Clinical algorithm for the management of intrapartum maternal urine abnormalities.

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Abstract

Aim: To develop an evidence based clinical algorithm for management of common intrapartum urinary abnormalities

Population: Women with singleton, term pregnancies in active labour and immediate postnatal period, at low risk of complications.

Setting: Health care facilities in low- and middle-income countries.

Search strategy: A systematic search and review were conducted on the current guidelines from WHO, NICE, ACOG and RCOG. Additional search was done on PubMed and The Cochrane Database of Systematic Reviews up to May 2020.

Case scenarios: Four common intrapartum urinary abnormalities were selected: proteinuria, ketonuria, glycosuria and oliguria. Using reagent strip testing, glycosuria was defined as ≥ 2+ on 1 occasion or of ≥ 1+ on 2 or more occasions, proteinuria as ≥ 2+ andpresence of ketone indicated ketonuria. Oliguria was defined as hourly urine output ≤ 30ml. Thorough initial assessment using history, physical examination and basic investigations helped differentiate most of the underlying causes, which include diabetes mellitus, dehydration, sepsis, pre-eclampsia, shock, anemia, obstructed labour, underlying cardiac or renal problems. A clinical algorithm was developed to facilitate intrapartum management and referral of complicated cases for specialized care.

Conclusions: Four simple, user friendly and evidence based clinical algorithms were developed to enhance intrapartum care of commonly encountered maternal urine abnormalities. These algorithms may be used to support health care professionals in clinical decision-making when handling normal and potentially complicated labour, especially in low resource countries.

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Keywords: Proteinuria; ketonuria; glycosuria; oliguria; pregnancy; intrapartum; labour

Tweetable abstract: An evidence based clinical algorithm was developed to enhance intrapartum management of commonly encountered urinary abnormalities**.**

Introduction

Reducing maternal and perinatal mortality remains a priority, especially in less developed countries where resources and access to specialized care are limited. Significant numbers of women have unfortunately died during the intrapartum and postpartum period because of obstructed labour, haemorrhage, sepsis and pre-eclampsia.[1] Such maternal death also directly affect the rate of stillbirth and neonatal deaths.[1,2]

International guidelines recommend that, during labour, the urinary volume, and presence or absence of protein and acetone should be recorded each time awoman voids.[3-5] Glucose testing in urine is not specifically recommended but some facilities may have reagent testing strips that also test for glucose. Such testing offers an opportunity to detect underlying maternal health conditions and potential complications. Proteinuria is an important feature of pre-eclampsia.[6]Intrapartum oliguria may signify acute renal failure secondary to pre-eclampsia, sepsis or obstetric haemorrhage.[7] Glycosuria or ketosis raise suspicion ofunrecognized diabetes in pregnancy, identify women at risk of macrosomia, obstructed labour and postpartum haemorrhage.[8,9] Earlier recognition, intensified monitoring, and prompt

management of these conditions could help optimize intrapartum care, to prevent serious complications, and improve maternal and perinatal outcome.

International recommendations for the management of urinary abnormalities during pregnancy focus mainly on those detected in the antenatal period but there is limited evidence on management during labour.[5,6,8,10] Criteria used to diagnose abnormal parameters vary among guidelines and may not be applicable for intrapartum use. Therefore, we reviewed international guidelines and the evidence base on four commonly encountered intrapartum urinary abnormalities associated with maternal and fetal complications: proteinuria, ketonuria, glycosuria and oliguria. The aim of this study was to summarise the evidence and develop clinical algorithms for diagnosis and management of abnormal intrapartum urinary findings, to guide health professionals.

Method

This work is part of a project commissioned by the World Health Organization, for the management of uneventful and complicated labours, to complement WHO intrapartum care guidelines, and facilitate the development of electronic evidence-based, decision-support tools by stakeholders, to improve labouroutcomes in low-resource settings.[11]

Search strategy

We searched for guidelines from the World Health Organization (WHO), National Institute for Health and Care Excellence (NICE), Royal College of Obstetricians and Gynaecologist (RCOG) and The American College of Obstetricians and Gynaecologist (ACOG). PubMed and The Cochrane Database of Systematic Reviews (CDSR) were also searched electronically, from inception to 01.05.2020, utilizing a combination of the keywords 1) proteinuria: 'protein OR

proteinuria' AND pregnancy and 'urinary tract infection' AND pregnancy, 2) glycosuria: 'glucose OR glycosuria OR diabetes' AND 'intrapartum', 3) oliguria: 'oliguria' or 'anuria' AND pregnancy, 4) ketonuria: pregnancy AND 'ketones or ketonuria'. The literature review was guided by a hierarchy of evidence and prioritised WHO guidelines followed by other international or national guidelines using GRADE methodology. In the absence of guidelines on a case scenario, a combination of existing studies and expert opinion was used to determine key points for consideration in the algorithm. The highest level of evidence found was used to support the decisions along the management pathway, in the order of up-to-date systematic review (with meta-analyses), up-to-date systematic review (without meta- analyses), any available systematic review, validated decision rules, randomized controlled trials, non-randomized controlled trials, observations studies, and consensus documents. Two reviewers (K.W.C. and L.N.T.) screened the title and the abstract, extending manual searching through the reference lists of relevant articles and extracted the recommendations and supporting evidences into an excel file independently, any inconsistencies were resolved by a third reviewer (S.M.).

Population and setting

The algorithms were developed to cover the assessment and management of pregnant women with singleton, term pregnancies considered to be at low risk of developing complications at admission to the birthing facility, with the diagnosis of active labour, regardless of stage of labour, until immediate postnatal period (including the first hour after childbirth). Health facilities in low- and middle-income countries were the priority. However, the algorithms are applicable to any health care setting, and possible adaptations that may be required were acknowledged. The target users for these algorithms are skilled health personnel providing care during childbirth working alone or as part of teams, particularly midwives, non-specialized clinicians (i.e. clinicians without

specialist training in obstetrics but who also provide care for women in labour), and specialists.

Development of the algorithm

After collating the evidence, a selection process for inclusion of the evidence in the algorithm took place. Selection was based on relevance of the evidence to the key decision points and severity of the condition targeted by an intervention. The selection also accounted for the strength of evidence and applicability and feasibility in a low to middle income countries context. If there were inconsistencies among guidelines, the most up-to-date guidelines and evidence were reviewed and used to inform consultation with experts. A list of inconsistencies was discussed at the WHO Intrapartum Care Algorithms Working Group meeting and a consensus reached on evidence for the algorithm.

Algorithms were structured to cover criteria that should be used to suspect a deviation from normal parameters in labour, initial assessment, probable causes and potential differential diagnosis, further assessments to reach the most probable diagnosis, and management of the condition. Draw.io, an open source diagramming software, was used to construct the algorithm in a flowchart format. The online software facilitated remote working by the WHO Intrapartum Care Algorithms Working Group. The algorithm was composed of standardised but variable shaped boxes, representing either a clinical state(rounded rectangle), decision point (hexagon or diamond), action task (rectangle), or link to a different algorithm (oval). Each box was numbered and joined to other boxes via arrows, to orientate the reader to the direction of flow. The numbers also corresponded to a table of evidence (see supplementary tables S1-S4), showing the evidence source for the action and decision points. They algorithms underwent internal

peer review by the WHO Intrapartum Care Algorithms Working Group and revisions where needed.

Results

Glycosuria

Search result

Five WHO and two international guidelines were found to be relevant.[8,12-17] There were 34 reviews identified by the search in the CDSR, but none were relevant to intrapartum management of glycosuria. Three additional guidelines were found through the search in PubMed and another three relevant articles on the capillary blood glucose cut-off values and low renal threshold for glucose.[18-23] (Figure S1). Evidence from the above was used to develop the algorithm for intrapartum glycosuria (Figure 1).

Condition

If glucose is detected by reagent strip in labouring women, a semi-quantitative assessment should be performed. Glycosuria was defined as 2+ or above on 1 occasion or 1+ or above on 2 or more occasions detected by reagent strip testing.[8,16]

Assessment

Glycosuria in labour should prompt further assessment for possible hyperglycaemia in pregnancy. WHO recommends antenatal universal screening for gestational diabetes mellitus (GDM) and pre-existing diabetes. It would be unusual for undiagnosed diabetes to first present with intrapartum glycaemia unless in countries with no routine screening, ie. low resources countries. There are no accepted diagnostic criteria to detect hyperglycaemia during labour which may be associated with adverse pregnancy or perinatal outcomes. GDM is usually diagnosed by fasting oral glucose

tolerance test,[8,14,16] which is not practical during labour and therefore either fasting or random venous plasma glucose, using standard cut-off, should be obtained to detect undiagnosed diabetes in labour. Levels above 7mmol/L for fasting or 11.1mmol/L for random glucose suggests presence of diabetes.[12,14] These cut offs were used in the algorithm rather than the WHO diagnostic criteria for GDM to diagnose diabetes in labour because i) risk of diabetic ketoacidosis is low in the GDM group, ii) intrapartum management of GDM will be the same as for pregnant women with diabetes if blood glucose levels are high (dextrose-potassium-insulin infusion is generally considered when capillary plasma glucose is > 7 mmol/l in labour),[16] iii) the diagnostic criteria for diabetes is standardized across guidelines/countries,[13] and iv) for GDM there are no agreed diagnostic criteria based on capillary blood glucose testing and diagnostic criteria of GDM after an oral glucose tolerance test is variable across guidelines.[8,16,17]

Treatment

Where previously undiagnosed diabetes is suspected in labour, a medical review, and dextrose-potassium-insulin infusion with hourly capillary glucose monitoring should be done. Testing for ketonuria should be done to rule out complications such as diabetic ketoacidosis. Newborns should be monitored for possible hypoglycemia.[16,22] If the venous plasma glucose reading is below the diagnostic cut-off of diabetes, it likely represents a low renal glucose excretion threshold during pregnancy and normal labour is allowed with no active intervention.[19]

Oliguria

Search result

Six WHO and six international guidelines and recommendations were found.[3-6,10,24-30] There were two reviews identified by the search in the CDSR, but none were relevant to intrapartum management of oliguria. Additional search in PubMed did not

reveal any relevant recent high quality reviews. (Figure S2). The evidence available was used to develop the algorithm for intrapartum oliguria (Figure 2).

Condition

Oliguria is defined as less than 30 mls of urine passed per hour.[3] Other guideline definitions included passing less than 400 mL in 24 hours (16.7mls per hour), less than 200 mL in 4 hours (50mls per hour) and less than 0.5ml/kg/hr.[3,4,10] The definition of urinary output less than 30mls per hour was more consistent with the minimum hourly urine output expected based on the average weight of a women in the low and middle income countries (60 kg) (0.5ml/kg/hr) rather than 50mls per hour of a 100kg woman. Approximate 17mls per hour seems to be a lot less than the expected hourly urine output of an adult. Using 30mls urine passed per hour is a simple definition that would also avoid calculation errors, and eliminate the need to obtain the actual weight of the woman.

Assessment

If oliguria is suspected during labour, obstruction of urine outflow should be ruled out by palpating the urinary bladder and catherization if necessary.[4] A detailed history taking, physical examination and measurement of vital signs of blood pressure, pulse and temperature, with basic investigations would help differentiate the underlying cause of oliguria, which includes dehydration,[4,10] sepsis,[25] pre-eclampsia,[3,6] renal failure secondary to shock,[3,10,25] and the rarer cardiac or renal diseases.[4,10] Symptoms and signs of heart failure are difficulty with breathing or unexplained cough when lying down, paroxysmal nocturnal dyspnea, palpitation, pale sweaty cool peripheries, irregular heartbeat, heart rate > 110 bpm, respiratory rate > 20 breaths per minute, hypotension, oxygen saturation < 95% on room air, raised jugular venous pressure, hepatomegaly, cardiac murmur or, on chest auscultation, reduced air entry, basal crackles or wheeze.[4,10] Signs of fluid retention could represent underlying renal disease and serum for renal function test should be done.

Treatment

Fluid resuscitation should be initiated in women with signs of dehydration or in septic or hypovolemic shock.[3,4,24,29,30] Cautious fluid replacement is needed in women with possible pre-eclampsia, cardiac/ renal disease especially if crepitations are heard by lung auscultation, and this may need to be done under diuretic cover.[6,10] Women should respond to fluid challenge and urinary output should be reviewed regularly. Persistent oliguria or other signs suggestive of a more sinister pathology, for example, refractory shock or severe pre-eclampsia, should prompt an urgent medical assessment with renal function testing and consider specialist referral.[6,25,31,32] Individual management should be directed to the underlying cause.

Proteinuria

Search result

Two WHO and five international guidelines and recommendations were found.[3,5,6,10,24,33,34] There were 98 reviews identified by the search in the CDSR, but none were relevant to intrapartum management of proteinuria. Four Cochrane reviews related to urinary tract infection in pregnancy. Two of these were already covered in the one international guideline, the third added no further guidance and the fourth falls under the sepsis link. Search in Pubmed revealed one additional relevant article.[35] (Figure S3). Evidence from these sources was used to construct the algorithm for intrapartum proteinuria (Figure 3).

Condition

Proteinuria was defined as urinary protein to creatinine ratio of 0.3mg/dL or greater, or two dipstick measurement of at least 2+ if quantitative method is not available. [3,6,34] Suspicion of proteinuria is defined as 1+ in some guidelines and further evaluation is recommended.[6] We have used 2+ as the threshold for proteinuria in the algorithm to increase specificity during labour where there is high risk of urine

contamination.[4,34] Confirmatory tests for significant proteinuria include a spot urine for protein/creatinine ratio, 24 hour urine collection or two dipsticks of 2+ protein six hours apart but these may not be feasibleduring labour because it is not practical to collect a 24 hour urine sample during labour, the result of the protein/creatinine ratio test may not be obtained during labour and subsequent urine voids may not occur after 6 hours or before the woman delivers. Therefore, a 2+ protein on a single urine dipstick has been chosen to guide further management of the woman, although confirmation may be done with second dipstick of 2+ at the 'the next urine void' as a pragmatic approach. Dipstick may not be available in low-resource setting and persistent cloudy urine on boiling also suggests proteinuria.[3] The definition of 24-hour urine sample of more than 300mg protein was not used in the algorithm as it would not be feasible and could not aid in immediate management during labour.

Assessment

Differential diagnoses include pre-eclampsia, urinary tract infection or pyelonephritis, severe anaemia, and previously undiagnosed renal or cardiac disease.[3,6,10,24,33-35] A history, examination and basic investigations should help point towards the likely diagnosis. Symptoms of urinary frequency, dysuria or flank pain, raised temperature, and presence of leucocyte esterase or nitrates on dipstick point towards urinary tract infection, whereas raised blood pressureand associated headaches, visual disturbances and epigastric pain suggest pre-eclampsia.[6,33] Particular attention should be paid to women with chronic hypertension on medication with proteinuria, who may develop superimposed pre-eclampsia during labour with a normal blood pressure and require close monitoring of blood pressure, urine output and blood tests. Mucosa should be checked for pallor to detect anaemia particularly in the presence of palpitations and dizziness.[3] A detailed medical review and physical examination should be performed to detect underlying kidney or cardiac disease especially in women with decreased urinary output.

Treatment

The choice of antibiotics for urinary tract infection during pregnancy differs among guidelines.[3,33] We have selected amoxicillin for treatment instead of nitrofurantoin for the algorithm because nitrofurantoin is usually not recommended at term due to the risk of neonatal hemolysis. Antibiotics should be given intravenously in the presence of fever and suspected sepsis, along with other supportive measures.[32] Pre-eclampsia requires careful monitoring and control of blood pressure with antihypertensives, fluid input / output and prevention or treatment of eclampsia, and details are available in the algorithm on management of blood pressure and heart rate abnormalities.[31] Where other causes have been ruled out, isolated proteinuria may be secondary to contamination, and regular monitoring of vital signs is otherwise sufficient during labour.

Ketonuria

Search result

Six WHO and four international guidelines and recommendations were found.[3-5,10,16,24,28-30,36] There were 151 reviews identified by the search in The Cochrane Database of Systematic Reviews, three were relevant. Two of these were already covered by one WHO guideline and the third provided no additional data.[37] Additional search in PubMed did not retrieve any relevant high quality reviews. (Figure S4). Evidence from these was used to develop the algorithm for intrapartum ketonuria (Figure 4).

Condition

Ketonuria is defined as presence of ketones in the urine, detected by a positive urine dipstix.[4]

Assessment

No guidance is available on the grading of severity of ketonuria or whether severity of ketonuria should influence how it is managed. Assessment of maternal condition

and labour progress should help differentiate between the diagnoses, which include dehydration secondary to reduced intake or excessive losses (vomiting or diarrhea), prolonged labour or previously undiagnosed diabetes.[3,4,16] It is important to rule out diabetic ketoacidosis to reduce adverse outcome for both the mother and baby.

Treatment

Oral rehydration should be encouraged and, if not tolerated or fails, intravenous route can be considered.[3-5,24] Ongoing fluid loss should be assessed, replaced and vomiting treated with antiemetic. Oral rehydration solution may be needed to replace salts and fluid in diarrhea, and a sample of stool should be sent for culture if infection is suspected. Ketones should be rechecked at the next urine void. Mild ketonuria could be physiological but persistent ketonuria >2 + mayneed a medical review.[36]

Discussion

Main findings

We have developed evidence-based algorithms for clinical management of four common maternal urine abnormalities during labour: glucosuria,

ketonuria, oligouria and proteinuria. Detection of these urinary abnormalities should trigger a comprehensive maternal and fetal assessment with history review, targeted physical examination, monitoring of vital signs and further investigation to exclude underlying medical conditions, such as dehydration, hypertensive disorders, sepsis, shock, undiagnosed diabetes, and pre-existing cardiac or renal diseases. These algorithms will provide guidance on how to approach these abnormalities particularly for less specialized birth attendant, when deviations from normal occur during labour. We have also clearly highlighted where medical review is indicated to refer women with complicated labour for specialist care.

Strengths

This is the first management protocol specifically focused on the intrapartum management of maternal urinary abnormality. We performed a robust and systematic search with predefined eligibility criteria. We evaluated a range of guidelines from international authorities and consulted experts to fill the gaps in research. We used the best available evidence to provide 'step by step' guidance and a systematic approach (for ease of the end user) to manage urinary abnormalities during labour.

Limitations

Our study had several limitations. Firstly, high-quality evidence on intrapartum management of specific urinary abnormalities is currently lacking in literature,and recommendations have been extrapolated and adapted from those generated for antenatal care. Secondly, discrepancies exist in the diagnostic criteria forurinary abnormalities among international guidelines; we have justified our decisions in selecting our recommended criteria for the algorithm where appropriate. Finally, these algorithms may not be applicable in complicated cases, or where there are multiple intrapartum problems where clinical decision making becomes complex; we have highlighted where a medical review is needed, and linked our algorithms to other relevant algorithms where appropriate.[31,32]

Interpretation

There is no epidemiological data on the prevalence of intrapartum urinary abnormalities in relation to their underlying cause and how they impact pregnancy outcome. Detection of urinary abnormality during labour in itself may be challenging. Unlike other vital parameters that permit regular intrapartum monitoring, women may not void during a short labour or at regular intervals and therefore intrapartum assessment of urinary volume, protein, ketones and glucose may not be possible in every case. Urinary catheterization may allow more accurate and timely

measurements but routine catheterisation is not recommended during normal labour. Moreover, false positive results may occur due to contamination with vaginal discharge or blood.

Although international bodies recommend recording of urine output and dipstick findings when a woman voids during labour, the evidence to support routine intrapartum urine dipstick screening and volumetry to improve pregnancy and neonatal outcome is currently lacking. The efficacy and cost effectiveness of such an approach needs to be evaluated in large randomized trials. There is also lack of evidence on what findings constitute normality specifically in labour, and which deviations are associated with poor intrapartum outcomes. Until better evidence becomes available, and as routine urine screening remains a part of intrapartum care, these clinical algorithms aim to provide a systematic and practical management pathway to support health care workers identify women who require closer monitoring and interventions and timely referral to tertiary centres, especially in low resource countries.

In the clinical setting, a woman's general condition and vital signs usually indicate the development of hypertensive disorders, dehydration, sepsis, and shock; such findings then prompt further testing for urine abnormalities to confirm diagnosis and its severity. However, detection of Intrapartum urinary abnormalities may also serve as the first indicator for previously undetected conditions that may be asymptomatic, such as severity of dehydration due to poor oral intake, evolving pre-eclampsia in labour where proteinuria precedes development of hypertension, or medical conditions such as renal or heart disease, or diabetes, particularly in the context of suboptimal antenatal care. An abnormal urine dipstick as an objective sign may then serve to alert health care professionals to assess and review the whole clinical picture.

Available resources in local settings may also impact on the implementation of these algorithms. For example, urine dipsticks may not be readily available. Additionally, serial observations and laboratory-based investigation results may not be available within this short period of time during labour to guide further management. Barriers to the implementation of these algorithms in different settings need further investigation.

Introducing these clinical algorithms in low resource countries, in facilities with less specialized birth attendants may improve maternal and perinatal outcomes. The algorithm could serve as a prompt to consider a range of differential diagnosis, and guide towards appropriate investigations and management, with timely referral for specialist care. However, these algorithms need to be tested in real life clinical scenarios to explore their impact on patient care. In future, incorporation of these linked intrapartum algorithms into interactive software or mobile applications may facilitate end users' application and implementation for management in labour.

Conclusion

We have developed evidence-based algorithms for clinical management of intrapartum urinary abnormalities. Implementing these algorithms in low resource settings with less recourse to specialized birth attendant can provide a systematic approach to timely investigation and management of underlying maternal conditions. Further research is needed to explore the feasibility of implementing these algorithms in real life scenarios in various settings, and their impact onreducing maternal and perinatal morbidity and mortality.

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Figures

Figure 1. clinical algorithm for intrapartum glycosuria

Figure 2. clinical algorithm for intrapartum oliguria

Figure 3. clinical algorithm for intrapartum proteinuria

Figure 4. clinical algorithm for intrapartum ketonuria