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ORIGINAL ARTICLE

Efficacy of antepartum fetal surveillance for stillbirth prevention

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ABSTRACT

Objective: In 2019 the American College of Obstetricians and Gynecologists (ACOG) issued specific recommendations for performance of antepartum fetal surveillance (AFS) based on individual risk factors. As similar recommendations were already in place at our institution, we have evaluated the impact of AFS on stillbirth (SB) occurrence in a 5-year cohort.

Methods: Retrospective cohort study of all deliveries between 7/1/2013 and 6/30/2018. Excluded were multiples, anomalous fetuses or newborns, and deliveries before 32 0/7 weeks' gestation. AFS was conducted from 32 weeks with a modified biophysical profile, with a complete biophysical profile as back-up for non-reactive non-stress tests. All cases of SB were prospectively identified and individually reviewed to verify the presence of risk factors, the results of fetal testing if done, and calculate the interval between last fetal test and delivery. The electronic medical records during the study period were queried to identify women who underwent AFS and those who did not. Chi-square was used to compare the rates of SB between the two groups.

Results: 16,827 women fulfilled the study inclusion and exclusion criteria, 5711 (34%) had risk factors which prompted AFS; 37% had 2 or more risk factors. SB occurred in 1.8‰ of them (10/5711) (3 had 1 risk factor, 5 had 2, and 2 had 3 risk factors). Rates of SB at ≥32.0 weeks were similar between women who had AFS and those who did not (1.8 vs. 2.3‰, $p=0.51$, OR = 0.75, 95%CI 0.36–1.55). The false-negative rate at <7 days of a reassuring AFS among compliant women was 1.4‰ (8/5711). Rates of preterm delivery were similar in the tested vs untested population (6.5 vs. 6.0%, $p=0.22$).

Conclusion: Implementation of AFS in women with risk factors similar to those recommended by the ACOG may lower the risk of SB from 32 weeks to that of low-risk pregnancies.

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Antepartum fetal surveillance; stillbirth; non-stress test; biophysical profile; risk factors

Introduction

Antepartum fetal surveillance (AFS) is recommended to reduce the risk of stillbirth in pregnancies with risk factors for fetal death. This recommendation is based on the consideration that fetal hypoxia and acidosis, which represent the final common pathway to fetal death in most high-risk pregnancies, may result in changes in amniotic fluid volume, fetal movements, and fetal heart rate characteristics, which can be detected by AFS. However, there is a paucity of evidence on the efficacy of AFS because of the challenges in conducting prospective trials in pregnancies at high risk for stillbirth. As a result, such evidence is largely circumstantial and is based on studies conducted more than 30 years ago, which showed that the rates of fetal death in tested populations were lower than the rates in women with untested contemporaneous pregnancies from the same institutions, or in women with pregnancies with similar complications managed prior to the advent of currently used techniques of AFS [1–4].

However, the indications for AFS have changed significantly over the past 20 years, due to the identification of risk factors previously unknown (e.g. maternal obesity; conception by in-vitro fertilization; advanced maternal age) [5,6]. AFS carries increased use of health care resources and it does not come without risks: false-positive findings at AFS may result in parental anxiety and may increase unnecessary interventions,

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such as premature or operative birth [7]. Therefore a fresh look at benefits and risks of AFS is needed.

In 2021, the American College of Obstetrics and Gynecology (ACOG) issued for the first time recommendations for AFS based on individual risk factors [5]. Evidence of benefits of AFS in its current form would thus be desirable. Since we had already implemented AFS for indications similar to those promoted by ACOG guidelines in our obstetric population, we have evaluated whether patients who receive AFS have a risk of stillbirth similar to a lower risk population not receiving AFS.

Materials and methods

All pregnant women who delivered at Inova Alexandria Hospital over a 5-year period (from 1 July 2013 to 30 June 2018) and had AFS at the Antenatal Testing Center of Inova Alexandria Hospital were included in the study. 1 July 2013 was chosen as initial date for the study because it coincided with the introduction of electronic medical records at the Institution. Deliveries from the second half of 2018 were excluded because the large randomized clinical trial ARRIVE published in August 2018 [8] led to official recommendations by the Society for Maternal Fetal Medicine that delivery at 39 weeks could be considered, even in low-risk pregnancies [8]. As such recommendations were implemented at our Institution, the stillbirth rate could have been affected as delivery would have eliminated the risk of stillbirth in ongoing pregnancies.

Excluded were twins and other multiples ($n = 395$), anomalous fetuses or newborns (two cases of anencephaly, one trisomy 13, two trisomy 18, and one with known severe diaphragmatic hernia), deliveries before 32 0/7 weeks' gestation, or occurring outside of our institution. Based on official recommendations and large clinical studies, AFS was initiated at or after 32 0/7 weeks of gestation, with sporadic exceptions (early and severe fetal growth restriction (FGR); early hypertensive disorders of pregnancy; antiphospholipid syndrome with prior poor obstetric history; and pregestational diabetes mellitus White class R).

AFS was conducted with a modified biophysical profile (i.e. non-stress test and sonographic documentation of maximum vertical pocket of amniotic fluid). All women undergoing AFS also underwent a fetal biometry scan if not done within the previous 4 weeks. Non-reassuring findings at AFS (i.e. non-reactive non-stress test or maximum vertical pocket of amniotic fluid ≤2 cm) prompted the performance of a complete biophysical profile (BPP) or admission to the Labor and Delivery unit for prolonged monitoring, contraction stress test or delivery, depending on the findings and gestational age. Interpretation of AFS and subsequent management recommendations were done by certified Maternal Fetal Medicine specialists. The indications for AFS are presented in Appendix Table A1 and they closely mirrored those recommended by ACOG [5] with the following differences: in our center obesity was an indication for AFS if body mass index (BMI) was ≥40 rather than ≥35; maternal age >40 years was an indication for AFS from 32 weeks and between 35 and 40 years AFS was offered starting at 36 weeks based on the evidence available at the time [9]. Frequency of testing was weekly, with the exception of gestational cholestasis, FGR with abnormal umbilical artery Doppler results, preeclampsia, poorly controlled gestational or pregestational diabetes mellitus, and mild oligohydramnios (amniotic fluid index <5 cm but maximum vertical pocket of fluid >2 cm), for which testing was repeated twice weekly.

All pregnancies resulting in stillbirth at ≥32 weeks and fulfilling the study inclusion criteria were identified from a prospectively-collected database of Obstetric Safety at our Institution; they were individually reviewed to verify whether they had undergone AFS. Electronic medical records (EPIC, Epic Systems Corporation) were queried using the Splicer-Dicer function to identify bulk data on the total number of women who delivered at ≥32 weeks and underwent AFS at the Antenatal Testing Center during the study period, as well the total number of women who delivered at ≥32 weeks and did not undergo AFS during the same period. Only women who underwent scheduled AFS at our Antenatal Testing Center were included in the cohort with AFS so as to exclude fetal testing done for obstetric emergencies or other indications in Labor and Delivery. Perinatal mortality was defined as the sum of stillbirths at ≥32 weeks and of neonatal deaths to hospital discharge.

Statistical analysis: Observed rates of stillbirths among women with high-risk conditions who underwent AFS and delivered at ≥32 weeks were compared with the similar rates among women who did not undergo AFS using Chi square. Among women who underwent AFS and experienced stillbirth, the interval from fetal testing and stillbirth was calculated. The distribution of stillbirths was compared between the first and second half of the study period to assess potential temporal variations. A p value <0.05 or an odds ratio (OR) with 95% confidence interval (CI) not inclusive of the unity were considered significant.

The study was approved by the Institutional Review Board (IRB) committee (study # U23-05-5075).

Results

A total of 17,663 women delivered during the study period; of them, 16,827 fulfilled the study inclusion and exclusion criteria and delivered at ≥32 weeks. AFS was implemented in 5711 of them (33.9%), whereas it was not in the remaining 11,116. The median number of AFS tests per patient was 3 (range: 1–17), the mean ± standard deviation (SD) was 3.5 ± 2.3. Table 1 displays the most common principal diagnoses as indications for AFS. Two indications for testing were present in 18.7% of women (1067/5711) and three or more indications in 14.4% (822/5711).

Table 2 displays the population characteristics in relation to whether AFS was done or not. As expected, women in the AFS group were older than those who did not undergo AFS. Of the 883 women ≥40 years of age at delivery, 87% underwent AFS; among the 3677 women between 35 and 40 years of age, 2486 (67.6%) accepted fetal surveillance. Women in the AFS group delivered at an earlier gestational age and had higher rates of cesarean delivery (OR = 1.6, 95% CI 1.5–1.7). Although gestational age at delivery was significantly different between the women who underwent AFS vs those who did not, the difference was clinically insignificant (2 days); moreover, rates of preterm delivery (between 32.0 and 36.6 weeks' gestation) were similar in the tested vs untested population (6.5% or 371/5711 vs. 6.0% or 669/11,116, $p = 0.22$) (Table 2). Neonates born from high-risk pregnancies undergoing AFS had a longer hospital stay (2.8 ± 2.8 vs. 2.5 ± 2.6 days, $p < 0.001$).

Stillbirths occurred in 10/5711 of the women who underwent AFS (1.8‰) and in 26/11,116 (2.3‰) of those who delivered at ≥32 weeks and did not undergo fetal testing. The difference in rates of stillbirth between the two groups was not statistically significant ($p = 0.51$, OR = 0.75, 95% CI 0.36–1.55). Women who experienced stillbirth despite AFS were older than those who did not undergo AFS and had a stillbirth (36.1 ± 4.9 vs. 31.6 ± 4.9 years, $p = 0.019$), but had similar gestational age at delivery (37.7 ± 2.3 vs. 36.4 ± 2.2 weeks, $p = 0.13$). Among the 10 patients with stillbirths despite AFS, 5 (50%) had only 1 risk factor, 3 had 2, and 2 had 3 risk factors (Table 3). The rate of multiple risk factors was similar in women with stillbirth despite AFS as in the remaining women in the AFS group (33.3 or 3/10 vs. 33.1% or 1886/5701, $p = 0.84$Among women who experienced stillbirths despite AFS, fetal deaths occurred at <7 days in 9/10 cases, with a median interval from the last normal test to the diagnosis of fetal death of 4 days (Table 3). Moreover, one of the fetal deaths (case #7) occurred in a patient with suboptimally controlled diabetes mellitus on oral hypoglycemic agent who refused intervention for delivery. Thus the false-negative rate at <7 days of reassuring AFS among compliant women was 1.4‰ (8/5711). Table 4 displays the characteristics of the women who did not undergo AFS and experienced a stillbirth.

The distribution of stillbirths was similar in the first vs second half of the study period in both groups (Table 5).

Table 1. First indications for antenatal fetal surveillance.

Indication	No of women tested	%
Advanced maternal age	2124	37.1
Poor obstetric hystory[a]	470	8.2
Obesity body mass index ≥40	429	7.5
Post term pregnancy	357	6.2
Fetal growth restriction	300	5.2
Hypertensive disorders	215	3.7
Gestational diabetes (on medications or poorly controlled)	208	3.6
Decreased fetal movement	181	3.1
Cord anomalies[b]	150	2.6
Amniotic fluid abnormalities[c]	142	2.4
Other indications	1270	22.2
Total	5711	100

[a]>1 If abruption, preterm delivery, fetal growth restriction, preeclampsia; 1 if stillbirth, cerebral palsy or neonatal encephalopathy. [b]Single umbilical artery, velamentous or marginal cord insertion. [c]Oligohydramnios or polyhydramnios.

Table 2. Population characteristics in relation to antenatal fetal surveillance (AFS).

Variable	AFS yes ($n = 5711$)	AFS no ($n = 11,116$)	p Value
Maternal age (years)	34.6 ± 5.5	30.2 ± 4.7	<0.001
Maternal age ≥40	769 (13.5%)	114 (1.02%)	
Gestational age at delivery (days)	273 ± 10	275 ± 10	<0.001
Delivery before 37.0 weeks	371 (6.5%)	669 (6.01%)	0.22
Mode of delivery			
Vaginal spontaneous	2964 (51.9%)	7011 (63.1%)	
Vaginal assisted	112 (1.96%)	241 (2.2%)	
Cesarean	2635 (46.1%)	3863 (34.7%)	<0.001
Baby length of hospital stay (days)	2.75 ± 2.8	2.51 ± 2.6	<0.001
Neonatal demise[a]	0	4 (0.04%)	0.15
Perinatal mortality[b]	9 (0.16%)	31 (0.28%)	0.12

[a]Four neonatal demises in the non-AFS group were due to severe metabolic acidosis secondary to abruption ($n = 1$), shoulder dystocia ($n = 2$), and hypoxic ischemic encephalopathy ($n = 1$). [b]Included cases of stillbirth and neonatal demise within one week of life.

Discussion

We have found that the risk of stillbirth in women at risk undergoing AFS is similar to that of low-risk pregnancies not undergoing AFS. Our findings provide support for the efficacy of the ACOG recommendations [5]: the criteria for initiation of AFS (≥32 weeks) and frequency of testing (weekly in the majority of cases) in our study closely reflected the recommendations of the recent ACOG guidelines for AFS [5]. Moreover, the

Table 3. Stillbirths among cases undergoing antenatal fetal surveillance (AFS).

Case #	Weeks at delivery	Indications for AFS	NST	BPP	Interval between last normal test and fetal death	Clinical findings at delivery.
1	40.3	Maternal age 39 years	NR	8/10	3 Days	Birth weight 4315 g.
2	37.3	Maternal age 41 years; high hCG (4.0 MoM) and inhibin A (13.35 MoM) at genetic screening test	R	NP	3 Days	Birth weight 3020 g. Preeclampsia diagnosed on admission for delivery.
3	34.4	Maternal age 38 years; IDDM; Gestational HTN	R	NP	7 Days	Birth weight 2760 g. Diabetic ketoacidosis on admission (preceded by nausea and vomiting for 5 days).
4	36.1	Maternal age 41 years; gestational HTN; Persistent DFM	R	8/10	4 Days	Birth weight 2840 g.
5	38.6	GDM on Glyburide	R	10/10	5 Days	Birth weight 3005 g.
6	34.2	Maternal age 35 years; history of stillbirth	R	10/10	4 Days	Birth weight 2865 g.
7	39.4	GDM on insulin	NR	8/10	5 Days	Birth weight 4450 g. Gestational HTN diagnosed on admission.
8	39.4	IVF	R	NP	4 Day	Birth weight: 3374 g.
9	40.5	Post term	R	NP	2 Days	Birth weight: 3210 g.
10	36.6	Maternal age 42 years; IVF	R	NP	1 Day	Birth weight: 2520 g. Massive abruption on admission.

Abbreviations BPP, biophysical profile; DFM: decreased fetal movements; GDM: gestational diabetes mellitus; hCG: human chorionic gonadotropin; HTN: hypertension; IDDM: insulin-dependent diabetes mellitus; IVF: *in vitro* fertilization; MoM: multiples of median; NR: non reassuring; NST: non-stress test; R: reactive. NP: Not performed.

Table 4. Stillbirths among cases not undergoing antenatal fetal surveillance.

Case #	Weeks at delivery	Risk factors for stillbirths	Birth weight (g)	Clinical findings at delivery
1	36.1	None	2270	None
2	35	None	2460	Gestational HTN
3	33.1	None	1800	None
4	35.1	None	1490	Fetal growth restriction
5	36.6	Maternal age 38 years. BMI 40.	3735	None
6	32.4	None	2140	Abruption; severe preeclampsia
7	35.4	None	2183	None
8	33	Maternal age 40 years	2400	None
9	39.3	BMI 40	3062	None
10	37.2	GDM on oral medications	3340	Declined AFS
11	32.4	None	1200	Fetal growth restriction
12	35.6	Maternal age 40 years	1530	Fetal growth restriction; declined AFS
13	37.6	None	3331	None
14	39.2	None	3120	Preeclampsia. True knot in umbilical cord.
15	40.6	Post-term	3827	None
16	41	Post-term	4544	None
17	37.2	None	2330	Severe preeclampsia. Hydrops.
18	37.6	None	3270	Velamentous cord insertion
19	36.4	History of abruption	2375	Massive abruption
20	37.4	None	2600	None
21	36.6	Maternal age 36 years	2460	True knot in the cord
22	36.3	None	2665	Severe preeclampsia
23	34.1	None	1420	Fetal growth restriction; no prenatal care
24	36.1	None	2800	None
25	37.4	None	2250	Fetal growth restriction
26	36.6	Maternal age 37 years, IVF	2520	Massive abruption. DIC

Abbreviations AFS, antepartum fetal surveillance; BMI: body mass index; GDM: gestational diabetes mellitus; DIC: disseminated intravascular coagulation; HTN: hypertension.

indications for AFS closely mirrored those recommended by ACOG, with the exception of obesity, which was an indication for AFS in our series if BMI was ≥40 whereas ACOG recommends AFS for BMI ≥35 [5]. Women who did not undergo AFS were predominantly at low risk for stillbirth, with the exception of those with BMI between 35 and 40, who did not undergo AFS at our center. Our findings should assuage the concern about the lack of evidence linking fetal testing for the recently expanded indications to improved outcomes [10].

Our study covered a 5-year period, starting with the date when electronic medical records were introduced at our facility and ending in mid-2018, when induction of labor at 39 weeks became an option, particularly for women with risk factors for stillbirth. The large number of aggregate data had adequate numerosity to allow the analyses for this study, whereas inclusion of pregnancies after 2018 would have suffered from the presence of an important confounder, as elective delivery at 39 weeks would have inevitably lowered the risk of stillbirth.

Table 5. Distribution of stillbirth cases in the first half vs second half of the study period.

Study interval	Stillbirths among AFS patients	Stillbirths among non-AFS patients	*p* Value
From 7/1/2013 to 12/30/2015	6/2584	14/6161	0.96
From 1/1/2016 to 6/30/2018	4/3127	12/4955	0.26
p Value	0.35	0.87	

It should be noted that some women in the non-AFS group had risk factors: for example, 1% of them were 40 years of age or older at delivery. Lack of AFS in such patients could have been due to a variety of reasons, such as geographic distance from our testing center, patient preference, time constraints or costs. However, even after removing such cases, the difference in stillbirth between those who underwent AFS vs those who did not remained statistically insignificant.

Our false negative rate (i.e. occurrence of stillbirth within 7 days of AFS in women with non-malformed singleton fetuses at ≥32 weeks) was 1.57‰, which is comparable to that reported in previous studies on AFS using the modified BPP, with false negative rates of 0.6‰ or 1/1753 [2,3], and 1.3‰ or 21/15,842 [4]. Previous studies excluded women non-compliant with recommendations of care; using the same criterion, our false negative rate would be lower (1.4‰). The efficacy of AFS with modified BPP is also similar to that of a complete BPP, which has a false negative rate of 0.6‰ or 8/12,620 [11].

The above comparisons have several limitations: the characteristics of the study populations and the indications for AFS have greatly changed in the decades since the publication of the initial studies on AFS. Of interest, the top 3 indications in our series (advanced maternal age, poor obstetric history, and maternal obesity) were not even listed as indications in older series since they had not been identified as risk factors for fetal death [3,4]. Not surprisingly, the rate of women considered at risk for stillbirth and undergoing AFS was higher in our series (34%) than in older series (e.g. 23%) [4]. Moreover, management of some at-risk conditions has changed over the decades: for example, umbilical artery Doppler is now standard of care in the monitoring and management of FGR, but it was not decades ago, and anticipation of delivery in several high-risk conditions is now recommended [12]. These considerations emphasize the importance of a contemporary series such as ours on AFS.

A common concern is that institution of AFS may results in adverse obstetric or neonatal outcomes due to the inevitable occurrence of false positive results (i.e. non-reassuring fetal testing) requiring additional testing or leading to obstetric interventions including induction of labor or cesarean delivery. The retrospective nature of our study and the retrieval of bulk data did not allow us to identify the rates of iatrogenic induction of labor or cesarean delivery due to non-reassuring AFS. In our study the rates of cesarean delivery were significantly higher in women undergoing AFS compared with the untested population; however, most risk factors for stillbirth are also known risk factors for cesarean delivery and for medically indicated delivery. More importantly, the gestational age at delivery was clinically similar (2 days difference) and the rates of preterm delivery were not different between the tested and untested population. This suggests that AFS does not increase iatrogenic preterm birth, with related neonatal morbidity. The risks of iatrogenic prematurity were minimized in our study by the implementation of a cascade of fetal surveillance tests in the presence of non-reassuring AFS in the preterm period: non-reactive non-stress tests at a modified BPP were followed by a complete BPP, contraction stress-test, or hospital admission for prolonged monitoring. Maternal Fetal Medicine specialists interpreted all the tests results and made recommendations for management and timing of delivery. Our results cannot be generalized to centers in which fetal surveillance is offered by providers other than MFM specialists. Not only did AFS not adversely affect overall prematurity, but it did not seem to impact meaningfully the neonatal outcome. Neonatal stay was prolonged by only 0.3 days, which could reflect the tendency by the obstetric providers to delay the newborn discharges in cases of cesarean deliveries.

A valuable clinical implication of our findings is that it offers an alternative to induction of labor particularly in pregnancies with risk factors that do not include medical indications for late-preterm and early term deliveries [12]. Whereas an initial randomized clinical trial suggested that anticipation of delivery to 39 weeks could lower the risks of perinatal death even in low risk women [13], more recent epidemiologic evidence has shown that the results of the initial trial may not translate into the "real world" (i.e. not the controlled environment of a trial) [14]. Such a lack of generalizability should better inform clinical decision-making and patient counseling.

It should be noted that AFS cannot represent a panacea to prevent all stillbirths: some SB may occur despite AFS and over half of SB occur before 28 weeks (according to the latest data from the National Center for Health Statistics) [15] i.e. at gestational ages in which AFS is not recommended except for rare indications.

Prospective studies are needed to assess the effects of false positive findings at AFS, such as need for additional testing, induction of labor, or other obstetric interventions.

As the most common cause of stillbirths at or near term is fetal hypoxia, most likely related to placental senescence [16]. Future studies should evaluate whether the addition of placental biomarkers may increase the detection of placental dysfunction and thus be incorporated into protocols of AFS to reduce the risk of term stillbirths [17]. Studies are also needed on the cost-benefit analysis of AFS for prevention of stillbirth.

A strength of our study is represented by the large sample size of the study population, which was assessed in single institution with a rigorous application of a shared, standardized protocol for AFS. The accuracy of the EPIC Splicer-Dicer function for the selection of study patient has not been tested. In order to verify its accuracy, we compared the cases of stillbirths identified using the Splicer-Dicer function of EPIC with the list of stillbirths which had been prospectively collected during the study period by the Institutional Obstetric Safety Committee: 3/34 (8.8%) cases had been incorrectly assigned by Splicer-Dicer as not having had AFS whereas they had undergone AFS, whereas there were no cases assigned to the AFS group which did not have AFS. This suggests that the EPIC Splicer-Dicer function had an approximate accuracy of 90%. Another limitation of our study is that some of the women who did not undergo AFS could have had risk factors for stillbirth. Given the retrospective nature of our study and the use of bulk data, the eligible patients for AFS (thus allowing an "intention-to-treat" analysis) could not be identified and their actual number could not be established: although we collected the principal ICD-10 codes at delivery, we could not establish whether any risk factors present were actually diagnosed antenatally or peripartum. However, this number is probably negligible, considering the rigorous application of a shared, standardized protocol for AFS at our institution and the exclusion of patients who were managed and delivered at other centers.

Implementation of AFS using criteria closely resembling those recommended by ACOG[5] may lower the risk of stillbirth without any appreciable increase in prematurity. Future studies may quantify the reduction in risk of stillbirth in a population undergoing AFS by comparing the observed rates of stillbirth with those expected based on the number and types of risk factors.

Author contributions

Substantial contributions to the concept and design or analysis and interpretation of data (AG, KV, AC, MC, SF, SO, NP, AL). Drafting the manuscript or revising it critically for important intellectual content (AG, KV, AC, MC, SF, SO, NP, AL). All authors have read and approved the version of the manuscript submitted.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Submission declaration

The work herein described has not been published previously and is not under consideration for publication elsewhere; its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out; if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder.

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Data availability statement

The data that support the findings of this study are available from the corresponding author, [SF], upon reasonable request.

References

[1] Clark SL, Sabey P, Jolley K. Nonstress testing with acoustic stimulation and amniotic fluid volume assessment: 5973 tests without unexpected fetal death. Am J Obstet Gynecol. 1989;160(3):694–697. doi: 10.1016/s0002-9378(89)80062-6.

[2] Nageotte MP, Towers CV, Asrat T, et al. Perinatal outcome with the modified biophysical profile. Am J Obstet Gynecol. 1994;170(6):1672–1676. doi: 10.1016/S0002-9378(94)70339-6.

[3] Nageotte MP, Towers CV, Asrat T, et al. The value of a negative antepartum test: contraction strss test and modified biophysical profile. Obstet Gynecol. 1994;84:231–234.

[4] Miller DA, Rabello YA, Paul RH. The modified biophysical profile: antepartum testing in the 1990s. Am J Obstet Gynecol. 1996;174(3):812–817. doi: 10.1016/s0002-9378(96)70305-8.

[5] American College of Obstetrics and Gynecology. Indications for outpatient antenatal fetal surveillance. Obstet Gynecol. 2021;137:e177–e197.

[6] Society of Obstetrician and Gynaecologists of Canada (SOGC). Guideline No. 441. Antenatal fetal health surveillance. J Obstet Gynaecol Can. 2023;45:665–677.

[7] American College of Obstetrics and Gynecology. Antepartum fetal surveillance. Obstet Gynecol. 2014;124(1):182–192.

[8] Grobman WA, Rice MM, Reddy UM, et al. Labor induction versus expectant management in low-risk nulliparous women. Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. N Engl J Med. 2018;379(6):513–523. doi: 10.1056/NEJMoa1800566.

[9] Society of Maternal-Fetal (SMFM) Publications Committee. SMFM statement on elective induction of labor in low-risk nulliparous women at term: the ARRIVE trial. Am J Obstet Gynecol. 2019;221(1):B2–B4. doi: 10.1016/j.ajog.2018.08.009.

[10] Reddy UM, Ko CW, Willinger M. Maternal age and the risk of stillbirth throughout pregnancy in the United States. Am J Obstet Gynecol. 2006;195(3):764–770. doi: 10.1016/j.ajog.2006.06.019.
[11] Johnson GJ, Clark SL, Turrentine MA. Antepartum testing for the prevention of stillbirth: where do we go from here? Obstet Gynecol. 2018;132(6):1407–1411. doi: 10.1097/AOG.0000000000002967.
[12] Manning FA. Fetal biophysical profile. Obstet Gynecol Clin North Am. 1999;26(4):557–577. doi: 10.1016/s0889-8545(05)70099-1.
[13] American College of Obstetrics and Gynecology . Medically indicated late-preterm and early -term deliveries. Obstet Gynecol. 2021;138:e35–e39.
[14] Clapp M. Lost in translation? Evaluating the generalizability of randomized controlled trial findings to broad clinical practice. Obstet Gynecol. 2023;142(2):236–238. doi: 10.1097/AOG.0000000000005268.
[15] CDC Department of Health and Human Services. Centers for Disease Control and Prevention. National Center for Health Statistics. Division of Vital Statistics. User guide to the 2021 period linked birth/infant death public use file. Available from: https://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/DVS/fetaldeath/2021fetaluserguide.pdf.
[16] Maiti K, Sultana Z, Aitken RJ, et al. Evidence that fetal death is associated with placental aging. Am J Obstet Gynecol. 2017;217(4):441.e1–441.e14. doi: 10.1016/j.ajog.2017.06.015.
[17] King VJ, Bennet L, Stone PR, et al. Fetal growth restriction and stillbirth: biomarkers for identifying at risk fetuses. Front Physiol. 2022;13:959750. doi: 10.3389/fphys.2022.959750.

Appendix A

Table A1. Indications for fetal surveillance in singletons at Antenatal Testing Center during the study period.

Indication	Weeks to start NST	Frequency	Suggested delivery by
Post term pregnancy	40.1 weeks	Once	41 Weeks
DFM	At diagnosis	None	No change
Chronic HTN			
– On medications	– At 32 weeks	Weekly	By 40 weeks
– All others	– At 36 weeks		
Gestational HTN	At diagnosis	Weekly	37 Weeks
Preeclampsia	At diagnosis	Semiweekly	37 Weeks
GDM			
– On diet alone	– Never	– None	By 41 weeks
– On medications	– 36 Weeks (earlier if LGA)	– Weekly	By 40 weeks
DM			
– Well controlled	– 36 Weeks	Semiweekly	– 39 Weeks
– Poorly controlled	– 32 weeks	Semiweekly	– 37–39 Weeks
– Requiring insulin	– 32 weeks	Semiweekly	
Oligohydramnios			
Mild (AFI <5 cm, MVP >2 cm)	At diagnosis	Semiweekly	41 Weeks
Severe (MVP <2 cm)	At diagnosis	Admit for hydration.	If persistent: delivery
Polyhydramnios (AFI >25 cm)	At diagnosis	Weekly	40 Weeks
Obesity BMI >40	36 Weeks	Weekly	40 Weeks
Previous stillbirth, cerebral palsy or neonatal encephalopathy	32 Weeks or 1 week before stillbirth	Weekly	40 Weeks
Poor obstetric history with >1 risk factor (abruption, PTD, FGR, preeclampsia)	36 Weeks	Weekly	40 Weeks
FGR (AC <10th centile)	At diagnosis	Weekly	37–38 Weeks
– Umbilical artery PI >95%		– Twice weekly	37 weeks
– AEDF		– Daily	When NR fetal testing
Gestational cholestasis	At diagnosis	Twice weekly	37 Weeks
Cord anomalies (velamentous or marginal cord insertion, single umbilical artery)	36 weeks	Weekly	40 Weeks
AMA			
>35 Years	36 Weeks	Weekly	41 Weeks
>40 Years	32 Weeks		40 Weeks
IVF	36 Weeks	Weekly	40 Weeks
Inherited thrombophilias[a]	36 Weeks	Weekly	40 Weeks
Placental anomalies[b]	36 Weeks	Weekly	40 Weeks
HIV on HAART	36 Weeks	Weekly	38 weeks
Severe maternal medical conditions[c]	32 Weeks	Weekly	39–40 Weeks
Severe fetal anomalies or trisomy 21	32 Weeks	Weekly	39–40 Weeks
Low PAPP-A, high hCG, high MSAFP at screening	36 Weeks	Weekly	41 Weeks

[a]Factor V Leiden, prothrombin gene mutation, AT III deficiency, Protein S or C deficiency; [b]bilobed placentas, succenturiate cotyledon, placental thickness >4 cm, circumvallate placenta, grade III placenta before 32 weeks. [c]Severe asthma, chronic renal disease, cyanotic heart disease, symptomatic hemoglobinopathy, poorly controlled epilepsy, uncontrolled thyroid disease; systemic lupus erythematosus, antiphospholipid syndrome, alloimmunization.

Abbreviations. BPP, biophysical profile; DFM: decreased fetal movements; GDM: gestational diabetes mellitus; DM: diabetes mellitus; AFI: amniotic fluid index; MVP: maximum vertical pocket of amniotic fluid; BMI: body mass index; PTD: preterm delivery; FGR: fetal growth restriction; AEDF: absent end diastolic flow; AMA: advanced maternal age; HIV: human immunodeficiency virus; HAART: Highly active antiretroviral therapy; PAPP-A: pregnancy-associated plasma protein A; hCG:human chorionic gonadotropin; MSAFP: maternal serum alpha-fetoprotein; HTN: hypertension; IVF: *in vitro* fertilization; MoM: multiples of median.