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Synoptic Reporting in Clinical Placental Pathology: A Preliminary Investigation Into Report Findings and Interobserver Agreement

Sonia R. Dancey[1], Samantha J. Benton[2], Anthea J. Lafreniere[3], Michal Leckie[4], Benjamin McLeod[4], Jordan Sim[5], Dina El-Demellawy[4], David Grynspan[6], and Shannon A. Bainbridge[1,7]

Abstract

Introduction: Placental pathology is key for investigating adverse pregnancy outcomes, however, lack of standardization in reporting has limited clinical utility. We evaluated a novel placental pathology synoptic report, comparing its robustness to narrative reports, and assessed interobserver agreement.

Methods: 100 singleton placentas were included. Histology slides were examined by 2 senior perinatal pathologists and 2 pathology residents using a synoptic report (32 lesions). Historical narrative reports were compared to synoptic reports. Kappa scores were calculated for interobserver agreement between senior, resident, and senior vs resident pathologists.

Results: Synoptic reporting detected 169 (51.4%) lesion instances initially not included in historical reports. Amongst senior pathologists, 64% of all lesions examined demonstrated fair-to-excellent agreement (Kappa $\geq$0.41), with only 26% of Kappas $\geq$0.41 amongst those examined by resident pathologists. Well-characterized lesions (e.g., chorioamnionitis) demonstrated higher agreement, with lower agreement for uncommon lesions and those previously shown to have poor consensus.

Discussion: Synoptic reporting is one proposed method to address issues in placenta pathology reporting. The synoptic report generally identifies more lesions compared to the narrative report, however clinical significance remains unclear. Interobserver agreement is likely related to differential in experience. Further efforts to improve overall standardization of placenta pathology reporting are needed.

Keywords:
placental pathology, histopathology, synoptic reporting, lesions, standardization, interobserver agreement

Introduction

The placenta is the critical organ of pregnancy, regulating fetal growth and development and modulating maternal adaptations during pregnancy to support the developing fetus.[1] Due to these fundamental roles, healthy placental developmental and function are vital for optimal outcomes of both mother and fetus/infant. Adverse pregnancy outcomes such as preterm birth, preeclampsia, fetal growth restriction, and stillbirth are leading causes of maternal and fetal/neonatal mortality and morbidity worldwide.[2-4] Moreover, these complications are linked to a number of insults and/or exposures that disrupt placental structure and function, such as infection, underlying maternal morbidities (i.e., hyperglycemia), abnormal vascular development, and immunomodulatory aberrations.[5-8] Placental health can be assessed following delivery by gross and histopathological examination of placenta, providing insight into potential etiologies of these adverse pregnancy outcomes, immediate and long-term impacts to maternal and neonatal health and potential recurrence risks.[9,10] In this regard, placental pathology has a critical role in the continuum of care for mothers and their infants.

[1]Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada
[2]Department of Health Sciences, Faculty of Science, Carleton University, Ottawa, ON, Canada
[3]Division of Pathology, The Hospital for Sick Children, Toronto, ON, Canada
[4]Department of Pathology, Children's Hospital of Eastern Ontario, Ottawa, ON, Canada
[5]Department of Pathology and Laboratory Medicine, The Ottawa Hospital, Ottawa, ON, Canada
[6]Department of Pathology and Laboratory Medicine, Vernon Jubilee Hospital, Vernon, BC, Canada
[7]Interdisciplinary School of Health Sciences, Faculty of Health Sciences, University of Ottawa, Ottawa, ON, Canada

Corresponding Author:
Shannon A. Bainbridge, Interdisciplinary School of Health Sciences, University of Ottawa, Roger Guindon Hall, Room 2116, 451 Smyth Road, Ottawa, ON K1H 8M5, Canada.
Email: shannon.bainbridge@uottawa.ca

As in other pathology specialties, issues in standardization, reporting practices and clinical translation are recognized limitations in the field of placental pathology.[11-15] Recent efforts to improve the quality and robustness of placental pathology in practice include the development of international consensus guidelines, such as the Amsterdam criteria, for lesion definitions and severity criteria, recommendations for standardized gross examination and uniform approaches for placental submission to Pathology.[16-18] Despite these efforts, lack of standardized reporting practices yielding potentially incomplete and biased placental evaluations remains a current problem.[19] To improve and advance this important clinical modality, a synoptic reporting approach in which a line-by-line evaluation of placental lesions is employed may increase the completeness and limit bias in the evaluation of histopathology lesions, as demonstrated in the field of oncologic pathology.[20] Synoptic reporting has become widespread in the field of oncopathology, increasing the quality and completeness of pathology reporting and allowing for the creation of uniform, multi-center databases that can be leveraged for large-scale research endeavors.[21-23] Recently, our group developed a novel synoptic report for placental pathology based on current literature and practice guidelines, as an extension of Amsterdam consensus criteria.[16,19] Our long-term goal in the development of this synoptic report is to guide the implementation of the Amsterdam consensus criteria into clinical practice and take initial steps in creating robust databases in placental pathology for large-scale analysis to explore clinical significance of a wide range of placental lesions. As first steps to the implementation of this synoptic tool in clinical practice, we conducted an internal audit of this synoptic report. Our objectives for the current study were 2-fold, we sought to: (1) evaluate and compare the use of the synoptic report to historical narrative reporting of placenta cases, and (2) assess interobserver agreement regarding lesion presence and severity between senior perinatal pathologists and resident pathologists. These 2 objectives were undertaken to both compare/contrast the type of information captured when using traditional narrative reporting vs proposed synoptic reporting, and to determine the similarity in data captured using this synoptic reporting tool when applied by users with different experiential and training backgrounds. Collectively, both pieces of information are needed for consideration prior to moving forward with the implementation of such a tool in either a clinical or research setting.

Materials and Methods

This was a retrospective cohort study of archived placenta pathology examination reports and accompanying histopathology tissue sections of placentas submitted to the Department of Pathology (Children's Hospital of Eastern Ontario, Ontario, Canada) between 2013 and 2014. This study was approved by the Children's Hospital of Eastern Ontario (CHEO) Research Ethics Board (REB#15/19X).

Case Selection and Retrospective Review of Historical Reports

Placentas sent to the Department of Pathology between October 1, 2013 and December 31, 2014 were randomly selected for inclusion in the study using a random number generator of uniquely assigned patient study numbers. During this time period, approximately 2200 placentas were received, and 100 placental cases from singleton pregnancy with a liveborn infant were selected for inclusion based on sample size calculation for clinical audits, accepting a 10% inaccuracy due to sampling.[24] Cases were excluded if the gestational age at delivery was not provided with the pathology requisition. Historical pathology reports signed out by pediatric pathologists at CHEO were reviewed for demographic data (maternal history, infant sex and birthweight, pregnancy diagnosis at delivery) as well as gross anatomical findings and information was entered in a secure Redcap study database.

For the retrospective review of historical placental pathology reports, each report was reviewed for histopathological findings noted by the original reporting pathologist. For each lesion indicated in the historical report, the severity description was recorded in a data collection form and included all descriptors (mild/moderate/severe; absent, etc).

Placental Assessments With Synoptic Report

Following review of the historical narrative report, accompanying H&E-stained placenta tissue slides were retrieved from the Eastern Ontario Regional Laboratory Association (EORLA) slide repository at CHEO. Representative tissue sections had been collected from the umbilical cord, fetal membranes and full-thickness tissue sections from each quadrant of the placenta according to EORLA standard operating procedures. Additional tissue blocks were collected when overt pathology was noted visually. Thus, each included case had a minimum of 6 tissue sections which were all reviewed in de novo fashion by the reporting pathologist and evaluated using the synoptic report.

The synoptic report provides diagnostic and severity criteria for 32 distinct placental lesions categorized into 9 etiological categories (maternal vascular malperfusion, maternal decidual arteriopathy, implantation site abnormalities, ascending intrauterine infection, placenta villous maldevelopment, fetal vascular malperfusion, utero-placental separation, maternal-fetal interface disturbance, and chronic inflammation), largely based on Amsterdam consensus statement criteria, with the addition of other histopathological lesions of interest. For each lesion, a definition based on current literature and consensus guidelines[16,19] is included in the

synoptic report, and the user is required to enter a semi-quantitative score based on the absence/presence and severity of each lesion (absent [score = 0]/present [score = 1], severity [score = 1–3]). A narrative text field at the end of the report allows for inclusion of additional findings.

The histology slides of each case were independently examined by 2 experienced perinatal pathologists (DG and DED) using the synoptic report (see Supplemental Appendix A). The pathologists were blinded to all clinical information (except for gestational age at delivery and placenta weight) and the historical pathology report. Gross placental findings were provided to the pathologists when needed in diagnosing microscopic lesions such as retroplacental adherent hematomas. Two anatomical pathology residents (AL, PGY3 at study conduction and JS, PGY5 at study conduction) reviewed the placental cases in the same manner as described above. The placentas selected for inclusion within this study (i.e., submitted to Pathology between 2013 and 2014) had initial historical reports created by the reporting pathologist prior to the publication and widespread implementation of Amsterdam consensus statement criteria. Thus, de novo examination of the placental slides with the proposed synoptic report acted as a method of objectively putting into practice the consensus statement criteria while additionally assessing other placental lesions of interest.

Statistical Analysis

Data were analyzed using Microsoft Excel 2010 for descriptive data and GraphPad QuickCalcs (https://www.graphpad.com/quickcalcs/kappa1/) to quantify agreement with kappas which uses equations 18.16 to 18.20 from Fleiss, Statistical Methods for Rates & Proportions, 3rd edition.[25] Descriptive data were expressed as means and standard deviations for normally distributed data or medians with interquartile ranges for non-normally distributed data.

To compare the reported findings between the synoptic report and the historical narrative reports, the proportion of lesions not mentioned in the historical narrative report but indicated as a positive finding on the synoptic report was calculated, and vice versa. A post-hoc analysis was also completed for senior pathologists' who participated in the study, to compare their diagnoses on the historic narrative report (DED, 26 cases and DG, 49 cases) to those that were found with the synoptic report. This data is presented in Supplemental Appendices 2 and 3.

Interobserver agreement between senior pathologists and between resident pathologists for each lesion was assessed using weighted kappa scores. Weighted kappa scores assume that categories are ordered and accounts for how far apart raters are, using linear weights.

To assess agreement between the residents and the senior pathologists, non-weighted "binary" kappa scores were calculated. The scoring of placental slides by each lesion, completed by the resident pathologists was reviewed and compiled. A masterlist was created for the resident pathologists and for each placental case if any one, or both, of the residents indicated the lesion present, the lesion was noted to be present (i.e., =1). If both residents indicated the lesion was absent, it was given a score of 0 in the masterlist. This same process was applied to the scoring of placental lesions by senior pathologists. Kappa scores were calculated using the masterlist to assess level of agreement between resident and senior pathologists regarding the presence/absence of each distinct placental lesion included within the synoptic report. A similar non-weighted, post-hoc analysis was completed to compare each resident pathologist's interobserver agreement to the senior pathologists.

Kappa scores were interpreted as follows: <0.40 indicated poor agreement between reviewers, 0.41–0.75 indicated fair to good agreement, and values >0.75 were considered excellent agreement.[25] Mean (SD) kappa scores were calculated for each category of placental lesions, stratified by the analyses stated above (senior pathologists, resident pathologists, and senior vs resident pathologists).

Results

Cohort Characteristics

Of the initial 100 placental cases that were randomly selected for inclusion in the study, 42 (42%) were missing gestational age at delivery. These cases were excluded and review of an additional 94 cases was required to achieve the complete cohort of 100 cases which met eligibility criteria. The demographics of the cohort are shown in Table 1. The most common indication for submission of the placenta for pathology examination was preterm birth (27%), followed by maternal history (18%) and fetal anomalies (17%). The majority of births were by vaginal delivery (62%). Median gestational and maternal ages at delivery were 37 weeks (Q1, Q3 [33, 39]), and 31 years (Q1, Q3 [27, 35]), respectively and mean birthweight percentile was 39.8 (Q1, Q3 [14.0, 58.0]).

Narrative vs Synoptic Reporting and Detection of Placental Lesions

Table 2 demonstrates the detection of placental lesions when using the synoptic report vs detection included in the historical narrative report. When comparing the narrative reports to the synoptic reports across all placentas and lesion categories, the synoptic reporting tool detected 169 instances of placental lesions that were missed in the narrative report, at a rate of 51.4%. Occasionally, cases were identified in the historical narrative report but not identified in the synoptic report, which occurred for a total of 32 instances, at a rate of 24.7%.

The results of our post-hoc analysis, comparing the diagnoses of the study pathologists original historic narrative reports to those from their de novo synoptic reports are

Table 1. Clinical Characteristics of the Audit Cohort.

Characteristic	Proportion (%)	Median (IQR)
Method of delivery[a]		
Vaginal	62 (62)	
Caesarean section	35 (35)	
Infant sex[b]		
Male	54 (54)	
Female	42 (42)	
Infant birthweight percentile		39.75 (14.00, 58.00)
Gestational age at delivery (wk)		36.93 (33.36, 39.04)
Maternal information		31.00 (27.00, 35.00)
Nulliparous	45 (45)	
Maternal age at delivery (y)		
Indication for submission to pathology		
Pre-term labor	27 (27)	
Maternal history	18 (18)	
Fetal anomalies	17 (17)	
Hypertensive disorders of pregnancy	16 (16)	
Intrauterine growth restriction	11 (11)	
Placenta anomalies	11 (11)	
Infection	10 (10)	
Maternal diabetes	9 (9)	
Caesarean section	5 (5)	

[a]Method of delivery not available for n = 3 of 100 cases.
[b]Infant sex not available for n = 4 of 100 cases.

presented in Supplemental Appendices 2 and 3. Interestingly, as shown in Supplemental Appendix 3, cases originally signed out by DED demonstrated a greater rate of instances of placental lesions recorded in the narrative report as compared to the synoptic report (average 45.6% across all lesions), with this difference most notable within the category of maternal vascular malperfusion lesions.

Interobserver Agreement Between Pathologists Using the Synoptic Reporting Tool

We examined interobserver agreement using the synoptic reporting tool comparing senior pathologists to each other, resident pathologists to each other, and comparing the residents to the senior pathologists to assess the consistency of information collected using this tool when applied by users with different experiential/training backgrounds—a metric required for consideration of future implementation of this tool in either clinical or research settings. When assessing interobserver agreement between senior pathologists using the synoptic reporting tool (Table 3), 4 out of the total 32 lesions were not identified in any of the placentas by the senior pathologists and thus no kappa was calculated for the following 4 lesions: villous stromal-vascular karyorrhexis, maternal floor infarct pattern, infectious villitis, and chronic intervillositis. Of the remaining 28 placental lesions, 18 (64.3%) demonstrated fair to excellent agreement ($k \geq 0.40$).

When the synoptic tool was used by resident pathologists, a considerably lower interobserver agreement was obtained, with reporting on only 8 of the total 31 placental lesions identified in the cohort (25.8%) demonstrating fair to excellent interobserver agreement. It should be noted that 1 lesion was not called by either resident pathologist using version 1.7 of the synoptic report, thus 31 kappas were calculated out of the 32 lesions in the report. Interestingly, a higher degree of interobserver agreement was observed between senior and junior pathologists, with 15 of 31 total identified placental lesions (48.4%) demonstrating fair to excellent interobserver agreement (kappa ≥ 0.40). Our post-hoc analysis examined the kappa scores between each resident pathologist and both senior pathologists together to determine if there were significant differences in reporting of placental lesions between residents. The results can be found in Table 4 and demonstrate similar average kappa scores across all categories.

When examining lesions with the highest degree of interobserver agreement between all pathologists (all levels of training/experience) the lesions associated with evidence of ascending intrauterine infection—including maternal and fetal inflammatory responses (category 4), demonstrated excellent agreement (all comparisons generated kappa scores ≥ 0.75).

Senior pathologists additionally had high levels of agreement for placental lesions in category 7—evidence of chronic utero-placental separation. The average kappa score for this category was (0.71, SD = ± 0.39), with strong interobserver

Table 2. Comparing the Use of a Synoptic Reporting Tool vs Historic Narrative Reporting System for Reporting Placental Pathology.

Lesion	% Cases missed in narrative report[a]	% Cases missed in synoptic report[b]	# Cases recorded in synoptic report	# Cases recorded in narrative report	Concordance (# cases identified in both synoptic and narrative report)	# Cases recorded present based on the synoptic report but not recorded in the narrative report)	# Cases recorded present in the narrative report but recorded as absent in the synoptic report)
Category 1: Evidence of maternal vascular malperfusion							
Placental infarct	20	20	15	15	12	3	3
Distal villous hypoplasia	45	54	11	13	6	5	7
Accelerated villous maturation	41	15	29	20	17	12	3
Increased syncytial knots	65	13	37	15	13	24	2
Villous agglutination	78	0	9	2	2	7	0
Focal perivillous fibrin deposition	61	25	23	12	9	14	3
Category 2: Evidence of maternal decidual vasculopathy							
Insufficient vessel remodeling	91	0	11	1	1	10	0
Fibrinoid change	33	20	6	5	4	2	1
Category 3: Evidence of implantation site abnormalities							
Microscopic accreta	75	0	4	1	1	3	0
Increased basement membrane fibrin	100	n/a	1	0	0	1	0
Category 4: Evidence of ascending intrauterine infection							
Maternal inflammatory response	38	5	29	19	18	11	1
Fetal inflammatory response	17	5	24	21	20	4	1
Category 5: Evidence of placenta villous maldevelopment							
Chorangiosis	67	0	6	2	2	4	0
Chorangioma	0	0	1	1	1	0	0
Delayed villous maturation	88	0	25	3	3	22	0
Category 6: Evidence of fetal vascular malperfusion							
Avascular fibrotic villi	82	33	11	3	2	9	1
Thrombosis	83	66	6	3	1	5	2
Intramural fibrin deposition	0	40	3	5	3	0	2
Villous stromal-vascular karyorrhexis	n/a	100	0	1	0	0	1
High-grade fetal vascular malperfusion	50	0	4	2	2	2	0
Category 7: Evidence of chronic utero-placental separation							
Chorionic hemosiderosis	0	0	1	1	1	0	0
Retroplacental adherent hematoma	22	0	9	7	7	2	0
Laminar necrosis of decidua capsularis	100	n/a	6	0	0	6	0
Category 8: Evidence of maternal-fetal interface disturbance							
Massive perivillous fibrin deposition pattern	0	0	1	1	1	0	0
Maternal floor infarct pattern	n/a	100	0	1	0	0	1
Intervillous thrombi	38	20	13	10	8	5	2
Category 9: Evidence of chronic inflammation							
Infectious villitis	n/a	n/a	0	0	0	0	0
Villitis of unknown etiology (VUE)	50	0	14	7	7	7	0
Chronic intervillositis	n/a	100	0	1	0	0	1
Chronic deciduitis	92	50	12	2	1	11	1
Average across all lesions[c]	51.4%				24.7%		

[a]The % cases missed in the narrative report was calculated as follows: (# Cases recorded present based on the synoptic report but not recorded in the narrative report/# Cases recorded in synoptic report) × 100%. Thus, cases marked as n/a has 0 cases recorded in the synoptic report.
[b]The % cases missed in the synoptic report was calculated as follows: (# Cases recorded present in the narrative report but recorded as absent in the synoptic report/# Cases recorded in narrative report) × 100%. Thus, cases marked as n/a has 0 cases recorded in the narrative report.
[c]Average across all lesions excludes those marked as n/a.

Table 3. Interobserver Agreement by Placental Lesion Comparing Senior Pathologists' Scoring (DG vs DED), Resident Pathologists' Scoring (AL vs JS) and Senior vs Resident Pathologist Scoring of Placental Lesions (DG, DED vs AL, JS).

Lesion	Interobserver agreement, senior pathologists (weighted Kappa)	Kappa interpretation[a]	Interobserver agreement, resident pathologists (weighted Kappa)	Kappa interpretation[a]	Interobserver agreement, senior vs resident pathologists (Kappa ± SE)	Kappa interpretation[a]
Category 1: Evidence of maternal vascular malperfusion						
Placental infarct(s)	0.627	Fair to good	0.384	Poor	−0.103 ± 0.034	Poor
Distal villous hypoplasia	0.342	Poor	0.183	Poor	0.279 ± 0.094	Poor
Accelerated villous maturation pattern	0.461	Fair to good	0.103	Poor	0.347 ± 0.101	Poor
Syncytial knots	0.418	Fair to good	0.379	Poor	0.473 ± 0.092	Fair to good
Focal perivillous fibrin deposition	0.483	Fair to good	0.027	Poor	0.019 ± 0.073	Poor
Villous agglutination	−0.034	Poor	0	Poor	0.035 ± 0.054	Poor
Average (SD)	0.38 (0.22)		0.18 (0.17)		0.18 (0.22)	
Category 2: Evidence of maternal decidual vasculopathy						
Insufficient vessel remodeling	0.254	Poor	0.296	Poor	0.616 ± 0.116	Fair to good
Fibrinoid change	0.442	Fair to good	0.501	Fair to good	0.541 ± 0.164	Fair to good
Average (SD)	0.35 (0.13)	Poor	0.40 (0.14)		0.58 (0.05)	
Category 3: Implantation site abnormalities						
Microscopic accreta	0.561	Fair to good	0.488	Fair to good	0.739 ± 0.177	Fair to good
Increased basement membrane fibrin	0	Poor	−0.018	Poor	0.126 ± 0.115	Poor
Average (SD)	0.28 (0.40)		0.24 (0.36)		0.43 (0.43)	
Category 4: Evidence of ascending intrauterine infection						
Maternal inflammatory response: stage	0.768	Excellent	0.687	Fair to good	0.699 ± 0.071	Fair to good
Maternal inflammatory response: grade	0.570	Fair to good	0.694	Fair to good	0.703 ± 0.071	Fair to good
Fetal inflammatory response: stage	0.894	Excellent	0.827	Excellent	0.916 ± 0.048	Excellent
Fetal inflammatory response: grade	0.801	Excellent	0.810	Excellent	0.917 ± 0.048	Excellent
Average (SD)	0.76 (0.14)		0.75 (0.07)		0.81 (0.12)	
Category 5: Evidence of placenta villous maldevelopment						
Chorangiosis	−0.027	Poor	1	Excellent	−0.018 ± 0.015	Poor
Chorangiomas	0	Poor	−0.010	Poor	1 ± 0	Excellent
Delayed villous maturation	0.269	Poor	0.309	Poor	0.342 ± 0.108	Poor
Average (SD)	0.08 (0.16)		0.43 (0.52)		0.44 (0.52)	
Category 6: Evidence of fetal vascular malperfusion						
Avascular fibrotic villi	0.647	Fair to good	0.176	Poor	0.487 ± 0.113	Fair to good
Thrombosis	0.481	Fair to good	0	Poor	0.159 ± 0.174	Poor
Intramural fibrin deposition	0.492	Fair to good	0.72 ± 0.223	Fair to good	0.74 ± 0.176	Fair to good
Villous stromal-vascular karyorrhexis	n/a	—	0	Poor	0	Poor
High-grade fetal vascular malperfusion	0.720	Fair to good	−0.01	Poor	0.26 ± 0.228	Poor
Average (SD)	0.59 (0.12)		0.18 (0.31)		0.33 (0.29)	
Category 7: Evidence of chronic utero-placental separation						
Chorionic hemosiderosis	1	Excellent	−0.01	Poor	−0.014 ± 0.010	Poor
Presence of retroplacental adherent hematoma	0.864	Excellent	0.138	Poor	0.628 ± 0.129	Fair to good
Laminar necrosis of decidua capsularis	0.26	Poor	0	Poor	−0.018 ± 0.015	Poor
Average (SD)	0.71 (0.39)		0.04 (0.08)		0.20 (0.37)	
Category 8: Evidence of maternal-fetal interface disturbance						
Massive perivillous fibrin deposition pattern	0	Poor	−0.010	Poor	0.492 ± 0.306	Fair to good
Maternal floor infarct pattern	n/a	—	−0.012	Poor	0	Poor
Intervillous thrombi	0.796	Excellent	0.046	Poor	0.423 ± 0.097	Fair to good
Average (SD)	0.40 (0.56)		0.01 (0.03)		0.31 (0.27)	
Category 9: Evidence of chronic inflammation						
Infectious villitis	n/a	—	0	Poor	0	Poor
Villitis of unknown etiology	0.660	Fair to good	0.296	Poor	0.417 ± 0.129	Fair to good
Chronic intervillositis	n/a	—	n/a	—	n/a	—
Chronic deciduitis	0.124	Poor	−0.025	Poor	0.049 ± 0.110	Poor
Average (SD)	0.39 (0.38)	Poor	0.09 (0.18)		0.15 (0.23)	

[a]Kappa scores were interpreted as follows: <0.40 indicated poor agreement between reviewers, 0.41–0.75 indicated fair to good agreement, and values >0.75 were considered excellent agreement.

Table 4. Interobserver Agreement by Placental Lesion Comparing Senior Pathologists' Scoring (DG and DED) vs Resident Pathologists' Scoring (AL, JS).

Lesion	Interobserver agreement, AL vs senior pathologists (Kappa ± SE)	Kappa interpretation[a]	Interobserver agreement, JS vs senior pathologists (Kappa ± SE)	Kappa interpretation[a]	Interobserver agreement, senior vs resident pathologists (Kappa ± SE)	Kappa interpretation[a]
Category 1: Evidence of maternal vascular malperfusion						
Placental infarct(s)	−0.041 ± 0.063	Poor	−0.071 ± 0.021	Poor	−0.103 ± 0.034	Poor
Distal villous hypoplasia	0.284 ± 0.141	Poor	0.313 ± 0.110	Poor	0.279 ± 0.094	Poor
Accelerated villous maturation pattern	0.322 ± 0.107	Poor	0.229 ± 0.106	Poor	0.347 ± 0.101	Poor
Syncytial knots	0.426 ± 0.096	Fair to good	0.406 ± 0.094	Fair to good	0.473 ± 0.092	Fair to good
Focal perivillous fibrin deposition	0.019 ± 0.073	Poor	0.048 ± 0.068	Poor	0.019 ± 0.073	Poor
Villous agglutination	0.052 ± 0.059	Poor	0	Poor	0.035 ± 0.054	Poor
Average (SD)	0.18 (0.19)		0.15 (0.19)		0.18 (0.22)	
Category 2: Evidence of maternal decidual vasculopathy						
Insufficient vessel remodelling	0.647 ± 0.114	Fair to good	0.362 ± 0.161	Poor	0.616 ± 0.116	Fair to good
Fibrinoid change	0.789 ± 0.145	Excellent	0.590 ± 0.165	Fair to good	0.541 ± 0.164	Fair to good
Average (SD)	0.72 (0.10)		0.48 (0.16)		0.58 (0.05)	
Category 3: Implantation site abnormalities						
Microscopic accreta	0.739 ± 0.177	Fair to good	0.739 ± 0.177	Fair to good	0.739 ± 0.177	Fair to good
Increased basement membrane fibrin	0.138 ± 0.124	Poor	−0.010 ± 0.007	Poor	0.126 ± 0.115	Poor
Average (SD)	0.44 (0.42)		0.36 (0.53)		0.43 (0.43)	
Category 4: Evidence of ascending intrauterine infection						
Maternal inflammatory response: stage	0.699 ± 0.071	Fair to good	0.827 ± 0.063	Excellent	0.699 ± 0.071	Fair to good
Maternal inflammatory response: grade	0.699 ± 0.071	Fair to good	0.827 ± 0.063	Excellent	0.703 ± 0.071	Fair to good
Fetal inflammatory response: stage	0.856 ± 0.062	Excellent	0.883 ± 0.057	Excellent	0.916 ± 0.048	Excellent
Fetal inflammatory response: grade	0.856 ± 0.062	Excellent	0.883 ± 0.057	Excellent	0.917 ± 0.048	Excellent
Average (SD)	0.78 (0.09)		0.85 (0.03)		0.81 (0.12)	
Category 5: Evidence of placenta villous maldevelopment						
Chorangiosis	−0.018 ± 0.015	Poor	−0.018 ± 0.015	Poor	−0.018 ± 0.015	Poor
Chorangiomas	1.000 ± 0.000	Excellent	1.000 ± 0.000	Excellent	1.000 ± 0.000	Excellent
Delayed villous maturation	0.343 ± 0.108	Poor	0.199 ± 0.096	Poor	0.342 ± 0.108	Poor
Average (SD)	0.44 (0.52)		0.39 (0.54)		0.44 (0.52)	
Category 6: Evidence of fetal vascular malperfusion						
Avascular fibrotic villi	0.434 ± 0.118	Fair to good	0.462 ± 0.157	Fair to good	0.487 ± 0.113	Fair to good
Thrombosis	0.159 ± 0.174	Poor	0	Poor	0.159 ± 0.174	Poor
Intramural fibrin deposition	0.795 ± 0.200	Excellent	0.740 ± 0.176	Fair to good	0.74 ± 0.176	Fair to good
Villous stromal-vascular karyorrhexis	0	Poor	n/a	—	0	Poor
High-grade fetal vascular malperfusion	−0.028 ± 0.014	Poor	0.390 ± 0.275	Poor	0.26 ± 0.228	Poor
Average (SD)	0.27 (0.34)		0.40 (0.30)		0.33 (0.29)	
Category 7: Evidence of chronic utero-placental separation						
Chorionic hemosiderosis	−0.010 ± 0.007	Poor	−0.010 ± 0.007	Poor	−0.014 ± 0.010	Poor
Presence of retroplacental adherent hematoma	0.628 ± 0.129	Fair to good	0.185 ± 0.160	Poor	0.628 ± 0.129	Fair to good
Laminar necrosis of decidua capsularis	−0.018 ± 0.015	Poor	0	Poor	−0.018 ± 0.015	Poor
Average (SD)	0.20 (0.37)		0.06 (0.11)		0.20 (0.37)	
Category 8: Evidence of maternal-fetal interface disturbance						
Massive perivillous fibrin deposition pattern	0.492 ± 0.306	Fair to good	1.000 ± 0.000	Excellent	0.492 ± 0.306	Fair to good
Maternal floor infarct pattern	0	Poor	0	Poor	0	Poor
Intervillous thrombi	0.423 ± 0.097	Fair to good	0.138 ± 0.124	Poor	0.423 ± 0.097	Fair to good
Average (SD)	0.30 (0.27)		0.38 (0.54)		0.31 (0.27)	
Category 9: Evidence of chronic inflammation						
Infectious villitis	0	Poor	n/a	—	0	Poor
Villitis of unknown etiology	0.468 ± 0.130	Fair to good	0.493 ± 0.136	Fair to good	0.417 ± 0.129	Fair to good
Chronic intervillositis	n/a	—	n/a		n/a	—
Chronic deciduitis	0.112 ± 0.121	Poor	0	Poor	0.049 ± 0.110	Poor
Average (SD)	0.19 (0.24)		0.25 (0.35)		0.15 (0.23)	

[a]Kappa scores were interpreted as follows: <0.40 indicated poor agreement between reviewers, 0.41–0.75 indicated fair to good agreement, and values >0.75 were considered excellent agreement.

agreement for lesions of chorionic hemosiderosis (k = 1.00, SD = ±0) and retroplacental adherent hematoma (k = 0.86, SD = ±0.094), although there was poor interobserver agreement seen for laminar necrosis of the decidua capsularis (k = 0.26, SD = ±0.228). Interestingly, the resident pathologists had very poor agreement for this same category of lesions with an average kappa score of 0.04, SD = ±0.08, and even one kappa score less than 0 (i.e., suggesting agreement worse than expected by chance) for chorionic hemosiderosis lesions.

The senior pathologists had the overall lowest agreement for lesions in category 5—evidence of placenta villous maldevelopment (average kappa score = 0.08, SD = ±0.16), which included all lesions subject to much interobserver variability: chorangiosis, chorangioma and delayed villous maturation. In comparison, the residents had a wide variation in levels of interobserver agreement for this same category of lesions, with an average kappa score of 0.43 (SD = ±0.52). Less than chance levels of agreement were observed for chorangioma (k = −0.010), but excellent consensus was reached for chorangiosis (k = 1.00).

Discussion

Placental histopathological examination is an often overlooked, but valuable clinical tool to investigate the etiology of adverse pregnancy outcomes.[12,26,27] Compared to other fields, placental examination is still in its infancy with a multitude of avenues for further work and improvement. Several challenges exist within the field of placenta pathology including poor interobserver reliability, reporting of lesions of unclear clinical significance and lack of consensus on diagnostic reporting criteria.[28-30] Until recently, with the establishment of the Amsterdam consensus statement criteria, there have been few efforts for international standardization of diagnostic criteria in placental assessments and there is a lack of implementation of synoptic reporting as compared to other areas of pathology.[15,16,19] Here we sought to assess the potential clinical and/or research utility of a synoptic reporting tool for placental pathology that builds on Amsterdam consensus criteria, by comparing the pathology findings reported when using a synoptic vs historical narrative approach. Moreover, we assessed interobserver agreement between resident and senior perinatal pathologists when using the synoptic tool to determine the reproducibility of data collected by users with varying experiential and training backgrounds.

Synoptic reporting, with a line-by-line evaluation of a data element followed by a response, has been incorporated into oncologic pathology reporting practices for decades and with the College of American Pathologists (CAP) as major driver, synoptic reporting is now a mainstay in the field of oncology.[20,31,32] Many studies to date, mainly in the field of oncology, have demonstrated the numerous benefits of synoptic reporting over traditional narrative reporting, including increasing the completeness of pathology reports, better reporting quality, higher degrees of satisfaction amongst the entire care team and the potential for data linkage and population-level research.[20,21,33,34] Although synoptic reporting has been the most widespread in cancer care, there have been reports of its uptake in other areas including operative reporting and radiology, which demonstrate similar benefits.[35-38] To date, however, there has been no clear evidence of the use or benefit of synoptic reporting in the domain of placenta pathology. With the movement toward international consensus on diagnostic criteria in placental pathology, the adoption of a synoptic report such as the one proposed by Benton et al[19] and utilized in this present study will be of particular benefit in this field.

In our study, using the synoptic reporting tool, 169 placental lesions across all cases were identified that were originally missed in the narrative report. The synoptic report also identified 100% of cases that were missed in the narrative report with respect to the lesions of increased basement membrane fibrin (1 case total) and laminar necrosis of the decidua capsularis (6 cases total). Although these lesions were relatively uncommon in our sample, this highlights the potential value of synoptic reporting for detection and reporting of more rare lesions, however the clinical utility of these additional findings remains to be determined. Previous work has demonstrated that laminar necrosis is a distinct form of necrosis and has been associated with placental hypoxia. As such, laminar necrosis can be seen in the setting of intrauterine growth restriction and hypertensive disorders of pregnancy, with potential for significant maternal and fetal morbidity and mortality.[39-41] While the Amsterdam Consensus Statement[16] notes that there is insufficient evidence to include these lesions under the category of maternal vascular malperfusion, including such a lesion in a comprehensive placenta pathology synoptic report such as ours, is important for further data collection in order to better define such lesions, clinical associations and recurrence risk for future pregnancies. The synoptic report essentially acts as a visual cue, helping to identify less common lesions which could be overlooked and not reported. Interestingly, even lesions that have been well-defined by the Society of Pediatric Pathology and the Amsterdam Consensus Statement[16] (namely maternal vascular malperfusion lesions, fetal vascular malperfusion lesions and maternal and fetal inflammatory responses in ascending intrauterine infection), were more frequently reported using the synoptic approach. It is important to note that these findings cannot be entirely attributed to the use of a synoptic report alone, as the de novo slide reviews conducted in this study were carried out following the publication and dissemination of the Amsterdam consensus criteria. As such, the pathologists reviewing these cases at time of this second review were familiar with and would have incorporated these consensus guidelines into their practice. Nevertheless, the embedding of the Amsterdam consensus diagnostic criteria into the synoptic reporting tool

most certainly could help ensure the appropriate implementation of the census guidelines into clinical and/or research practice in the field.

Regarding distal villous hypoplasia, these lesions were more frequently picked up in the narrative report as compared to de novo slide review with the synoptic report. As shown in the post-hoc analysis with senior pathologist DED, maternal vascular malperfusion lesions were overall more frequently recorded in the narrative report as well, as compared to the synoptic report. Again, practice changes and familiarity with Amsterdam consensus statement criteria likely are at play here, however it is possible that having the diagnostic criteria readily available and clearly outlined within the synoptic report may lead to less "over-calling" of these placental lesions.

The synoptic report tested in the current study is quite extensive and includes a wide range of diverse placenta lesions, and as such future work will need to focus on refining this tool to ensure included lesions demonstrate clinical importance. In oncologic pathology, the success of synoptic reporting is certainly the result of widespread and international body consensus regarding the types of lesions to report on and their clinical utility. In the field of placenta pathology this same degree of practice consensus will be needed to encourage clinical uptake. The research presented here is an important first step in assessing the potential utility of such a tool in this field, however it will be the results of ongoing research endeavors by our group and others, which aim to engage all relevant stakeholders—including pathologists, obstetricians/midwives, neonatologists, placental biologists, and patients alike—that will ultimately help to refine and fine-tune a synoptic reporting tool that will demonstrate strong clinical utility that can serve to improve clinical management and patient counseling following an adverse pregnancy outcome. Certainly, a strong case can be made for the use of a synoptic tool, such as the one tested here in its present form, for the collection of robust and standardized research data. Ultimately it will be the collection of these comprehensive placenta pathology datasets, which can be linked to maternal and neonatal health outcomes and/or biological measurements, that will allow us to determine the clinical significance of different placenta pathology findings.

Our second objective with the current study was to assess interobserver variability between senior perinatal pathologists and pathology residents using the synoptic report for reproducibility and practicality purposes. In this analysis it was noted that agreement was weaker among resident pathologists, with only 26% of lesions demonstrating fair to excellent agreement, compared to 64% of placental lesions for senior pathologists. Among residents, good consensus was reached for well-defined lesions such as maternal and fetal inflammatory response in ascending intrauterine infection, however rarer lesions such as massive perivillous fibrin deposition, maternal floor infarct pattern, chorionic hemosiderosis, and chorangioma demonstrated poor agreement, likely speaking to a differential in experience and exposure between resident pathologists. It is unsurprising that subspecialty-trained perinatal pathologists reached better overall agreement than the residents as pathology is a highly visual specialty and experience is known to make a difference in diagnostic accuracy.[42,43]

For all pathologists, poor agreement was seen for lesions that were less common in our sample (incidence <5 cases) such as chorangioma, and lesions that have been historically difficult to achieve consensus, such as distal villous hypoplasia.[44] Thus, despite the additional training and expertise in the field of perinatal pathology, there appears to be subjectivity and/or misunderstanding that underlies lower levels of agreement. When reviewing placenta cases, senior pathologists likely approach cases with a differential in training experiences and style of reporting. Even with the synoptic report acting as a guiding tool, some placental lesions have diagnostic nuances that are inherently subjective. In a study by Redline et al,[45] in which placental cases were examined for 11 lesions by 8 perinatal pathologists, interobserver agreement ranged from kappa values of 0.25 to 0.61 with lowest agreement for increased intervillous fibrin lesions. Authors noted several factors contributing to variability including differing interpretations of diagnostic criteria, personal biases, and lacking standardized measuring devices. Furthermore, in a single-center study by Al-Adnani et al,[46] an audit of 164 singleton placentas by 4 perinatal pathologists was completed to assess for delayed villous maturation (DVM). From the 38 cases that were reported to show DVM by at least 1 pathologist, consensus with at least 3 pathologists was found only in 14 cases. Issues in concordance were postulated to be due to conflicting diagnosis criteria and degree of placental immaturity deemed significant. While the implementation of a synoptic report would mitigate the possibility of competing differences in diagnostic criteria, assessing the severity of lesions is still nuanced and practices can vary. To improve agreement and generalizability in using the synoptic reporting tool, our team is working to convert the synoptic report into an electronic form with representative sample images embedded to serve as a reference/template for reporting pathologists.

In our study, resident pathologists served as surrogates for non-subspecialty trained pathologists. The results reinforce the notion that placental pathology is a field where advanced training and experience makes a difference in the accuracy of understanding diagnostic and severity criteria. The synoptic tool, however, can be important in histopathology education and training, highlighting where training may be lacking, and which lesion diagnostic criteria could be refined. Additional subspecialized training specific to perinatal pathology could be an important avenue for general pathologists in community-based non-academic settings. Continuing professional development courses are currently available

through the College of American Pathologist and similar organizations. Future work to develop additional training in perinatal pathology could provide a background for non-subspecialty pathologists to review placenta cases. With the complement of a synoptic reporting tool as a guide and framework, trainees and non-subspecialty-trained pathologists could refer to the tool when producing a report, helping to make placental pathology more accessible.

Strengths of this study include the examination of placentas by both resident and senior subspecialty-trained perinatal pathologists to examine the functionality of the synoptic reporting tool with respect to various stages of training. Additionally, all pathologists were blinded to previous placental examination records, clinical information and reviews were conducted separately by each pathologist. Our study was a preliminary investigation and was limited by sample size, thus for lesions that were uncommon, disagreement on one placenta had a greater negative impact on the overall kappa score. Additionally, narrative reports included within the study were signed out by any of the pediatric pathologists at CHEO at that time and the analysis was not restricted to those reports signed out by senior perinatal pathologists DED or DG who performed de novo review of the placenta cases using the synoptic report. It is also important to consider the fact that reporting practices and habits may have naturally evolved in the time between the initial narrative report and de the novo review with the synoptic report. Importantly, in the context of a retrospective review of pathology cases for the purposes of this research study, it is likely that the of de novo placenta pathology report findings would be superior to historical reports to some extent, due to the widespread dissemination and clinical uptake of the Amsterdam consensus.

Despite the potential benefits of synoptic reporting, an important consideration is the perceived and/or realized increase in workload with the completion of a comprehensive synoptic report. We recognize that the synoptic report tested within this study is lengthy and would be burdensome to reporting pathologists, thus is most appropriate for research settings in its present form. As discussed above, refinement of this tool with an emphasis on lesions with high clinical relevance, and potential incorporation into a template for electronic medical records would serve to reduce such burden. It will further be of high priority to envision and develop machine learning algorithms capable of combining key elements of the pathology report into a "top-line" diagnosis, meaning a clinically significant and meaningful output that is beneficial to all stakeholders. This area of work is already underway by our group and others, including work by Freedman et al[47] who is formulating meaningful placental phenotypes based on MVM, FVM, and chronic inflammatory lesions. The results of these ongoing projects will certainly help to move this field forward, envisioning a future in which the systematic collection of placenta pathology data can be used to better understand the disease process, recurrence risk in future pregnancies, and future health risks for mother and infants following an adverse pregnancy outcome.

In this study, we sought to evaluate a novel synoptic reporting tool for placental pathology, building on the Amsterdam consensus statement criteria. We propose that synoptic reporting is one method to help address the current issues in standardization and reporting of placental lesions. We demonstrated that this tool can help in categorizing captured placental pathology data for research purposes and generally helped to identify more lesions than historical narrative reporting (although this finding was not uniform). Kappa analysis was completed to assess the reliability and reproducibility amongst pathologists when using the synoptic tool, and demonstrated fair reproducibility of results when the tool is used by senior pathologist users. Future directions include engagement with key stakeholders to further refine the synoptic report to ensure clinical utility, and the application of synoptic reporting tools to capture robust placenta pathology data in research settings to better understand placenta-mediated diseases of pregnancy and the clinical importance of different placental lesions for the management and counseling of patients following an adverse pregnancy outcome.

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Authorship

S.R. Dancey: Acquisition of data; analysis and interpretation of data; drafting of article for intellectual content, manuscript editing, and final approval of the version to be published. S.J. Benton: Conception and design; acquisition of data; analysis and interpretation of data; drafting of article for intellectual content, revising for intellectual content; manuscript editing and final approval of the version to be published. A.J. Lafreniere: Acquisition of data; analysis and interpretation of data; manuscript editing and final approval of the version to be published. M. Leckie: Acquisition of data; analysis and interpretation of data, manuscript editing, and final approval of the version to be published. B. MacLeod: Acquisition of data, manuscript editing and final approval of the version to be published. J. Sim: Acquisition of data, manuscript editing, and final approval of the version to be published. D. El-Demellawy: Conception and design; acquisition of data; revising for intellectual content; manuscript editing and final approval of the version to be published. D. Grynspan: Conception and design; revising for intellectual content; manuscript editing and final approval of the version to be published. S.A. Bainbridge: Conception and design; revising for intellectual content; manuscript editing and final approval of the version to be published.

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ORCID iDs

Sonia R. Dancey https://orcid.org/0000-0003-0714-2899
Shannon A. Bainbridge https://orcid.org/0000-0002-8947-8152

Supplemental Material

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