p<0.001)] and at SO2 > 95% [30.8% (n= 331)] Vs SO2 ≤ 95% [15.3% (n= 144)] [OR 2.0 95% CI (1.3 - 3.1)] (p < 0.001). Cases with pathological glycaemia had elevated cortisol [281.1 nmol/L (87.6)] (n=118) Vs normal glycaemia [261.1 nmol/L (71.1)] (n= 156)] (p= 0.024).

Conclusion: The prevalence of pathological glycaemia was higher at <1700 m altitude corresponding to the atm > 82% and when the SO2 was >95%. After adjustment, blood glucose was no longer correlated with temperature.

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Introduction

Geographical conditions of altitude and/or temperature have an impact on glucose metabolism [1, 2]. Elevation in altitude would be a determining factor of glucose homeostasis and would be inversely related to the prevalence of diabetes [1, 3, 4]. High altitude has an impact on pregnancy outcome [5, 6]. The prevalence of gestational diabetes may experience seasonal influences related to temperature fluctuations and this is noticeable for other situations of hyperglycemia [7-9]. The same is true of altitude, which can influence the prevalence of gestational diabetes [10]. The metabolism would be impacted, the cortisol level is modified, among other things, by the rise in altitude but the adrenal axis normalizes due to acclimatization after 4 to 5 weeks of exposure (around 5000m) [11]. The impact of temperature and/or altitude is increasingly analyzed around the world. In Canada, it was noted that an increase in the outside temperature of 10°C increased the probability of gestational diabetes even between two pregnancies in the same woman [8]. In the USA, although there was no difference in the prevalence of gestational diabetes between mid and high altitude, the difference in the characteristics of pregnant women with gestational diabetes between the mid and high altitude groups was suggestive of a difference in glucose metabolism of these two groups [12]. In China, the adaptation to high altitude of Tibetans consisted, among other things, in the modulation of glucose metabolism [13]. To our knowledge, the analysis of the prevalence of gestational diabetes in relation to both altitude and temperature is not documented in our environments in the DRC and in sub-Saharan Africa, whereas the differences in the prevalence of gestational diabetes noted in the study sites in Eastern DRC would be due, among other things, to the geographical conditions of altitude and temperature [14].

Objective

Explore the geographic determinants of gestational diabetes in eastern DRC, including altitude, temperature and atmospheric pressure in Goma, Idjwi, Ngungu and Rutshuru and to seek confounding factors.

Materials and Methods

This study is the continuation of the study on "Prevalence of gestational diabetes in the Eastern of the Democratic Republic of Congo" whose material and methods are superimposable to a certain degree [14].

Study Design and Site

This cross-sectional and multicenter study was conducted from 04/25/2019 to 02/02/2021 in eastern DRC in sites chosen for their geographical characteristics of altitude and temperature. These include Mapendo Health Center in Goma, Ngungu Reference Health Center and Rutshuru Health Center in North Kivu Province and Bunyakiri Health Center on Idjwi Island in the province of South Kivu located respectively at 1500m, 2419m, 1400m and 1700m above sea level and where the average temperature of 30 days preceding the sampling was respectively 20.5-23.7°C, 21.5 -22.9°C, 16.5-21.6°C and 20.6-22.8°C [14].

Study Population

This study involved pregnant women whose term of pregnancy was between 24 and 28 weeks of amenorrhea who had followed the first prenatal consultation in the sites and during the study period [14].

Sample Size and Sampling

The prevalence of type II diabetes, generally accepted as the closest reflection of the likelihood of GDM because it is parallels to it. The prevalence of type II diabetes in the DRC being 18.4%, a proportion of 20% was considered as a reference. We then adjusted a 10% margin for non-respondents. Thus, for a prevalence of 20%, taking a confidence level of 95% and a margin of error of 5%, the sample size should be $n = t2 \times p \times (1\text{-}p) / m\ 2$ is $1.96\ 2 \times 0.2 \times 0.8 / 0.05\ 2 = 245.8$. Considering a margin of 10% for non-respondents: 245.8 + 10% (24.58) = 270.3. The minimum number for the purposes of the study was therefore 270 subjects. But given the diversity of the DRC and the sectoral nature of the data available on diabetes, we have, for reasons of simplicity and to have enough subjects, retained a sampling proportional to the cases expected on the different sites. The number of participants per health center was calculated based on the relative contribution of each center to the total number of women attended for antenatal care (ANC) per site during the six months preceding data collection. The total number of pregnant women who attended the ANC for the first time during this period was 6895. The relative frequency of ANC by health facility was used to calculate the following indices: 0.345 for Goma; 0.140 for Idjwi; 0.280 for Ngungu and 0.235 for Rutshuru. For convenience and in order to obtain at least 50 participants per site, the indexed proportion was multiplied by 1.45 to obtain a total number of 392 pregnant women [14].

Data Collection

Staff at the various sites had been trained to standardize data collection. Data collection was done using a standard survey form. Informed consent was systematically requested for the collection of personal data, guaranteeing anonymity by a code participating in the processing of data in order to respect the principles of confidentiality and human dignity. The socio-anthropometric data of the pregnant women, the gestation and the parity, the history of diabetes in the family and of a child with a weight ≥ 4000 g at birth were collected on a data collection sheet. Due to the lack of standard laboratory equipment and trained laboratory personnel in these remote and rural health facilities, only capillary blood glucose determination was technically possible [14]. The serum for the cortisol level assay in the other sites were kept in the refrigerator and sent to Goma within seven days of collection for analysis. In order to be in the conditions for blood glucose and cortisol sampling, the blood sample was taken between 07:30 and 09:00 in the morning. The parameters were taken in two waves depending on the hot or cold season of the sites, after 30 days of exposure to the conditions of the season. Cortisol was measured in any pregnant woman with a blood sugar level ≥ 92 mg/dL, to which a pregnant woman of the same term with a blood sugar level between 60 and 91 mg/dL was matched by site. Blood glucose between 92 and 125mg/dL was defined as gestational diabetes. Pregnant women with elevated blood glucose ≥ 92 mg/dl received lifestyle and dietary counseling and were seen again two weeks later.

Inclusion and Exclusion Criteria

Inclusion

- Being pregnant of 24 – 28 weeks of amenorrhea.
- Live in the survey site for at least 30 days.
- Agree to answer the survey questionnaire and freely consent to the sampling conditions during the study periods.

Exclusion

- Being pregnant with one or more pre-existing chronic disease(s) such as diabetes and/or at a term other than 24-28 weeks.
- Not fasting for at least 8 hours and/or presenting after 9:00 a.m.
- Being on corticosteroid therapy

Laboratory Methods and other Samples

Blood glucose was measured using a glycose oxidase technique by the commercial blood glucose meter (SAFE-ACCU Blood Glucose Monitoring System, Changsha Sinocare, Inc., PRC) [15]. The accuracy and precision of the meter have been assessed using quality control materials (Acusera, Randox Laboratory Ltd, Crumlin, UK). Quality control was performed upon opening each batch of 50 test strips. GDM has been defined as blood sugar between 92 and 125 mg/dl and normal blood sugar between 60 and 91.9 mg/dl [14]. Cortisol level was measured using an immunoassay technique and following the recommendations of the manufacturer of I-Chroma II Boditech Med Inc. 43, Geodudanji 1-gil, Dongnae-myeon, Chuncheon-si, Gang-won-do, Korea [16]. On run days, system performance was checked by the system check cartridge as recommended. Oxygen saturation (SO2) was measured by LED technique using a commercial Fingertip pulse Oximeter, YK-80A, Xuzhou Yonker Electronic Technology Co., Ltd., China [17]. The average temperature of thirty days preceding the sampling had been calculated from data of www.accuweather.com site for Goma, Idjwi and Rutshuru and from www.lachainemeteo.com site for Ngungu. Atmospheric pressure (atm) was determined based on site altitude and temperature using the air pressure calculator www.mide.com/air-pressure-at-altitude-calculator.

Statistical Analyzes

The data collected was encoded in Excel and analyzed using SPSS version 23 software. As a dependent variable, capillary glycaemia was studied according to altitude, atmospheric pressure, oxygen saturation, socio-anthropometric parameters: age, pregnancy and parity, mid-upper harm circumference (MUAC) and family history of diabetes and of newborn weight ≥ 4000 g. The synthesis of the variables, whose distribution in the sample was asymmetrical, was made in terms of median accompanied by its range of variation or after transformation into categories, expressed in proportion (%) like the qualitative variables. ANOVA was used to compare means. Pearson's Chi2 and/or Fisher's exact test were used to compare proportions. The Wilcoxon-Mann–Whitney test was applied for the comparison of medians. The significance level was set at 0.05 [14]. To control confounding factors and test possible interactions, logistic regression was used. The variables retained in the logistic regression model of gestational diabetes were selected by a degressive procedure based on the likelihood ratio. A model integrating, in addition to the variables selected by this procedure, the interactions of order 2, was established and the interactions were tested according to a degressive procedure. The model retained is the one with the highest Nagelkerke R-square value in which the data of more than 95% of the subjects of the sample were included. The verification of the fit of the final model to the data was carried out using the Hosmer-Lemeshow test and an examination of the residuals was carried out.

Results

Sample Description

Out of 2687 pregnant women in antenatal consultation (ANC) for the first visit during the sequential periods of data collection, 392 had been enrolled, i.e. a proportion of 14.6%. The distribution of the 392 pregnant according to the geographical parameters was 23.5%, 34.4%, 14.0% and 28.1% respectively at the altitude of 1400 m, 1500m, 1700m and 2419m. The atmospheric pressure was 85%, 84%, 82% and 75% respectively at the altitude of 1400m, 1500m, 1700m and 2419m. The average temperature of the sites for the 30 days preceding the sampling varied from 16.5 to 23.7°C (Table 1).

Table 1: Nutritional, Obstetrical, Geographic and Sociodemographic Parameters

Parameter	Proportion
Age of the pregnant women(n=392)	
≥ 25 years	56,6
< 25 years	43,4
Family history of diabetes (n = 385)	
Yes	5,2
Family history of macrosomia (n = 351)	
Yes	4,6
Gestation (n = 392)	
> 4	39,3
3 - 4	23,5
< 3	37,2
Parity (n = 392)	
> 4	26,0
3 - 4	23,7
< 3	50,3
MUAC (n = 378)	
< 220 mm	4,8
≥ 220 mm	95,2
Serum cortisol (n = 188)	
> 275 nmol/L	62,2
≤ 275 nmol/L	37,8
Temperature (n = 392)	
> 19°C	86,0
≤ 19°C	14,0
Oxygen saturation (n = 391)	
< 95%	30,9
≥ 95%	69,1
Altitude (n = 392)	

< 1700 m	57,9
≥ 1700 m	42,1
1400 m	23,5
1500 m	34,4
1700 m	14,0
2419 m	28, 1
Atmospheric pressure (n = 392)	
> 82	57,9
≤ 82	42,1

Prevalence of Gestational Diabetes

Overall, only oxygen saturation and cortisol level showed thresholds associated with the prevalence of gestational diabetes. This prevalence was 1.84 times higher in those whose cortisol level was >275 nmol/L [49.1% (n = 116)] compared to those whose level was ≤ 275 nmol/L [26.8% (n = 71)] [PR 1.84 95% CI (1.20-2.81)] (p = 0.002)] and low 0.62 times in those whose oxygen saturation was < 95% [15.0% (n = 120)] compared to those whose saturation was ≥ 95% [24.2% (n = 269)] [PR 0.62 95% CI (0.39-0.99)] (p = 0.042)]. Age, parity, gestality and mid-upper arm circumference (MUAC) were not associated with the prevalence of gestational diabetes. Pregnant women with a MUAC greater than 280 mm represented 20.6% (n = 378). (Table 2).

Table 2: Gestational Diabetes According to Different Demographic and Clinical Parameters

Parameter	%	RP (IC à 95%)	p
Age of the pregnant woman			
≥ 25 years (n = 220)	19,1	0,79 (0,54 – 1,16	0,30
< 25 years (n = 170)	24,1	1	
Gestality			
> 4 (n = 152)	23,7	0,94 (0,63 – 1,39)	0,019
3 – 4 (n = 92)	10,9	0,43 (0,22 – 0,82)	
< 3 (n = 146)	25,3	1	
Parity (n = 392)			
> 4 (n = 100)	22,0	0,99 (0,63 – 1,54)	0,72
3 – 4 (n = 93)	18,3	0,82 (0,50 – 1,35)	
< 3 (n = 197)	22,3	1	
MUAC (n = 378)			
< 280 mm (n = 299)	18,7	0,69 (0,45 – 1,06	0,09
≥ 280 mm (n = 77)	27,3	1	
< 220 mm (n = 18)	16,7	0,81 (0,28 – 2,31)	0,99
≥ 220 mm (n = 358)	20,7		
Serum cortisol			
> 275 nmol/L (n = 116)	49,1	1,84 (1,20 – 2,81)	0,002
≤ 275 nmol/L (n = 71)	26,8	1	
Oxygen Saturation			
< 95% (n = 120)	15,0	0,62 (0,39 – 0,99)	0,042
≥ 95% (n = 269)	24,2		

Gestational Diabetes based on History

The proportion of pregnant women with gestational diabetes was almost three times higher in those who had a family history of diabetes [52.6% (n = 19)] compared to those without this history [19.0% (n = 364)] [PR 2.79 95% CI (1.72- 4.47)] (p < 0.001)] and slightly more than twice as many in those with macrosomia history [43.8% (n = 16)] compared to those without this history [18.3% (n = 333)] [RR 2.38 95% CI (1.31-4.35)] (p = 0.021)] (Table 3).

Table 3: Gestational Diabetes according to History

Parameter	%	RP (IC à 95%)	p
Family history of diabetes			
Yes (n = 19)	52,6	2,79 (1,72 – 4,47)	< 0,001
No (n = 364)	19,0	1	
History of macrosomia			
Yes (n = 16)	43,8	2,38 (1,31 - 4,35)	0,021
No (n = 333)	18,3	1	

Geographic Factors Associated with MGD

The prevalence of gestational diabetes was 2.5 times higher in pregnant women exposed to an average temperature >19°C [23.2% (n = 336)] compared to those exposed to a temperature ≤ 19°C [9.3 % (n = 54)] [RR 2.51 95% CI (1.51-5.91)] (p = 0.020)]. It was twice as high in pregnant women living at an altitude of < 1700 m corresponding to an atmospheric pressure of > 82% [27.0% (n = 226)] compared to those living at an altitude ≥ 1700 m corresponding to an atmospheric pressure ≤ 82% [13.4% (n = 164)] [RP 2.01 95% CI (1.29- 3.14)] (p = 0.001)] (Table 4).

Table 4: Gestational Diabetes According to Geographical Parameters

Parameter	%	RP (IC à 95%)	p
Temperature			
> 19°C (n = 336)	23,2	2,51 (1,06 – 5,91)	0,020
≤ 19°C (n = 54)	9,3	1	
Altitude			
< 1700 m (n = 226)	27,0	2,01 (1,29 – 3,14)	0,001
≥ 1700 m (n = 164)	13,4	1	
Atmospheric pressure			
> 82 (n = 226)	27,0	2,01 (1,29 – 3,14)	0,001
≤ 82 (n = 164)	13,4	1	

Determinants of DGM

After adjusting for family history of diabetes, only atmospheric pressure and altitude remained significantly associated with gestational diabetes. Gestational diabetes was 3.62 times more in case of ATCD of diabetes in the family [(n = 383)] [OR 3.62 95% CI (1.39-9.43)] (p = 0.009)] and almost 2 times more when the altitude was <1700m, which corresponded to an atmospheric pressure > 82% [(n = 383) OR 198.0 95% CI (1.14 - 3.46)] (p = 0.016)]. Temperature was no longer associated with gestational diabetes (Table 5).

Table 5: Multivariate Analysis of Geographic Parameters and Family History of Diabetes Associated with Gestational Diabetes (n = 383, Gestational Diabetes = 79)

indicators	RC (IC à 95%)	p
History of diabetes		
Yes	3,62 (1,39 – 9,43)	0,009
No	1	
Altitude		
< 1700 m	1,98 (1,14 – 3,46)	0,016
≥ 1700 m	1	

Discussion

The prevalence of gestational diabetes was different according to the different study localities by their geographical conditions of altitude and temperature [14].

In this study, oxygen saturation < 95% (hypoxia) was associated with a low prevalence of gestational diabetes. Speaking of intermittent hypoxia, Amandine Thomas at al. found that hypoxia was accompanied by anorexia, impaired insulin resistance in its target organs, and improved glucose tolerance throughout the body [18]. While had found that this hypoxia was more at the basis of the induction or aggravation of insulin-resistance, glucose intolerance and an inflammatory environment including in the pancreas [19]. Hypoxia is not an isolated factor for effects on glycaemia, in altitude conditions where the effects of temperature and lifestyle also combine, among other things [20]. Moreover, this may explain the results of this study.

A cortisol level of >275 nmol/L was associated in this study with a higher prevalence of gestational diabetes. As this study involved pregnant women who had been living in the sites for at least 30 days, their metabolism would therefore no longer be due to changes in altitude as demonstrated by certain results whose authors had respectively found that the endocrine response to altitude normalized in the five days following the climb, in particular the cortisol level and that the variations in the cortisol level stabilized after a stay of 30 days or more at high altitude [21, 22]. Interested in adapting to stress had noted that the average cortisol level was higher in pregnant women with gestational diabetes: 502.75 ± 124 nmol/L Vs 464.62 ± 110 nmol/L in the absence of gestational diabetes [23]. This is consistent with the results of our study despite the relative low cortisol level in the study settings. The difference in cortisol level with the results of Yan Feng at al. could be explained by the fact that his study concerned pregnant women subjected to a certain degree of stress.

Pregnant women with an arm circumference greater than 280 mm represented 20.6% (n = 378) and had a non-statistically significant high prevalence of gestational diabetes compared to those with a lower arm circumference [14]. The mechanisms of low weight at altitude are incompletely elucidated had explained it by the increase in physical activity and energy expenditure when traveling in these sometimes difficult environments and in addition, the low temperatures that reign there increased energy expenditure for thermogenesis [20]. The different geographical conditions of altitude at 1372m an annual average temperature of 20°C with a maximum variation of 5.9 °C; which would not modify the local atmospheric pressure of 86.1% in Arusha would explain the difference in our results from those of who found in Arusha that a MUAC ≥ 280 mm was associated with hyperglycemia during pregnancy [24, 25].

In this study, the prevalence of gestational diabetes was higher in pregnant women exposed to an average temperature of 30 days prior to sampling at >19°C. Gerngroß C For temperature does not modify the activity of brown fat [26]. Francesco S Celi an increase in fasting insulin levels and a slight but significant drop in postprandial glycaemia after a short exposure to a temperature drop of 5°C [27]. Even if the glycaemia was dosed once, the pregnant women included in this study had been subjected to the seasonal temperature for at least 30 days and in this study, the temperature ≤19°C was associated with an altitude of 2419m corresponding to a pressure 75% atmospheric. This could explain the results of this study.

The prevalence of gestational diabetes was higher in pregnant women living at an altitude of < 1700 m corresponding to an atmospheric pressure of > 82%. These results corroborate those of had suggested that significant physiological modifications were necessary for adaptation to an altitude ≥1500m[20] , to those of for whom high altitude (1500 to 3500) was associated with a lower probability of having diabetes than at an altitude ≤ 500m and those of who also found that altitude was inversely associated with the risk of diabetes in Tibetans [28]. This inverse association between altitude and diabetes was not verified in women by the results [1]. Even though had not found a difference in the prevalence of gestational diabetes between high and medium altitude, he had noted that the differences in the characteristics of pregnant women were suggestive of a subtle difference in glucose metabolism at high altitude [12]. After adjustment for confounding factors, noted that fasting blood glucose levels were elevated when the altitude was ≤ 2000m in both men (1.80; 95% CI, 1.32–2.46) and women (1.55; 95% CI, 1.24–1.93) [29]. The differences in geographical conditions of altitude and the low variation in average temperature of 30 days preceding the sampling of the study sites could explain our results.

In this study, gestational diabetes was more common in cases of family history of diabetes and history of macrosomia [14]. After adjusting for family history of diabetes, unlike altitude and atmospheric pressure, temperature was no longer associated with gestational diabetes. This is in line with the observations of who had found that there was no association between the average temperature of the weeks preceding the sampling and blood sugar whereas this association was strong if the variations in temperatures during the previous weeks were used, especially if the variation was at the rise [30]. However, the temperature remains an interesting factor in that it enters with the altitude into the calculation of the atmospheric pressure even though the study environments experienced a small inter-seasonal fluctuation in temperature; insufficient to modify the local atmospheric pressure.. After adjustment, atmospheric pressure and altitude remained significantly associated with gestational diabetes. These results corroborate those of who noticed that fasting glycaemia was high when the altitude was ≤ 2000m [29].

The Limits of this Work

This work did not look for other factors that could influence blood sugar such as the level of physical activity and/or stress or even eating habits. Moreover, he was only interested in the average temperature of thirty days before sampling. From its sample, the work had failed to establish whether cortisol levels were also a mechanism by which geographical factors would influence blood sugar levels.

The Merits of this Work

This work is among the few studies on gestational diabetes based on geographic conditions in our environments including atmospheric pressure, a factor that incorporates local altitude and temperature.

Conclusion

The differences in the prevalence of gestational diabetes in the different study settings would be due to the differences in climatic conditions of altitude and atmospheric pressure. The prevalence of pathological glycaemia tended to be higher at <1700 mm altitude corresponding to atmospheric pressure > 82% and when SO2 was >95%.

What is Known?

Glucose metabolism is influenced by altitude and temperature, the mechanisms of which have not yet been fully elucidated.

What is the Contribution of this Study?

This work demonstrated that the difference in the prevalence of gestational diabetes in our environments would also be due to the different geographical conditions of altitude and atmospheric pressure and that relative hypoxia would protect against gestational diabetes. Atmospheric pressure would be a more inclusive geographic determinant of gestational diabetes and in addition would be a more standard parameter for comparison between different environments and seasons in order to understand glucose homeostasis in particular.

References

1. Woolcott OO, Ader M, Bergman RN (2015) Glucose Homeostasis During Short-term and Prolonged Exposure to High Altitudes. Endocr. Rev 36: 149-173.
2. Verburg PE, Tucker G, Scheil W, Erwich JJHM, Dekker GA (2016) Seasonality of gestational diabetes mellitus: a South Australian population study. BMJ Open Diabetes Res. Care 4: e000286.
3. Castillo O, Orison O Woolcott, Elizabeth Gonzales, Victoria Tello, Lida Tello, et al. (2007) Residents at High Altitude Show a Lower Glucose Profile Than Sea-Level Residents Throughout 12-Hour Blood Continuous Monitoring. High Alt. Med. Biol 8: 307-311.
4. Woolcott OO, Castillo OA, Gutierrez C, Elashoff RM,

Stefanovski D, et al. (2014) Inverse association between diabetes and altitude: A cross-sectional study in the adult population of the United States: Diabetes at High Altitude. Obesity 22: 2080-2090.
5. Grant ID, Giussani DA, Catherine E Aiken (2021) Fetal growth and spontaneous preterm birth in high-altitude pregnancy: A systematic review, meta-analysis, and meta-regression. Int. J. Gynecol. Obstet 13779.
6. Bailey BA, Donnelly M, Bol K, Moore LG, Julian CG (2019) High Altitude Continues to Reduce Birth Weights in Colorado. Matern. Child Health J 23: 1573-1580.
7. Moses RG, Wong VCK, Lambert K, Morris GJ, San Gil F (2016) Seasonal Changes in the Prevalence of Gestational Diabetes Mellitus. Diabetes Care 39: 1218-1221.
8. Booth GL, Luo J, Park AL, Feig DS, Moineddin R, et al. (2017) Influence of environmental temperature on risk of gestational diabetes. Can. Med. Assoc. J 189: E682-E689.
9. Ouellet V, Annick Routhier-Labadie, William Bellemare, Lajmi Lakhal-Chaieb, Eric Turcotte, et al. (2011) Outdoor Temperature, Age, Sex, Body Mass Index, and Diabetic Status Determine the Prevalence, Mass, and Glucose-Uptake Activity of 18F-FDG-Detected BAT in Humans. J. Clin. Endocrinol. Metab 96: 192-199.
10. Hassan B (2020) Interpretation of maternal blood glucose during pregnancy at high altitude area, Abha-Saudi Arabia. J. Fam. Med. Prim. Care 9: 4633.
11. Von Wolff M, C T Nakas, M Tobler, T M Merz, M P Hilty, et al. (2018) Adrenal, thyroid and gonadal axes are affected at high altitude. Endocr. Connect 7: 1081-1089.
12. Anna G Euser, Andrew Hammes, Jared T Ahrendsen, Barbara Neshek, David A Weitzenkamp, et al. (2018) Gestational Diabetes Prevalence at Moderate and High Altitude. High Alt. Med. Biol 19: 367-372.
13. Ge RL, Simonson TS, Gordeuk V, Prchal JT, McClain DA, et al (2015) Metabolic aspects of high-altitude adaptation in Tibetans: Metabolic aspects of high-altitude adaptation in Tibetans. Exp. Physiol 100: 1247-1255.
14. Rogatien Mwandjalulu Kisindja, Pierrot Lundimu Tugirimana, Mitangala Ndeba Prudence, Katenga Bosunga, Jean-Jeannot Juakali Sihalikyolo, et al. (2022) Prevalence of gestational diabetes in Eastern. Democratic Republic of Congo. BMC Pregnancy Childbirth 22: 645.
15. Yuchan Zhang, Yixin Liu, Liang Su, Zhonghua Zhang, Danqun Huo, et al. (2014) CuO nanowires based sensitive and selective non-enzymatic glucose detection. Sens. Actuators B Chem 191: 86-93.
16. Pinkney S, Suman Bains, Goyal A, Gupta N, John Bolodeoku (2017) Evaluating a Membrane Based Rapid Plasma Separation Device (RPSD) for Immunoassay Point-of-Care Testing (POCT) for Estimations of Cortisol, D-Dimer, Myoglobin and Thyroxine. Ann. Clin. Lab. Res 5: 196.
17. Rong Chang, Jinchun Wu, Cheng Han, Yanmin Liu, Xiangbo Liu, et al. (2021) Correlation of aspirin resistance with serological indicators in patients with coronary heart disease in the plateau. Am. J. Transl. Res 13: 9024-9031.
18. Amandine Thomas, Elise Belaidi, Sophie Moulin, Sandrine Horman, Gerard C van der Zon (2017) Chronic Intermittent Hypoxia Impairs Insulin Sensitivity but Improves Whole-Body Glucose Tolerance by Activating Skeletal Muscle AMPK. Diabetes 66: 2942-2951.
19. Uchiyama T, Ota H, Ohbayashi C, Takasawa S (2021) Effects of Intermittent Hypoxia on Cytokine Expression Involved in Insulin Resistance. Int. J. Mol. Sci 22: 12898.
20. Koufakis T, Karras SN, Mustafa OG, Zebekakis, Kotsa K (2019) The Effects of High Altitude on Glucose Homeostasis, Metabolic Control, and Other Diabetes-Related Parameters: From Animal Studies to Real Life. High Alt. Med. Biol 20: 1-11.
21. Kimberly E Barnholt, Andrew R Hoffman, Paul B Rock, Stephen R Muza, Charles S Fulco, et al. (2006) Endocrine responses to acute and chronic high-altitude exposure (4,300 meters): modulating effects of caloric restriction. Am. J. Physiol.-Endocrinol. Metab 290: E1078-E1088.
22. Woods D, Stacey M, Hill N, Alwis ND (2011) Endocrine Aspects of High Altitude Acclimatization and Acute Mountain Sickness. J. R. Army Med. Corps 157: 33-37.
23. Yan Feng, Qi Feng, Hongmei Qu, Xinna Song, Jianwei Hu (2020) Stress adaptation is associated with insulin resistance in women with gestational diabetes mellitus. Nutr. Diabetes 10: 4.
24. Ladislaus Benedict Chang'a, Lovina Peter Japheth, Agnes Lawrence Kijazi, Elisia Hamisi Zobanya, Leila Francis Muhoma (2021) Trends of Temperature Extreme Indices over Arusha and Kilimanjaro Regions in Tanzania. Atmospheric Clim. Sci 11: 520-534.
25. Msollo SS, Martin HD, Mwanri AW, Petrucka P (2019) Prevalence of hyperglycemia in pregnancy and influence of body fat on development of hyperglycemia in pregnancy among pregnant women in urban areas of Arusha region, Tanzania. BMC Pregnancy Childbirth 19: 315.
26. Gerngroß C, Schretter J, Klingenspor M, Schwaiger M, Fromme T (2017) Active Brown Fat During 18 F-FDG PET/CT Imaging Defines a Patient Group with Characteristic Traits and an Increased Probability of Brown Fat Redetection. J. Nucl. Med 58: 1104-1110.
27. Francesco S Celi, Robert J Brychta, Joyce D Linderman, Peter W Butler, Anna Teresa Alberobello, et al. (2010) Minimal changes in environmental temperature result in a significant increase in energy expenditure and changes in the hormonal homeostasis in healthy adults. Eur. J. Endocrinol 163: 863-872.
28. Shaopeng Xu, Qing Wang, Jie Liu, Bo Bian, Xuefang Yu, et al. (2017) The prevalence of and risk factors for diabetes mellitus and impaired glucose tolerance among Tibetans in China: a cross-sectional study. Oncotarget 8: 112467-112476.
29. Juna CF, Cho YH, Joung H (2020) Low Elevation and Physical Inactivity are Associated with a Higher Prevalence of Metabolic Syndrome in Ecuadorian Adults: A National Cross-Sectional Study. Diabetes Metab. Syndr. Obes. Targets Ther 13: 2217-2226.
30. Ravi Retnakaran , Chang Ye , Caroline K Kramer , Anthony J Hanley , Philip W Connelly, et al. (2018) Impact of daily incremental change in environmental temperature on beta cell function and the risk of gestational diabetes in pregnant women. Diabetologia 61: 2633-2642.