Progression of Pregnancy Induced Diabetes Mellitus to type two Diabetes Mellitus, an Ambidirectional cohort study.

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Research article

Keywords: Glucose intolerance, pregnancy induced diabetes mellitus, progression, type 2 DM

Posted Date: June 8th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-30572/v1

Version of Record: A version of this preprint was published at Primary Care Diabetes on June 1st, 2021.
See the published version at https://doi.org/10.1016/j.pcd.2020.11.016.

Abstract

Introduction:

Diabetes Mellitus (DM) is a metabolic disorder characterized by elevated level of blood glucose. It affects more than 422 million people globally. In resource limited settings, the progression of gestational diabetes (GDM) to DM was not well investigated and this research work was conducted to estimate the incidence of DM after GDM and their predictors in resource limited settings.

Methods

Both retrospective and Prospective cohort studies were implemented from January 2010 until December 2019. The data were collected using patients chart review, interview and collecting blood sample. Initially, baseline data were collected from GDM and GDM free women and update data were collected every 3 months. Clinical nurses were used to extract the necessary data from medical charts and to collect the data using patient interview. Laboratory technologists were used to measure the blood glucose level of the study participants. The study was conducted in pregnant women presenting themselves in the referral hospitals of Amhara regional state. The sample size was calculated using Epi-info software. Descriptive statistics were used to describe the profile of study participants. Kaplan Meier survival curve and life-table were used to estimate the survivals of study participants. Incidence density was used to estimate the incidence of DM. Cox regression was used to identify the predictors DM.

Results

A total of 4892 women were followed giving for the response rate of 88.62%. The mean age of study participants at the start of the study was 28.34 years with standard deviation [SD] ± 7.48 years. DM was associated with Gestational diabetes mellitus [AHR(adjusted hazard ratio) ;2.53, 95% CI: 2.14–2.99], Frequency of breastfeeding [AHR; 0.72, 95% CI: 0.69–0.74], age [AHR; 1.04, 95% CI: 1.03–1.05], Parity [AHR; 1.14, 95% CI: 1.07–1.21], Regular physical exercise [AHR; 0.45, 95% CI: 0.37–0.55], Family history of DM [AHR; 2.04, 95% CI: 1.76–2.37],Stillbirth increases [AHR;1.67: 95% CI: 1.34–2.07], Abortion [AHR; 2.64, 95%CI: 2.25–3.09].

Conclusion

The progression of GDM to DM was very high and special follow up should be implemented for women with a history of abortion, stillbirth, and family history of DM.

Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by impaired metabolism of glucose fat and proteins. It is generally classified as Gestational diabetes mellitus (GDM), type 1 diabetes mellitus, and type two diabetes mellitus. GDM is a high blood glucose level first detected in pregnancy and it disappears after 42 days post-partum. Type 1 DM occurs when the pancreas produces little or no insulin and common in childhood. Type two diabetes mellitus is the most common type of DM and characterized by insulin resistance and latter on insulin deficiency [1–3].

World health organization (WHO) estimates that about 422 million people are diabetes and its prevalence will increase with a high rate in the coming years. The number of DM patients increase by four folds since 1980. Yearly, 1.6 million people were dying as a result of DM. The mortality and morbidity of DM were higher in low and middle- income countries [4].

DM has acute and chronic complications; the acute complication resulted from the mismatch between the available insulin and its demand and includes hypoglycemia, hyperosmolar hyperglycemic state (HHS), and diabetes ketoacidosis (DKA) [5]. Chronic complication attacks years later and it affects all parts of the body, particularly affecting the eyes, nerves, kidneys, feet, arm, mouth, and skin [6].

The expert recommends using one of the following modalities to diagnose DM; fasting blood glucose level (> 126 mg/dl), random blood glucose level (> 200 mg/dl), measuring glycated hemoglobin (HbA1c > 6.5 at two different spots) or oral glucose tolerance tests at two different spots [7].

In resource-limited settings, the progression of GDM to DM was not well investigated and this research work was conducted to estimate the incidence of DM after GDM and their predictors in resource-limited settings.

Methods And Materials

Both retrospective and Prospective cohort studies were implemented. The study was conducted starting from January 2010 until December 2019; starting from January 2010 to February 2015 the study participants were followed retrospectively, meaning reviewing the medical charts. And starting from March 2015 to December 2019 the study participant's status was checked every 3 months prospectively. A Simple random sampling technique was used to select both GDM and GDM free women using their registration chart ID as a sampling frame. The data were collected using patients chart review, interview and collecting a blood sample. Initially, baseline data were collected from GDM, and GDM free women and update data were collected every 3 months. The DM status of each study participant was checked every 3 months using the random plasma glucose (RPG) test [8]. Each study participant was followed for a total of 10 years (January 2010 to December 2019).The event of this study was DM. Study participants withdrew from the study before the event was considered as censored. Clinical nurses were used to extracting the necessary data from medical charts and to collect the data using the patient interviews. Laboratory technologists were used to measuring the blood glucose level of the study participants.

The International Physical Activity Questionnaire tool (IPAQ) was used to measure regular physical [9]. The random blood glucose level was measured using Random Plasma Glucose (RPG) test adhering to the standard operating procedures [8]. The whole data collection procedures were closely supervised.

Pregnant women receiving antenatal care in the year 2010 and diagnosed GDM were considered as an exposed group. Pregnant women receiving the ANC service and declared GDM free in the year 2010 were considered as non-exposed. For the first phase (starting from January 2010 to February 2015), study participants were followed retrospectively from their medical chart. For the second phase from March 2015 to December 2019, the study participants were followed prospectively. The study was conducted in pregnant women presenting themselves in the referral hospitals of Amhara regional state (Gondar university hospital, Felegehiwote referral hospital, Debreberhane hospital, Dessie referral hospital, and Debremarkose referral hospital) DM was diagnosed using American diabetes association, random blood sugar > 200 mg/dl at two different spots was labeled as DM patient [7]. The sources of the data were hospital registers and primary data from each participant. To increase the response rate of the study, each study participant was informed about the study and its merits to the community.

The sample size was calculated using Epi-info software using the assumption of 95% CI, 90% power, the ten-year risk of diabetes mellitus after gestational diabetes of 50% [10], the ratio of women with GDM and GDM free of 1: 2, 15% non-response rate gives 1840 women with GDM and 3,680 women free from GDM.

Data were analyzed using STATA software version 14. Descriptive statistics were used to describe the profile of the study participants. Kaplan Meier survival curve and life-table were used to estimate the survivals of study participants. Incidence density was used to estimate the incidence of DM. Cox regression was used to identify the predictor's DM, Adjusted Hazard Ratio (AHR) with their 95% CI were used to declare the determinants. Multiple imputations were used to handle the missing data [11].

Ethical clearance was obtained from Bahir Dar University College of medicine and health science ethical review board with an ethical approval number of CMHS/IRB/93/2014. A support letter was obtained from the Amhara regional state health bureau. A permission letter was obtained from each hospital. Written informed consent was obtained from each study participant. Pretest and posttest counseling was given for each study participant. A study participant diagnosed with DM was linked to the chronic care.

Results

A total of 4,892 women were followed giving for the response rate of 88.62%, the records of 324 study participants were incomplete, 108 study participants changed their resident and 196 study participants were not volunteer to participate in the study. The mean age of study participants at the start of the study was 28.34 years with standard deviation [SD] ± 7.48 years (Table 1).

Table 1
Profile of the study participants (n = 4892)

Serial Number	Variables		GDM		Free from GDM	
			Frequency	**Percentage**	**Frequency**	**Percentage**
1.	Family history of DM	Present	217	65.2	116	34.8
		Absent	1432	31.4	3127	68.6
3.	Regular physical exercise	Present	421	24.5	1295	75.5
		Absent	1228	38.7	1948	61.3
5.	History of abortion	Present	158	48.9	165	51.1
		Absent	1491	32.6	3078	67.4
	History of stillbirth	Present	105	72.9	39	27.1
		Absent	1544	32.5	3204	67.5

Incidence Of Diabetes Mellitus

The incidence of DM in women with a history of GDM was 705/10355 person year; that means, if we follow 10355 GDM women for a year, 705 women will develop DM at the end of the year.

The incidence of diabetes mellitus for women free from GDM was 349/25501 person year; if we follow 25501 GDM free women for a year, 349 women will develop DM at the end of the year (Fig. 1).

Table 2
Life table for DM (n = 4892)

Interval in months	Total	DM	Lost	Survival	Standard error	95% CI	
						Lower limit	Upper limit
48–49	4892	51	0	0.9896	0.0015	0.9863	0.9921
51–52	4841	24	0	0.9847	0.0018	0.9808	0.9878
57–58	4817	124	0	0.9593	0.0028	0.9534	0.9645
60–61	4693	174	0	0.9238	0.0038	0.9160	0.9309
63–64	4519	0	205	0.9238	0.0038	0.9160	0.9309
66–67	4314	88	0	0.9049	0.0042	0.8963	0.9128
69–70	4226	0	222	0.9049	0.0042	0.8963	0.9128
72–73	4004	112	279	0.8787	0.0048	0.8690	0.8877
75–76	3613	242	0	0.8198	0.0058	0.8082	0.8308
81–82	3371	24	0	0.8140	0.0058	0.8022	0.8251
84–85	3347	0	443	0.8140	0.0058	0.8022	0.8251
87–88	2904	133	0	0.7767	0.0064	0.7639	0.7890
94–95	2771	0	644	0.7767	0.0064	0.7639	0.7890
97–98	2127	0	788	0.7767	0.0064	0.7639	0.7890
99–100	1339	29	0	0.7599	0.0070	0.7459	0.7733
104–105	1310	0	826	0.7599	0.0070	0.7459	0.7733
108–109	484	53	431	0.6099	0.0193	0.5709	0.6465

After adjusting for age, history of abortion, history of stillbirth, frequency of breastfeeding, regular physical exercise, parity after GDM, family history of DM, GDM, and other chronic illnesses; DM was associated with a history of abortion, history of stillbirth, regular physical exercise, family history of DM, age, GDM, frequency of breastfeeding (Table 3).

Table 3
Cox regression output for the determinants of DM (N = 4892).

Variables	Hazard Ratio	Std. Err.	z	P > z	95% CI for HR	
					Lower	Upper
Frequency of breast feeding	0.72	0.01	-20.26	< 0.01	0.70	0.74
Age	1.04	0.00	9.86	< 0.01	1.04	1.05
Parity	1.14	0.04	4.00	< 0.01	1.07	1.21
GDM	2.53	0.22	10.89	< 0.01	2.14	2.99
Regular physical activity	0.45	0.05	-7.71	< 0.01	0.37	0.55
Family history of DM	2.04	0.15	9.43	< 0.01	1.76	2.37
History of stillbirth	1.67	0.18	4.62	< 0.01	1.34	2.07
History of abortion	2.64	0.21	12.04	< 0.01	2.25	3.09

Discussion

Gestational diabetes increases the risk of DM by 2.53 folds higher [AHR; 2.53, 95% CI: 2.14–2.99]. The progression of GDM to DM is 705/10355 person-year, if we follow 10,355 GDM women for a year, 705 women will develop DM at the end of the year. This finding agrees with finding from Sri-Lanka [12]. This is due to the linear associations of gestational diabetes mellitus and peripheral insulin resistance [13].

The risk of diabetes mellitus decreases by 28% per unit increase in the frequency of breastfeeding per 24 hours [AHR (adjusted hazard ratio); 0.72, 95% CI: 0.69–0.74]. This finding was in line with the research finding from Canada[14]. This is because of the fact that breastfeeding increases insulin sensitivity and improves glucose metabolism to women [15].

The risk of diabetes mellitus increases by 4% per year increase in the age of the women [AHR; 1.04, 95% CI: 1.03–1.05]. This finding agrees with research from the USA [16]. This is because of the fact that older age increases the resistance of insulin and impaired pancreatic islet functions [17].

A unit increase in the parity of the women increases the probability of DM by 14% [AHR; 1.14, 95% CI: 1.07–1.21]. This result agrees with evidence from China [18]. This is due to the reason that high parity is associated with higher maternal age that increases the resistance of insulin[19].

Regular physical exercise decreases the risk of DM by 2.22 folds [AHR; 0.45, 95% CI: 0.37–0.55]. This finding strengthens the previous research conclusion [20]. This is due to the effects of exercise in preventing obesity and increasing the endocrine actions of insulin [21].

The family history of DM increases the risk of acquiring DM by two folds [AHR; 2.04, 95% CI: 1.76–2.37]. This finding agrees with researcher's work from Nepal [22]. This is due to the familial tendency in insulin secretory defects [23].

Stillbirth increases the risk of DM by 67% [AHR; 1.67: 95% CI: 1.34–2.07]. This finding agrees with finding from Italy [24]. This is due to the effects of stillbirth on disturbing the normal endocrine action of women [25].

The hazard of DM increases by 2.6 folds in the presence of abortion [AHR; 2.64, 95%CI: 2.25–3.09]. The finding was in line with the expert's work from China [26]. This is due to the multi-system effects of abortion on women's health, like cardiovascular problems which finally make the women become obese and acquire insulin resistance [27].

The main limitation of this study was a failure to identify the effects of gestational diabetes on the progression of other chronic illnesses.

Conclusion

The progression of GDM to DM was very high and special follow up should be implemented for women with a history of abortion, stillbirth, and family history of DM.

Abbreviation

AHR-Adjusted hazard ratio

ANC- antenatal care

CI-Confidence interval

DM- diabetes mellitus

GDM- gestational diabetes mellitus

HbA1c- hemoglobin A 1c

HR- hazard ratio

IPAQ- International Physical Activity Questionnaire tool

Mg/dl- milligram per-deciliter

ML- Milliliter

SD-Standard deviation

SOP- standard operating procedures

WHO- World health organization

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from Bahir Dar University College of medicine and health science ethical review board with an ethical approval number of CMHS/IRB/93/2014. A support letter was obtained from the Amhara regional state health bureau. A permission letter was obtained from each hospital. Written informed consent was obtained from each study participant. Pretest and posttest counseling was given for each study participant. A study participant diagnosed with DM was linked to the chronic care.

Consent for publication

Not applicable

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interest

The authors declare that they have no competing interests.

Funding

This research work was financially supported by the University of Bahir dar and Federal democratic republic of Ethiopia ministry of health. The funder has no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Author contribution

BEF and TEF conceived the experiment; BEF, MBK, WGA, AG, and TEF performed the experiment, BEF, TEF, WGA, AAN, HAE and DA plan the data collection process, BEF, MBK, DA WGA and TEF analyzed and interpreted the data. BEF, TEF, WGA, AG, and AAN wrote the manuscript and all authors approved the final draft for publication.

Acknowledgements

We would like to acknowledge the Amhara regional state health bureau for their unreserved contribution during the field work. Our heartfelt appreciation also goes to the referral hospitals for their cooperation during the data collection process. At last not least, we would like to thanks all organizations and individuals that had an input for this work.

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Figures

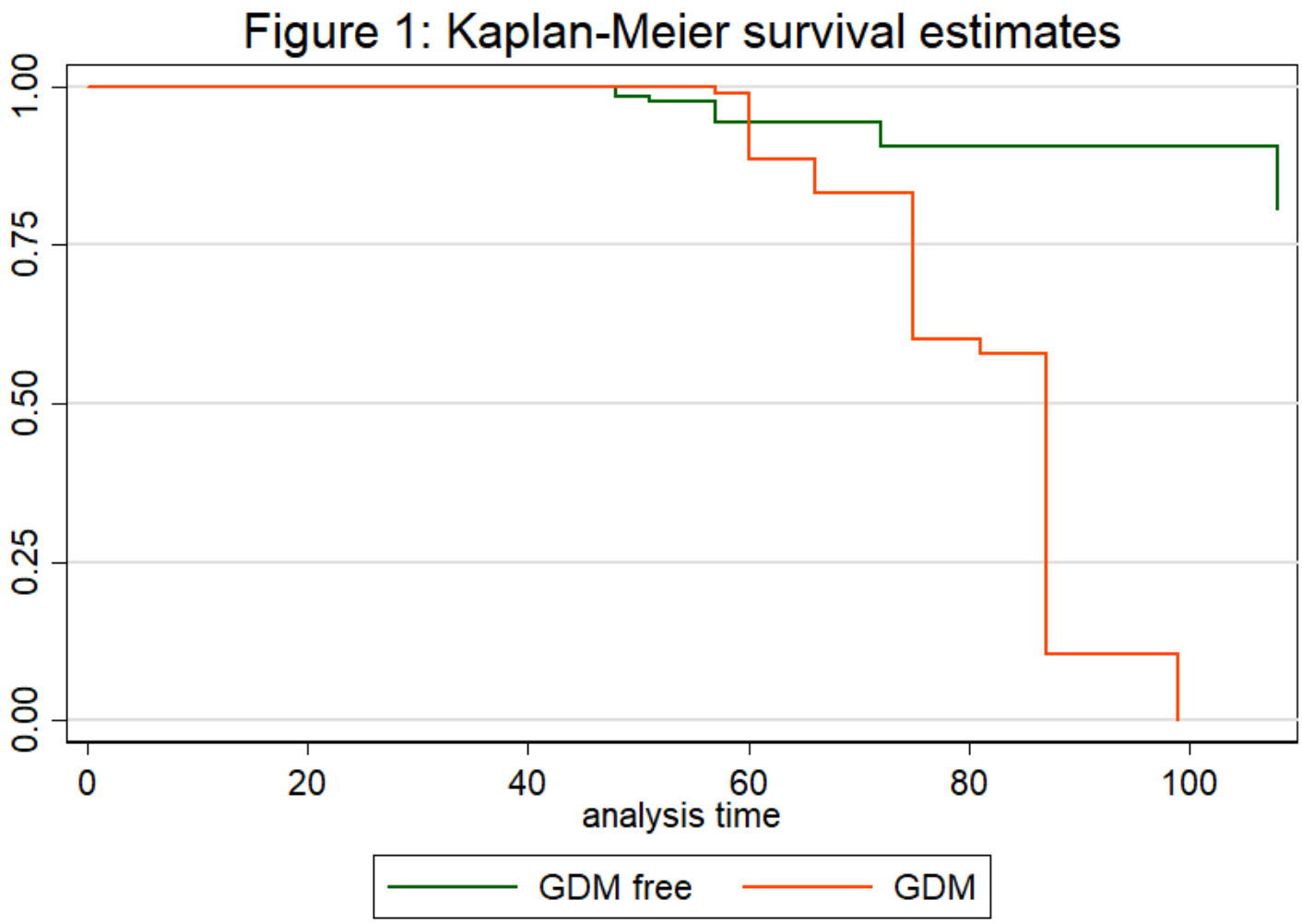

Figure 1

Kaplan Meier survival estimates

Supplementary Files

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