ORIGINAL ARTICLE

Risk Factors Associated with Maternal and Fetal Complications: A Cross-Sectional Study in the West Bank, Palestine

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ABSTRACT

Background: Fibrocalculous pancreatic diabetes (FCPD) is a unique form of diabetes reported from tropical countries. Though classically described in young, lean and malnourished people from tropical countries with a low socioeconomic background, recent evidences suggest that this classical presentation of FCPD is changing. ***Objective:*** The present study aims to explore detail clinical presentations of encountered FCPD cases in a tertiary hospital in Eastern India. ***Methods:*** A prospective observational study included cases fulfilling the diagnostic criteria of FCPD. Each included patient was interviewed for their basic demographic profile, body mass index, family history and duration of diabetes mellitus. Clinical, biochemical and radiological investigations were done. ***Results:*** A total of 11 patients were studied. Mean age observed was 26.18 years, with majority having their disease diagnosed before the age of 30years. The classical triad of pain abdomen, steatorrhea and DM was present in only 3 cases. On clinical examination, only 1 patient was found to be hypertensive. All patients had HbA1c more than 7% with 5 of them having HbA1c >=8%. Neuropathy was the most common complication detected, followed by nephropathy and retinopathy. Straight X-ray Abdomen after proper bowel preparation showed presence of diffuse calcification involving the head, body and tail region in all the 11 cases, thus confirming the diagnosis. All the cases were managed medically with injectable insulin. ***Conclusion:*** Although insights have been gained into its natural history, the etiopathogenesis continues to be elusive. Despite the low prevalence of the disease, clinicians practicing in tropical countries should always keep in mind FCPD as a differential diagnosis during evaluation of a young diabetic patient, especially if patient is lean and there is a history of abdominal pain or steatorrhea with absence of ketosis.

Keywords: Fibrocalculous pancreatic diabetes, diabetes mellitus, clinical presentation

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INTRODUCTION

With all the improvements and advancements in the managed care, plenty of women still experience health problems during pregnancy. These health problems lead to complications that can affect the health of both mother and or fetus[1]. The World Health Organization (WHO) reported that around 15% of all pregnant women are prone to develop potentially life-threatening complication and require extended medical care or a major obstetrical intervention to survive[2]. On top of it, a pregnant woman from developing countries is up to 36 times higher risk suffering from pregnancy-related complications than a pregnant woman from a developed country[3].

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There are plenty of complications that arise during pregnancy ranging from mild to severe[1]. The severe ones are more complicated, require periodic but continuous monitoring, and are potentially life-threatening if left unattended or even with appropriate treatment. Among these, gestational diabetes mellitus (GDM), pregnancy-induced hypertension (PIH), and preeclampsia are a few to name maternal complications[4,5]. Apart from these, some complications are also associated with the outcome of the pregnancy and include preterm labor (PTL) which is considered the most frequently observed complication which increases the risk of prenatal mortality and creates health issues among newborns[6]. Similarly, PIH is considered a major cause of mother and infant mortality, maternal morbidity such as PTL, and fetal morbidity such as intrauterine growth retardation[7].

Meanwhile, the possible reported complications relating to the fetus during pregnancy include small for gestational age (SGA), large for gestational age (LGA), intrauterine growth restriction (IUGR), and intrauterine fetal death (IUFD)[7-9]. These fetal complications impose equal risk to the pregnant women and fetus. As an example, LGA can cause major problems during labor and delivery such as prolonged labor, arrest of labor, and also associated with increased neonatal morbidity[10].

In Palestine, data on the prevalence of pregnancy and fetal related complications are lacking. Therefore, we intended to record baseline characteristics by identifying the commonly observed fetal and pregnancy complications among pregnant women and their fetuses in Palestine. Furthermore, the study also planned to identify the risk factors of having fetal and pregnancy complications during the pregnancy period.

METHODS

A multicenter prospective, observational study was conducted at primary health care centers in the Nablus district of the West Bank, Palestine, which include four major antenatal clinics. The clinics were run under the supervision of the Palestinian Ministry of Health (MOH). All pregnant women at the age ≥ 17 years, registering at MOH antenatal clinics during their first trimester were included. The data was collected between September 2017 and July 2018.

Pregnant women at first trimester of spontaneous pregnancy were included in the study. Women with pre-existing chronic comorbidities (eg: hypertension and diabetes mellitus), having multi-fetuses' pregnancy, having induced pregnancy via intrauterine fertilization or intrauterine injection, or refused to participate were excluded from the cohort. Face and content validity of the questionnaires was conducted by 2 independent researcher, 2 obstetrics and gynecology doctors, and 2 senior midwives. To ensure the reliability of the questionnaire, Cronbach's alpha was calculated with a result of (0.90).

Acquired data were recorded on a developed structured questionnaire. It covered sociodemographic information including the education status of the mother, smoking status, and monthly income. For clinical information, women's current obstetric history such as the number of gravidities, parity, abortion, and last menstrual period was also recorded from medical files. Self-reported pre-pregnancy body weight at the first antenatal visit were noted. To determine the individuals' pre-pregnancy body mass index (BMI), their heights were also measured. Socioeconomic and baseline clinical data were collected at the beginning of the study. Included participants were followed during their regular visits to the antenatal clinics until delivery. It is important to emphasize that the Palestinian MOH follows WHO recommendations and regulations for antenatal care and pregnancy assessment (number of ultrasound scans, prenatal visits, etc.).

Maternal associated pregnancy complications included in the study were: gestational diabetes mellitus (GDM), pregnancy-induced hypertension (PIH), preterm labor (PTL), pre-eclampsia, abortion, and stillbirth. Fetal complications included in the study were: small for gestational age (SGA), large for gestational age (LGA), intrauterine growth restriction (IUGR), intrauterine fetal death (IUFD) and stillbirth. In Palestine, all these atypical consequences are classified and diagnosed according to the WHO standards.

Any maternal or fetal complication was recorded as a dichotomous (i.e., yes or no). A negative response was only recorded when a respondent experienced no maternal or fetal complication. Age was recorded as a continuous variable and

was later graded further into groups. For the purpose of the study, parity was categorized into four classes, i.e. nulliparity (did not give birth before), low multi-parity (history of previous 1 to 3 live births), grand multi-parity (history of previous 4 to 6 live births), and high parity (history of more than 6 live births).

Binary logistic regression was used to analyze the data. Odds ratio (OR) along with their respective 95% confidence intervals (CI) were recorded to compare the magnitude of different risk factors for both pregnancy and fetal complications. A p-value ≤ 0.05 was considered statistically significant. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS version 26.0), SPSS Inc., Chicago, IL, USA.

RESULTS

A total of 896 pregnant women registered at antenatal clinics in Nablus district during the study period. Among them, 380 pregnant women agreed to participate in the study. More than half of the participants (n=209) were aged between 26 and 32 years originating from the city (50.2%) (Table 1). Most women had at least one gravidity (28.7%) and 45.8% fell in the category of low multi-parity. There were 18 participants that had more than 6 parties as well. Similarly, more than half (52.1%) fell into the ideal BMI category while nearly every 2 out of five women (38.2%) had a history of smoking. Anemia was observed as the most prevalent (36.9%) health problem at the first visit (Table 1). 77(20.3%) pregnant women had at least one (one or more) pregnancy complication, while 303 women continued their pregnancies without any complications. PTL was the most common type complication (11.3%) observed followed by GDM and PIH, i.e. 7.9% each. Among fetal complications, LGA and SGA were the most common fetal complications with a percentage of 11.6% and 10.5%, respectively (Table 2). Maternal complications associated with pregnancy was found to increase the odds of having pregnancy-associated complications (OR = 2.35; 95% CI 1.02- 5.45). Similarly, having first-time pregnancy (OR = 14.9; 95% CI 1.09-202.5) or reaching parity one through three times (OR = 16.8; 95% CI 1.47- 192.5) had significantly higher odds of having maternal pregnancy complication than the other groups. Contrarily, a higher value of gravidity (>4) reduced the risk to have pregnancy complications (OR = 0.11; 95% CI 0.03- 0.47) (Table 3). An increase in age gradually but significantly increased the odds of acquiring such complications despite were the youngest age group's highest negative odds, i.e. OR = 0.04 (95% CI 0.08- 0.23). In other words; age younger than 41 years is a protective factor for fetal complications, because odds are <1. Although any trend was not visible in the parity-based grouping, four to six parities posed a significantly higher risk (OR=36.17; 95% CI 4.88-268) for fetal complications. Similarly, smoking borderline increased the odds (OR=1.25; 95% CI 1.0-3.07) of having fetal complications (Table 4).

Table 1: Demographic and baseline clinical characteristics of pregnant women at the beginning of the study.

Variables	Category	Frequency (Percentage)
Age (in years)	17-25	83 (21.8)
	26-32	209 (55)
	33-41	72 (18.9)
	> 41	16 (4.2)
Residency	Camps	16 (4)
	Villages	120 (45.6)
	City	244 (50.2)
Gravidity	1	109 (28.7)
	2	76 (20)
	3	54 (14.2)
	4	50 (13.2)
	>4	91 (23.9)
Parity	Zero	133 (35)
	1-3	174 (45.8)
	4-6	55 (14.5)
	>6	18 (4.7)
BMI (kg/m² (pre-pregnancy)	<18.5	12 (3.2)
	18.5-24.9	198 (52.1)
	25-29.9	101 (26.6)
	≥ 30	69 (18.1)
Smoking Status	Smokers	145 (38.2)
	Non smoking	235 (61.8)
Anemia	Anemia	140 (36.9)
Family monthly income	NIS <1000 (low income)	4 (1.1)
	1000-4000 NIS (middle income)	249 (65.5)
	NIS >4000 (high income)	127 (33.4)
Education level	Less than high school	65 (17.1)
	High school	112 (29.5)
	Diploma	91 (23.9)
	Bachelor	107(28.2)
	More than bachelors	5 (1.3)

BMI=body mass index; NIS=New Israeli Shekel

Table 2: Common pregnancy and fetal complications during pregnancy

Variables	Type of complication	No.	%
Pregnancy complications	PTL	43	11.3
	GDM	30	7.9
	PIH	30	7.9
	Preeclampsia	15	3.9
	Abortion	2	0.5
	Stillbirth	2	0.5
Fetal complications	LGA	44	11.6
	SGA	40	10.5
	IUGR	8	2.1
	IUFD	6	1.6

PIH=pregnancy induced hypertension; PTL=Preterm labor; GDM=gestational diabetes mellitus; LGA=Large for gestational age; SGA=Small for gestational age; IUGR=Intrauterine growth restriction; IUFD=Intrauterine fetal death.

Table 3: Binary logistic regression analysis for women complications during pregnancy

Variables	p-value	O.R (95% CI)
Age Categories (in years)		
> 41 [Reference group]	0.58	1.38 (0.18-10.69)
17-25	0.76	1.68 (0.23-12.08)
26-32	0.61	2.53 (0.33-19.27)
33-41	0.37	
BMI Categories		
>30 Kg/m^2 [Reference group]	0.72	
< 18 Kg/m^2	0.48	0.53 (0.09-3.11)
18-24.9 Kg/m^2	0.27	0.64 (0.29-1.40)
25-29.9 Kg/m^2	0.51	0.76 (0.34-1.70)
Place of Residence		
City [Reference group]	0.13	1.24 (0.64- 2.38)
Village	0.51	2.35
Camp	0.05*	(1.02- 5.45)
Monthly family income		
High: (>4000 NIS) [Reference group]	0.58	
Low: (< 1000 NIS)	0.83	0.31 (0.11-15.0)
Middle: (1000-4000 NIS)	0.33	0.75 (0.42-1.34)
Gravida		
>4 [Reference group]	0.06	0.44 (0.10-2.0)
1	0.28	0.39 (0.12-1.21)
2	0.10	0.45 (0.14-1.42)
3	0.17	0.11 (0.03-0.47)
4	0.003*	
Parity		
>6 [Reference group]	0.11	14.9 (1.09-202.5)
Zero	0.04*	16.8 (1.47-192.5)
1-3	0.023*	6.04 (0.58- 63.2)
4-6	0.133	
Anemia [yes versus no]	0.64	0.87 (0.50-1.54)
Smoking [yes versus no]	0.66	0.88 (0.50-1.55)

BMI =body mass index; NIS=New Israeli Shekel.

Table 4: Binary logistic regression analysis for fetal complications during pregnency

Variables	p-value	O.R (95% CI)
Age Categories (in years)		
> 41 [Reference group]	0.003	
17-25	0.000*	0.04 (0.08-0.23)
26-32	0.001*	0.06 (0.01-0.32)
33-41	0.008*	0.10 (0.02- 0.55)
BMI Categories		
> 30 Kg/m^2 [Reference group]	0.122	
< 18 Kg/m^2	0.416	1.9 (0.41-8.67)
18-24.9 Kg/m^2	0.439	0.73 (0.34-1.61)
25-29.9 Kg/m^2	0.070	0.45 (0.19-1.07)
Place of Residence		
City [Reference group]	0.659	
Village	0.626	0.5 (0.44- 1.63)
Camp	0.399	0.67 (0.27-1.68)
Monthly family income		

Variables	p-value	O.R (95% CI)
High: (>4000 NIS) [Reference group]	0.906	
Low: (< 1000 NIS)	0.798	0.72 (0.06-8.71)
Middle: (1000-4000 NIS)	0.688	0.89 (0.50-1.60)
Gravida **>4** [Reference group] 1 2 3 4	 0.201 0.470 0.609 0.858 0.070	 1.70 (0.40-7.13) 1.36 (0.42-4.37) 1.12 (0.33-3.82) 0.29 (0.07-1.11)
Parity >6 [Reference group] Zero 1-3 4-6	 0.003 0.020* 0.023* 0.000*	 12.43 (1.48-104.1) 10.14 (1.38-74.5) 36.17 (4.88- 268)
Anemia [yes versus no]	0.105	0.63 (0.36-1.10)
Smoking [yes versus no]	0.049*	1.76 (1.0-3.07)

BMI-=body mass index; NIS-=New Israeli Shekel

DISCUSSION

To our knowledge, this is the one of the first study reporting the baseline data of pregnancy complications among Palestinian pregnant women. It establishes that more than 20% of Palestinian pregnant women have at least one complication with PTL being most frequent and GDM and PIH, equally, being second most frequent. Among fetal complications, LGA and SGA were the most commonly recorded complications during pregnancy. Results from the current study indicate that participants in our group depicted sort of similar complications that are prevalent in the region or neighboring countries. For example, a retrospective study from Dubai also reported PIH and GDM as the most identified complications[11]. Apart from that, PTL was the most commonly observed complication in a Jordan[12].

Among fetal pregnancy complications, the current study identified SGA and LGA as the most common fetal complications during pregnancy. This finding was also consistent with previous studies identifying these complications as the most prevalent ones affecting fetuses during the pregnancy[13,14].

Regarding risk factors of pregnancy complications, we found that both nulliparity and low multi-parity women had higher risk of having complications during pregnancy when compared to high parity (>6) women. This means, both nulliparity and low parity were risk factor of complications during pregnancy. Parity has an inconclusive effect on pregnancy complications. Some studies showed different results and somewhat discrepancies regarding parity and pregnancy complications. Parities of three and above are considered a risk factor for GDM[15], while PTL was reported in some studies among high multiparity (≥5) women (9, 16). On the other hand, nulliparous women are also reported to be at a greater risk of having pregnancy complications than women with other parities[13,16-18]. A significant association between different parity levels and pregnancy complications (including GDM, PIH, and PTL) was also reported by Bai et al.[19]. The study showed that the risk of any obstetric complications was higher among nulliparous women compared to parity one women. However, the study also revealed that multiparous women (>4) were also at a higher risk of pregnancy complication as compared to women with parity one. A recent meta-analysis of the Asian population identified only multiparity as a risk factor of GDM[20]. Moreover, Shechter-Maor et al. reported that primiparous women (having 1 previous live birth) were at higher risk of having pregnancy complications than multiparous women[21]. The conflicting results of parity in different studies pointed to the complexity of the association between possible risk factors of pregnancy complications. This means, there may be a possible influence of further factors that contribute to a higher risk of these complications, such as ethnicity, socio-economic status, family history, and previous history of these complications.

An interesting result from the current study was gravida not having any adverse association with pregnancy complications. Instead, it depicted a statistically significant negative effect against pregnancy complications (O.R =0.11). The results identified pregnant women, mainly of gravida 4, being at lower risk of having pregnancy complications than higher gravida women. The degree of gravida or gravida status is rarely reported in previous studies as a risk factor or protective factor of pregnancy complications. In this context, Heaman and colleagues reported that being a primigravida is a risk factor of PTL[22]. However, the said study also showed that being a multigravida woman with a previous history

of PTL was a common risk factor for PTL and eclampsia as well. Additionally, primigravid women are previously highlighted by another researcher from Australia as well in a way that primigravid women have much higher rates of maternal complications[19]. However, a recent study from South India showed that gravidity was not associated with high-risk pregnancy and included complications such as anemia, PIH and GDM[18].

The current study revealed that pregnant women living in camps had greater risk of having pregnancy complications (O.R =2.35) as compared to women living in cities. The possible explanation might be due to lagging pregnant women living in camps in getting health care services regularly due to social, educational and economic conditions which are known to be much lower in Palestinian camps than cities and towns.

Regression analysis of current study results missed the age as a common risk factor for having complications during pregnancy. It was contrary to the Jordanian study that identified older women (age > 40) to be at high risk of such adverse pregnancy complications[12]. Similarly, many other international studies have also reported that advancing age (women ≥40 years) is a potent risk factor of pregnancy complications[23,24]. Advanced age was also identified to be a risk factor for having specific complications during pregnancy such as GDM, pre-eclampsia, and PIH[17,25,26]. However, the current study did not find age as a risk factor for maternal pregnancy complications; this might be due to the small number of pregnant women with advanced age in our study sample.

Contrarily, the regression model for fetal pregnancy complications from current data managed to identify younger age (17-40 years) as a protective factor of fetal complications during pregnancy. This indicated that these complications were more common to be seen among mothers with older age (>41 years). This has previously been reported by some studies where fetuses of older-age women (≥40 years) are prone to endure complications such as IUFD, IUGR, and LGA[24,27,28]. Yet, some other studies reported age of 35 years and above as the cut-off for increased risk of complications such as LGA, but this cut-off point did not found age as a risk for SGA fetal complications[14].

However, both LGA and SGA have indecisive trend across the studies. As an example, LGA was more commonly reported among women aged 40 years old and more when compared to younger pregnant women aged between 30 and 34 years[29]. However, the result was insignificant when comparing women aged women 35-39 years with the reference group pregnant women (30-34 years). Moreover, other showed women age 30 to 34 years old had lower rates of SGA compared with women aged between 20 and 29 years[30]. This phenomenon was also established when SGA was more frequently reported among women aged between 35 and 40 years old compared with women aged between 20 and 24 years[31]. Yet another angle of the relationship between age and fetal complications is that young age women (<19 years) had a lower risk of having fetal complications such as LGA (32). Nonetheless, current results indicate that advanced age women are at higher risk of having fetal complications during pregnancy, which is also reported in several earlier studies[24,27,29,31].

The results of the current study showed a relationship between parity status and fetal complications; fetal complications were more commonly seen among mothers with nulliparity, low multi-parity and high multi-parity compared to the reference group, indicating women with high parities had a lower risk of fetal complications in our sample. Some studies reported that nulliparous women had significant associations with adverse fetal complications compared with multiparous women[13,32], where nulliparous women depict significant adverse association with SGA (33). Additionally, the increased risk of fetal complications such as SGA (14) and IUGR is also reported to be higher among primiparous mothers than multiparous mothers[21]. Contrarily, there has been a study indicating LGA as more common to see among very high parity women (10-14 parities), but a lower risk of SGA was reported among this group[9]. However, since the study did not include nulliparous women in the analysis, it is difficult to compare our results with it. Moreover, a meta-analysis concluded that women who were both multiparous (≥3) and had their age ranging between 18-34 years had some protective effect against SGA[13]. Similarly, another study showed that only nulliparous women aged ≥30 years but not multiparous women were at higher risk of having SGA when compared with nulliparous women aged between 20 and 29 years[31]. This

may indicate that not only the level of parity may affect fetal complications, but the explanation of this could also be due to the existence of other influencing factors such as maternal age or the existing relationship between specific parity levels with specific fetal complications.

The current study revealed that the continuation of smoking during pregnancy is quite common among Palestinian pregnant women. The high prevalence of smoking could be attributed to the increase in the Shisha smoking practice among all Arab countries which itself is becoming an acceptable attitude among both men and women. Regression analysis showed that smoking women were at a higher risk of having fetal complications during pregnancy than non-smokers. This result confirmed previous findings whereby smoking in pregnancy is an established risk factor for fetal complications such as SGA, and IUGR in plenty of previous studies as a risk factor[17,22,25,34]. It is well known that cigarette smoking during pregnancy decreases the carrying capacity of oxygen for both fetal and maternal blood, which in turn diminishes the oxygen available to the fetus at the tissue level and further effect fetal oxy-hemoglobin dissociation[35]. Hence, the current study, once again, confirms the importance of smoking as a major risk factor for fetal complications during pregnancy.

This being one of the first studies to report baseline data regarding maternal and fetal pregnancy complications among Palestinian pregnant women, also has some limitations need to be addressed. There was no information collected about the history of previous pregnancy complications such as previous pre-eclampsia, abortion, PIH or GDM. Moreover, pregnant women who had pre-existing medical problems such as hypertension, diabetes, and epilepsy were not included in the study; this can underestimate the prevalence of complications during pregnancy. However, despite these limitations, we believe this study contributes to the literature related to the identification and evaluation of complications and risk factors of complications occurring during pregnancy.

CONCLUSION

Fetal and pregnancy complications are prevalent among Palestinian pregnant women. LGA and SGA were mostly reported as fetal complications while pregnant women were more likely to suffer from GDM, PIH and PTL as pregnancy complications. Based on findings, age <41 years was a protective factor for fetal complications, but not the complications of pregnancy. Additionally, fetal complications were more prevalent among smoking mothers and women with ≤6 previous live births. In the further context of parity, parity ≤3, and living in camps were risk factors that increase the risk of pregnancy complications. However, it was equally interesting to note that gravida 4 was a protective factor for pregnancy complications. We strongly recommend better pregnancy monitoring and early screening of pregnant women to identify the risk for these complications which can help to either avoid or timely action against those risky situations.

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Ethical Approval: The study was approved by the Institutional Review Board (IRB) of An-Najah National University, Nablus, West Bank, Palestine, and the Ministry of Health, Palestine.

Authors' Contributions: All authors contributed to the study conceived and designed the study. Nihal Al-Natour and Mariam Al-Tell contributed to data collection and assisted in completing the study. Nihal Al-Natour and Sana' AL Aqqad analyzed the data. Sana' AL Aqqad interpreted the data and wrote the final draft of the manuscript. The authors have read and approved the manuscript.

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