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Original article

Infants of Diabetic Mothers and Associated Complications in Neonatal Intensive Care Unit in Misurata Center

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ABSTRACT

Infants of diabetic mothers (IDM) are at an increased risk of various complications. The aim of this study is to evaluate the prevalence, demographic and clinical characters of IDM admissions to the neonatal intensive care unit, and the factors associated with morbidity and mortality. The study is a 1-year retrospective observational study involving all the cases of IDM admitted to the neonatal intensive care unit at Misurata. The study examined the association of the following ante- peri- and postnatal factors to the morbidity and mortality rate of IDM. A total of 103 IDM were admitted to the NICU with mother age range of 31- 35 years. About 84% of the mothers had multiple pregnancies, 81.5% of the IDM were born through C-section. 72% of the mothers had gestational diabetes. 59% of IDMs were females. Median gestational age was 36 – 38 weeks which was associated with higher mortality rate (p = 0.041) ,40% of them were post term. Macrosomia was the most common complication; 41%. About 22% had hypocalcemia and 12% had RDS. Six cases had congenital heart disease (CHD). About 26% of the cases required intravenous fluid (IVF) which had a significantly higher mortality rate (25% vs. 1.3%) (p = 0.008). IDM are at a higher risk of congenital and acquired morbidities and mortality. Delayed birth and the mode of delivery (elective or urgent C-section) are associated with the severity of the gestational diabetes which is significantly associated with higher mortality rate.

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INTRODUCTION

Infants of diabetic mothers (IDM) are newborns who are exposed to high blood glucose levels during pregnancy due to maternal diabetes [1]. This condition has significant implications for the health and development of the newborn, significantly increasing the risk of mortality and morbidity [1]. Therefore, it is a topic of great importance in epidemiology. Understanding the etiology of IDM is crucial for identifying the prevalence, risk factors, and potential interventions to improve outcomes for these infants.

Diabetes during pregnancy is a common medical condition affecting approximately 1-14% of pregnancies worldwide [2]. It can be either gestational or pre-gestational (Type 1 or type 2) [3]. The prevalence of maternal diabetes has been on the rise due to various factors such as increasing rates of obesity and sedentary lifestyles [4, 5]. This upward trend highlights the need for a deeper understanding of IDM and its associated risks on the newborn, as well as the importance of addressing obesity and promoting healthy lifestyles.

The impact of maternal diabetes on the infant's health is multifaceted. IDM are at an increased risk of macrosomia, which refers to excessive birth weight (weight >4000g) and subsequent birth trauma during delivery [6], resulting in an

increased rate of caesarian section [7]. Additionally, they are more likely to experience respiratory distress syndrome, hypoglycemia, hypocalcemia, hyperbilirubinemia [7, 8], and most importantly, they have a 3 to 4 times higher risk for congenital anomalies than other babies born to non-diabetic mothers [9]. These complications can have both short- and long-term consequences on the infant's health and development. Fortunately, these risks can be minimized by optimal maternal glycemic control before and throughout the pregnancy [10].

By studying the epidemiology of IDM, we can identify populations at higher risk, develop strategies for prevention and early detection, and implement interventions to improve outcomes for these infants. This research aims to provide descriptive data on the prevalence, demographics, and outcomes of IDM cases admitted to the NICU, emphasizing the importance of understanding the prevalence, risk factors, and potential interventions to reduce the burden of this condition.

METHODS

Setting and duration

A descriptive cross-sectional study in the neonatal intensive care unit at Misurata Teaching Hospital was conducted. The admissions records from January to December 2022 were retrospectively analyzed. Inclusion criteria includes cases admitted to the NICU at Misurata Teaching Hospital during the target study period who have been born to diabetic mothers in the records were included. Exclusion criteria were cases admitted before or after the target period, and/or those whose maternal glycemic state (Diabetic or not) was not reported or could not be verified were excluded.

Patients

During the study period 103 infants born to 103 different mothers with diabetes were identified and included in the study. This included children born to mother with gestational diabetes or pre-gestational diabetes of either types (1 or 2).

Data collection

The authors reviewed the existing records in the archives of the hospital. First, sorting through the medical records by the target year. After identifying the files of the admissions of the year 2022, the maternal and antenatal history section of each record was reviewed for the diagnosis of gestational diabetes or pre-gestational diabetes. Incomplete files were included. The complete files were selected for data collection according to a checklist that included the following variables: Maternal characteristics: age, parity, mode of delivery, type of diabetes, and mode of control. Neonatal characteristics: sex, gestational age, and birth weight were recorded, Macrosomia (defined as birthweight ≥ 4kg). Clinical findings: The Apgar score and results of a physical examination were also documented. Laboratory investigations: Hypoglycemia (≤ 35 md/dL), which is common among IDM due to hyperinsulinemia through pregnancy, Hypocalcemia (≤ 7 mg/dL), and hyperbilirubinemia (≥ 5 mg/dL). Hypocalcemia and hyperbilirubinemia are common comorbidities in IDM.

Statistical analysis

Data was initially collected in a checklist by the authors then it was entered into IBM SPSS 25 for windows for statistical analysis. Measures of central tendency and dispersion were used to describe numerical data, while frequencies and percentages were used to describe categorical data. Association between variables was tested using chi-square test (or Fischer's exact test when the cell count was not suitable) and it was considered significant at ($p < 0.05$, CI:95%).

Ethical considerations

The records were reviewed and data was collected after obtaining relevant ethical approval from Misurata Teaching Hospital's Committee of Scientific Affairs.

RESULTS

This study analyzed the monthly distribution of neonatal mortality and live births over a one-year period to identify potential trends and variations. Data revealed an average of 0.83 deaths per month (SD = 0.83) and 7.5 live births per month (SD = 5.6). Interestingly, significant fluctuations were observed throughout the year, with the lowest mortality and case count occurring in June (0 deaths, 0 cases) and the highest in February (3 deaths) and October (18 cases), respectively (Figure 1).

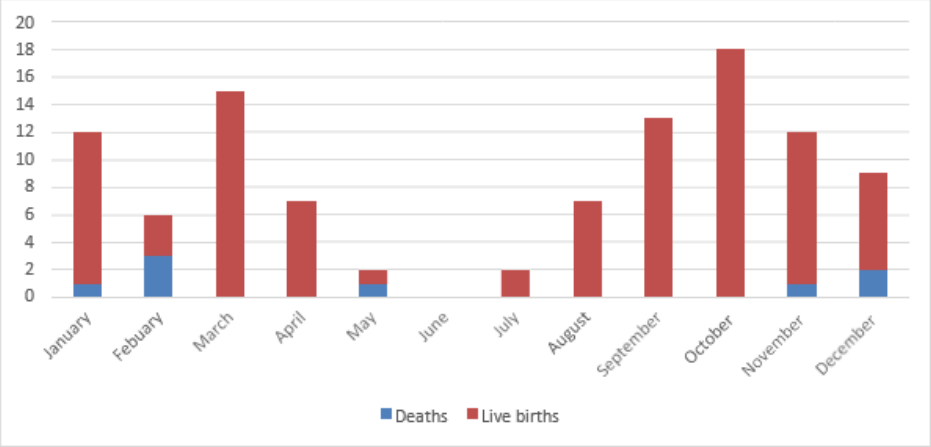

Figure 1. Case admissions per month and mortality indicated by numbers

Most of the infants were females 61 female (59%). Forty two cases were males (41%). There was no significant difference in mortality rates between males and females in the study (p = 0.91). The distribution is show in (Table 1).

Table 1. Sex distribution of the study population

Sex	Deaths	Live births	Number	Percentage (%)
Male	5	37	42	41
Female	3	58	61	59
Total	8	95	103	100

The median age group for the dataset, consisting of frequencies of different age groups, was determined to be 31-35 years. However, the greatest proportion of the mothers included in this study was 38 cases (36.9%) at the age group '36-40' years. Only two mothers (1.9%) were younger than 20 years old. There was no significant association between maternal age and infant mortality rate (p=0.45). The distribution of maternal age is given in (Figure 2).

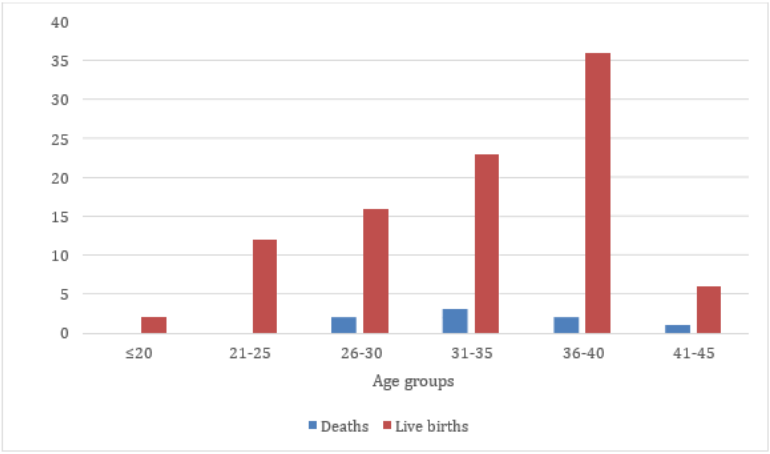

Figure 2. Distribution of the maternal age of the infants

Caesarian Section was the predominate mode of delivery in the study population was 84 cases (81.5%). Of those, 50 cases (48.5%) were elective C/S, and 34 cases (33%) were born through urgent C/S. There was no significant association between mortality and the mode of delivery (P >0.44). The details are shown in (Table 2).

Table 1. Distribution of IDM according to the mode of delivery

Mode of delivery	Deaths	Live births	Total	Percentage	P-value
NVD	1	17	18	17.5	0.44
Instrumental delivery	0	1	1	1.0	
Elective C/S	7	43	50	48.5	
Urgent C/S	0	34	34	33.0	
Total	8	95	103	100	

NVD: Normal Vaginal Delivery, C/S: Caesarian Section.

The median gestational age was between (36 – 38) weeks. The vast majority of the case were born in full- term 61 cases (59.2%). Only 1 case (<1%) was extremely pre-term (28 weeks of gestation). Gestational age was significantly associated with the infant mortality (P < 0.05) (Table 3).

Table 2. Gestational age of the IDM

Gestational age (weeks)	Deaths	Live births	Total	Percentage (%)	P- value
≤24	0	0	0	0.0	0.034
-26	0	0	0	0.0	
-28	1	0	1	1.0	
-30	0	0	0	0.0	
-32	0	2	2	1.9	
-34	0	4	4	3.9	
-36	0	19	19	18.4	
-38	5	56	61	59.2	
-40	2	12	14	13.6	
>40	0	2	2	1.9	

A very small proportion of the study population was born with a lower-than-normal birthweight 10 cases (9.7%). Nearly half the population 51 (49.5%) were born within the normal birthweight (2.5 – 3.5 kg). However, macrosomia was documented in 42 cases (40.8%). Of VLBW and LBW was significantly associated with deaths of IDM (p = 0.041). (Table 4)

Table 3. The birthweight in the IDM

Birthweight category	Deaths	Live births	Total	Percentage	P-value
VLBW	1	0	1	1.0	0.041
LBW	1	8	9	8.7	
Normal birthweight	4	47	51	49.5	
Macrosomia	2	40	42	40.8	

VLBW: Very Low Birth Weight, LBW: Low Birth Weight.

About 93.2% of the study population had an APGAR score ≥7 and only 5.8% of them have APGAR score < 7 (Table 5). The mortality rate was not significantly associated with the APGAR score (p = 0.068).

Table 5. Distribution of infants of diabetic mothers according to Appearance, Pulse, Grimace Response, Activity, Respiration (APGAR) score

APGAR score	Deaths	Live births	Total	Percentage	P-value
<7	0	6	6	5.8	0.068
≥7	8	88	96	93.2	
Unknown	0	1	1	1.0	

About 74 cases (71.8%) were hyperglycemic at the time of admission, while only 7 cases (6.8%) were hypoglycemic (Table 6). Hyperglycemic infants had a significantly higher mortality rate compared with normoglycemic patients (p = 0.011).

Table 6. Neonatal First blood sugar (mg/dL) measurement results of the study population

First blood sugar measurement (mg/dL)	Deaths	Live births	Total	Percentage	P-value
<35	2	7	9	6.8	0.011
35-45	0	14	14	13.6	
>45	6	74	80	71.8	

The use of IVF was significantly associated with mortality in this study (p = 0.008). However, only 26.2 of the study population required intravenous fluids (IVF) control. Most of the study population didn't require IVF 73.8% (Table 7).

Table 4. Distribution of infants of diabetic mothers who required IVF during admission

IVF replacement	Deaths	Live births	Total	Percentage	P-value
Used	7	20	27	26.2	0.008
Not used	1	75	76	73.8	

IVF: Intra-venous Fluid

Table 8 lists the complications and comorbidities, hypercalcemia and RDS were associated with the highest number of deaths, with 3 deaths each, representing 13.0% and 23.1% mortality rates within those groups, respectively. Notably, no deaths were recorded among neonates diagnosed with ASD, PDA, TR, hyperbilirubinemia, neonatal sepsis, or TTN.

Table 8. Neonatal complications and associated comorbidities among infants of diabetic mothers.

Complications	Number (number of deaths)
ASD	3
PDA	2
TR	1
Hyperbilirubinemia	4
Hypercalcemia	23 (3)
RDS	13 (3)
Neonatal sepsis	5
TTN	3

ASD: *Atrial Septum* Defect, ***PDA:*** *Patent Ductus Arteriosus,* ***TR:*** *Tricuspid Regurgitation,* ***RDS:*** *Respiratory Distress Syndrome,* ***TTN:*** *Transient Tachypnea of the New Born*

Out of the total 103 cases, the Chronic DM group accounted for 30 cases. Among these, 1 case (1%) resulted in death, while 25 cases (24.3%) had live births, with the remaining cases being classified under insulin and OHG treatments. The OHG treatment group consisted of 4 cases (3.9%) with live births and no reported deaths. Diet Control showed no reported deaths or live births among the chronic DM cases.

For Gestational DM, there were a total of 73 cases. Among these, 17 cases (16.5%) resulted in live births, while 7 cases (6.8%) resulted in deaths. Insulin treatment accounted for 14 live births (13.6%) and 3 deaths (2.9%). OHG treatment resulted in 20 live births (19.4%) and 1 death (1%). Diet Control had the highest number of live births, with 32 cases (31.1%) and 3 deaths (2.9%) (Table 9).

Table 9. Distribution of IDMs according to the type of DM and the used treatment

Type of DM	Treatment	Deaths	Live births	Total
Chronic	Insulin	1	25	26
	OHG	0	4	4
	Diet control	0	0	0
Gestational	Insulin	3	14	17
	OHG	1	20	21
	Diet control	3	32	35

DM: Diabetes Mellitus, OHG: Oral Hypo-Glycemic agents

In the Other Chronic Diseases category, there were a total of 6 cases. Among these, 5 cases (4.9%) were associated with HTN and resulted in live births, while 1 case (1%) was associated with Hypothyroidism and also resulted in a live birth. No deaths were reported in either category (Table 9).

Mothers with higher parities (1-5 or >5) have significantly higher live birth rates (74 and 11, respectively), they also experience no deaths, suggesting potential protective effects. Conversely, the P0 PG group exhibits the highest death rate (20%) despite still experiencing live births (8). This finding highlights the need for further investigation, particularly focusing on P0 PG>1, which demonstrates successful pregnancies after initial complications (2 live births and 0 deaths) (Table 10).

Table 10. Parity distribution of IDMs

Parity	Deaths	Live births	Total
P0 PG	2	8	10
P0 PG>1	0	2	12
1-5	6	74	80
>5	0	11	11

DISCUSSION

During the study period, 103 IDMs were admitted to the NICU. This finding closely parallels the outcomes of a similar study conducted in 2015 [11]. It is noteworthy that the prevalence of IDM has remained somewhat stable over the past four decades, as evidenced by earlier study [12] that was conducted from 1984 to 1991 [12]. The study reported 988 cases of gestational diabetes [12]. Additionally, a more recent study in the city of Benghazi, was conducted over a year-long period, documented a prevalence of 120 cases of IDMs [13].

This study identified gestational diabetes as the most common cause of diabetes in IDMs, consistent with all the previous studies mentioned above [11-13]. Notably, the study also identified several chronic conditions with established associations with diabetes mellitus (DM), such as hypertension (HTN) [14] and hyperthyroidism [15].

The impact of maternal diabetes type and glycemic control methods on IDM mortality and morbidity falls outside the scope of this present study [16, 17]. Nonetheless, it's worth noting that our findings indicated a lower mortality rate among infants born to mothers with chronic diabetes compared to those born to mothers with gestational diabetes. This association could potentially be incidental, as previous studies have shown that infants born to mothers with gestational diabetes have lower morbidity and mortality rates [16,17].

The median age group for the study participants was 31-35 years old; however, the largest proportion of mothers included in the study fell within the 36-40 age range (38 cases, 36.9%). Only two mothers (1.9%) were younger than 20 years old. While no significant association between maternal age and infant mortality rate was observed (p=0.45), the relatively small sample size could potentially mask the actual association. Large-scale epidemiological studies have previously demonstrated a direct correlation between maternal age and the risk of gestational diabetes [18].

Most IDMs in the study were females (59%) [19, 20]. This difference was not associated with a significant difference of morbidity or mortality. This finding aligns with existing literature, which suggests that fetal sex does not influence outcomes for births of diabetic mothers, regardless of whether the diabetes is pre-gestational or gestational [19, 20].

Caesarean section (C/S) was the predominant mode of delivery in the study population, with 84 cases (81.5%) delivered by C/S [21]. Among these, 50 cases (48.5%) were elective C/Ss, while 34 cases (33%) were urgent C/Ss. Notably, only 18 cases (17%) were delivered through vaginal delivery (NVD). The C/S rate in this study exceeds the international standard set by the World Health Organization (WHO) for pregnant women in general (diabetic and non-diabetic) [21]. This discrepancy suggests that not all C/Ss in the study population were necessarily related to the maternal glycemic state or diabetes, particularly considering the high proportion of elective C/Ss (50 cases). This hypothesis is further supported by the relatively lower C/S rates observed in dedicated studies on diabetic mothers [21].

Despite the median gestational age in the present study falling within the full-term range, the study population largely skewed towards the upper limit of normal gestational age. Post-term deliveries were significantly more common than pre-term or premature deliveries. These findings mirror those of Farooq et al., who investigated the maternal and fetal effects of gestational diabetes [27].

The vast majority of mothers in the study were multiparous (around 80%). Notably, multiparous mothers also exhibited the highest mortality rate compared to other parity categories [22]. The association between multiple pregnancies and gestational diabetes is well-established, not only in terms of incidence but also in terms of severity [22]. The larger placental mass associated with multiple pregnancies potentially amplifies the placenta's diabetogenic effect, consequently increasing the likelihood and severity of gestational diabetes [22].

Similar to the findings for gestational age, the birthweight of IDMs in this study primarily fell within the normal birthweight range (49.5%), largely concentrated near the upper limit. Macrosomia was not uncommon (40.8%), but interestingly, lower birth weights were significantly associated with higher mortality rates. This finding diverges from the study by Yogev et al., who observed a higher risk of both short-term and long-term complications, including increased morbidity and mortality rates, in infants born to mothers with gestational diabetes mellitus (GDM) compared to infants born to non-diabetic mothers [23].

In the present study, the most common complications observed in IDMs were macrosomia (40.8%), followed by hypocalcemia (22%), respiratory distress syndrome (RDS) (13%), hypoglycemia (9.8%), congenital heart anomalies (CHD) (6%), transient tachypnea of the newborn (TTN) (3%), and hyperbilirubinemia (4%) [11, 24, 25, 26]. These rates differ slightly from a similar study conducted in 2015, which reported higher rates of several complications [11].

The observed RDS and TTN rates are consistent with the high C/S rate seen in this study (81.5%), as C/S is a known risk factor for these complications [24]. Additionally, the 22% RDS rate aligns with findings from other studies [22-23]. RDS is further recognized as an indicator of poor glycemic control [24]. The slightly lower TTN rate compared to previous studies (8.6%) reported by Salima might be due to differences in study populations or methodologies.

Hypocalcemia was observed in a significant proportion of IDMs in this study (22%), possibly due to parathyroid hormone disturbances associated with diabetes [25]. Notably, the rate of neonatal jaundice (4%) was considerably lower than reported in similar studies, such as Opara et al. who found a prevalence of 63.8% [22, 26]. This discrepancy could be related to specific regional factors or differences in screening and diagnosing hyperbilirubinemia, which is known to be more frequent in macrosomic IDMs [22].

Finally, 26.2% of IDMs in this study required intravenous fluid (IVF) replacement, and these infants had a significantly higher mortality rate (26%) compared to those who did not require IVF (1.3%) ($p = 0.008$). This finding suggests that the need for IVF is a strong indicator of the severity of the infants' condition and could potentially be linked to poorly controlled diabetes during pregnancy.

CONCLUSION

The outcome of pregnancy and neonatal effects on IDMs is associated with both more infant morbidity and mortality rates. Ante- and perinatal factors like hypocalcemia, CHD, Macrosomia and hyperbilirubinemia are directly associated with higher mortality rates. Other factors are associated indirectly with gestational diabetes like RDS, and TTN as they are more common among IDMs because of the higher rate of C/S. The national data on the subject are very limited and efforts must be coordinated between multiple centers to lay the framework for further studies with more sophisticated designs to explore the demographic and epidemiological characters of IDMs.

Conflicts of Interest

The authors declare no conflicts of interest.

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أطفال الأمهات المصابات بالسكري والمضاعفات المصاحبة له في وحدة العناية المركزة لحديثي الولادة بمركز مصراتة

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قسم طب الأطفال وحديثي الولادة، كلية الطب، جامعة مصراتة، مصراتة، ليبيا

المستخلص

الأطفال حديثي الولادة لأمهات مصابات بالسكري معرضون لخطر متزايد للإصابة بمضاعفات مختلفة. يهدف هذا البحث إلى تقييم معدل الانتشار والخصائص الديموغرافية والكلينيكية لقبول حديثي الولادة لأمهات مصابات بالسكري في وحدة العناية المركزة لحديثي الولادة والعوامل المرتبطة بالمرض والوفيات. هذه دراسة استرجاعية لمدة عام تشمل جميع حالات حديثي الولادة لأمهات مصابات بالسكري المقبولة في وحدة العناية المركزة لحديثي الولادة في مصراتة. بفحص الدراسة العلاقة بين ما يلي:العوامل ما قبل والولادة وبعد الولادة معدل المراض والوفيات لدى حديثي الولادة لأمهات مصابات بالسكري. خلال فترة الدراسة، تم إدخال 103 حديثي الولادة لأمهات مصابات بالسكري إلى وحدة العناية المركزة لحديثي الولادة تتراوح أعمار أمهاتهن بين 31 و 35 عامًا. حوالي 84٪ من الأمهات لديهن حالات حمل متعددة ، و 81.5٪ من حديثي الولادة لأمهات مصابات بالسكري ولدن من خلال عملية قيصرية. 72٪ من الأمهات مصابات بسكري الحمل. 59٪ من حديثي الولادة لأمهات مصابات بالسكري من الإناث. متوسط عمر الحمل '36 - 38' أسبوعًا والذي ارتبط بمعدل وفيات أعلى (ص = 0.041). 40٪ منهم ولدوا بعد الموعد. تضخم المشيمة هو أكثر المضاعفات شيوعًا لهذه الحالة بنسبة 41٪. 22٪ يعانون من نقص كالسيوم الدم و 12٪ يعانون من متلازمة الضائقة التنفسية لدى حديثي الولادة. 6 حالات مصابة بعيوب خلقية بالقلب. 26٪ من الحالات احتاجت إلى استبدال السوائل الوريدية والذي كان له معدل وفيات أعلى بكثير (25٪ مقابل 1.3٪) (ص = 0.008). الأطفال حديثي الولادة لأمهات مصابات بالسكري معرضون لخطر أكبر للإصابة بأمراض ومضاعفات خلقية ومكتسبة والوفيات. يرتبط تأخر الولادة وطريقة الولادة (عملية قيصرية اختيارية أو طارئة) بشدة سكري الحمل الذي يرتبط ارتباطًا وثيقًا بمعدل وفيات أعلى.

الكلمات الدالة. الرضع والأمهات المصابات بالسكري، وحدة العناية المركزة لحديثي الولادة، مصراتة.