Background

Intrauterine growth restriction (IUGR) represents pathological inhibition of fetal growth and failure of the fetus to attain its growth potential [1]. There is a strong association between stillbirth and fetal growth restriction [2]. The etiology and risk factors for stillbirth and IUGR largely overlap [3,4]. Both the conditions are the result of complex pathology resulting from a recognizable interaction among maternal conditions, placental dysfunction and hormonal regulation [2,4]. For example, maternal smoking, low educational level, advanced maternal age, nulliparity, and black race are associated with increased risk of fetal growth restriction and stillbirth [2,4,5]. The same is the case for maternal medical conditions like gestational hypertensive disorders, pre and gestational diabetes, systemic lupus erythematosus, chronic renal disease, and thyroid disorders [2,3,6]. Further evidence of strong association between IUGR and stillbirth comes from the fact that prior delivery of a growth restricted infant is among the strongest risk factors for stillbirth, comparable to the history of prior stillbirth [3].

IUGR has been used as a marker to assess complications of pregnancy [7]. There is however, no standard definition of IUGR. It has been defined as a birth weight < 2 standard deviations below the median for gestational age, whereas others use a threshold of 3rd or 5th percentile of weight for age for the given population [7,8]. The term small for gestational age (SGA), usually defined as having a birth weight below the 10th percentile of an accepted reference standard, is often used as a proxy measure for IUGR [8]. These two terms are however not synonymous as some SGA infants may merely represent the lower tail of the 'normal' fetal growth distribution, while others who hah1atibn9(e)-eionhaft1-2(c484(--12(el)]TJT311Tf.031T20.56150082980Tdi(en)-4(umatond)]TJT11

inclusion in the review in which Doppler ultrasound of fetal and umbilical vessels was performed. Studies addressing utero-placental circulation were excluded however where umbilical artery or fetal Doppler was combined with utero-placental Doppler, the study has been included in this review.

For the fetal movement monitoring, we included randomized controlled trials, quasi-randomized and observational studies. The included studies either compared different methods of fetal movement monitoring vs. no fetal movement monitoring, mixed or undefined monitoring. Studies addressing effectiveness of fetal movement counting in high risk pregnancies and/or unselected populations were considered.

Da a ab ac a d a d a e e

All relevant data from final studies were abstracted on a standardized Excel spreadsheet (Additional file 2). Key variables extracted included study design, setting, allocation concealment, blinding, loss to follow-up, details of the intervention and comparison groups and the outcomes. The studies were assessed and graded according to the CHERG adaptation of the GRADE technique [12]. This method of assessment is based on strengths and limitations of individual studies. The studies are graded as 'high' 'moderate' 'low' or 'very low' quality based on study design, study quality, relevance to the objectives of the review and consistency across studies [11]. A randomized or cluster randomized trial initially received a high score which was downgraded to moderate if study design limitations or biases were present. In addition, studies having intent-to-treat analysis or a statistically significant

Some of the methods used to predict and monitor growth of the fetus include maternal BMI screening, symphysis-fundal height measurement and routine ultrasound [15]. Maternal BMI screening had been proposed as an effective method of predicting fetal growth by a group of experts [16]. Two Cochrane reviews on routine ultrasonographic evaluation in early (before 24 weeks of gestation) and late pregnancy (after 24 weeks) showed no effect in reducing overall peri-natal mortality [17,18]. Early pregnancy ultrasound (before 24 weeks) however was beneficial in detecting multiple pregnancies and reducing rates of induction of labor for post-term pregnancies [18]. Another Cochrane review on effectiveness of symphysis-fundal height measurement was inconclusive as only one trial was included and no recommendations in favor or against of the intervention were made [19].

For detection of IUGR, our approach was based on the results of a previous review conducted by us on different screening interventions during pregnancy [15]. On the basis of this review and other related evidence, a set of three interventions was proposed [15,16]. These interventions include (a) maternal BMI screening, (b) symphysis-fundal height measurement and (c) targeted ultrasound. The current evidence for these interventions is described based on our previous review and a summary of results is presented below.

Maternal anthropometry can be used to help predict adverse perinatal outcomes including low birth weight and preterm birth [16,20]. Appropriate detection and management of maternal malnutrition can significantly reduce the occurrence of IUGR and related perinatal adverse outcomes [21]. One of the nutritional interventions that have a proven effect in reducing incidence of SGA/IUGR is balanced protein energy supplementation

and abstracts, 84 were found to be appropriate and finally 14 studies were chosen for final data extraction. We evaluated studies on the basis of antepartum or intrapartum stillbirth and perinatal mortality as outcomes. Additional file 3 gives characteristics of included studies of fetal movement monitoring. There were four randomized controlled trials assessing fetal movement counting [26-29]. Three of these trials were conducted in developed countries [26,28,29] and one in a developing country [30]. Data were not pooled due to gross clinical heterogeneity in the assessment of fetal movement monitoring and the comparison group. Two of these trials compared different fetal movement counting methods, and measured the acceptability, the compliance and other outcomes [29,30]. No intrauterine death was reported in any of these two trials. In another trial fetal movement counting (modified Cardiff method) was compared with hormonal analysis. Only one stillbirth was reported (in the fetal counting group). However the fetal movement counting group had significantly fewer visits to the hospital antenatally compared to the group undergoing hormone analysis (RR 0.26, 95% CI 0.20 to

women comparing fetal counting (Cardiff method) versus no instruction to monitor fetal movements. There was no significant difference in the mean antepartum stillbirth rate per cluster in the intervention versus control group (2.90/1000 vs. 2.67/1000). The routine antenatal care guidelines of the UK National Institute for Health and Clinical Excellence (NICE) [31] that do not recommend fetal movement monitoring in uncomplicated pregnancies were largely dictated by the findings of this trial [32].

In addition, we identified four other intervention studies [33-36] and six observational studies [37-42]. A quasi-randomized trial by Neldam showed a statistically significant difference in antepartum stillbirth rates among women told to monitor fetal movements compared to those not being asked to monitor movements (0/1125 vs. 8/1125) [34]. The three before-after studies all showed a significant decline in stillbirth rates after formal introduction of fetal movement monitoring into clinical practice [33,35,36].

According to the observational study by De Muylder, high-risk women whose previously normal kick charts became abnormal had significantly higher antepartum stillbirth (194/1000 vs. 7/1000) and perinatal mortality (222/1000 vs. 27/1000) rates compared to women whose kick charts remained normal till delivery [37]. Other observational studies have mixed data regarding stillbirth outcome. Lema showed that poor fetal monitoring results had higher rates of stillbirths (5/27 vs. 1/83) [40], while a recent study by Sinha [42] found no deaths in the two groups of women with decreased and normal fetal movements (0/90 vs. 0/90) similar to the result of the study by Romero Gutierrez on perinatal mortality [41].

(2) D e e c e

Our literature search yielded 908 titles (Figure 2). Initially 25 studies were considered for inclusion in the review. Seven of these studies were excluded because the trial participants were described as 'unselected population' or of 'low risk' [43-49]. Two studies were excluded due to insufficient data [50,51]. Finally 16 studies were included in the review [52-67].

Additional file 4 presents the characteristics of included studies of Doppler velocimetry. All the studies were conducted in high income countries except one that was conducted in South Africa [64]. Pooled results for impact on stillbirth showed a reduction of 35 % [RR 0.65, 95 % CI 0.41-1.04]; however the results did not reach the conventional limits of statistical significance (Figure 3).

Pooled results from sixteen studies showed that Doppler velocimetry of umbilical and fetal arteries in 'high risk' pregnancies leads to a reduction of 29 % [RR 0.71, 95 % CI 0.52-0.98] in perinatal mortality compared to no Doppler velocimetry (Figure 4). There was no heterogeneity (I^2 =0) in both the pooled estimates.

Table 1 gives an overall qualitative assessment of studies addressing fetal movement monitoring and Doppler velocimetry. Data were not pooled for fetal movement monitoring due to gross clinical heterogeneity in the intervention and control groups of the included studies. We have not recommended fetal movement monitoring for inclusion in the LiST model due to insufficient data in favor or against the use of intervention (GRADE quality very low).

For Doppler velocimetry, there was a significant reduction of 29% in perinatal mortality and non-significant reduction of 35% in stillbirths in high risk pregnancies. The results across studies were consistent in both estimates and there was no significant heterogeneity in the pooled data (I^2 =0). The overall grade quality for reduction in perinatal mortality was that of 'moderate' level due to inadequate methods of sequence generation and allocation concealment in some of the included studies. Although the direction of effect (i.e. towards reduction) was similar for stillbirths, the overall grade quality of evidence for reduction in stillbirths was that of 'moderate' level. Keeping in mind the magnitude and direction of effect of these estimates, we recommend reduction in perinatal mortality [29 % (95 % CI 2% to 48%)] as a proxy for reduction in stillbirths with conversion of its overall quality grade from 'moderate' to 'low' level. This was to follow the theme of CHERG guidelines i.e. to select the most conservative estimate from the available data. The effect size for perinatal mortality (29%) was more conservative than that of stillbirth (35%). These recommendations can be interpreted as "Surveillance of high risk pregnancies with Doppler velocimetry of umbilical and fetal arteries with appropriate timely obstetric intervention leads to a reduction of 29 % (95 % CI 2% to 48%) in stillbirths".

Discussion

Maternal BMI screening is one of the methods that have been suggested to predict growth of fetus and related

Almstrom 1992
Biljan 1992
Burke 1992
Giles 2003
Haley 1997
Hofmeyr 1991
Johnstone 1993
Neales 1994
Newnham 1991
Nienhuis1997
Norman 1992
Ott 1998
Pattinson 1994
Trudinger 1987
Tyrrell 1990
Williams 2003

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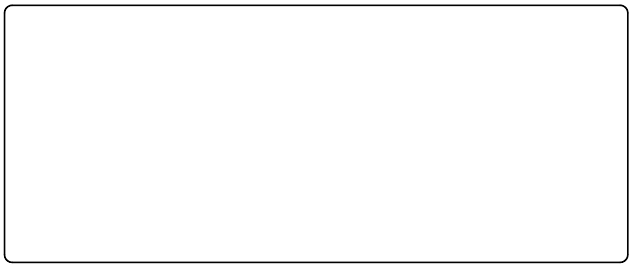
occurrence of low birth weight, and other perinatal adverse outcomes [16,20,21,68-73]. A Cochrane review on effectiveness of measurement of symphysis fundal

Doppler velocimetry is considered as one of the most objective methods to assess fetal wellbeing in cases of intrauterine growth restriction (IUGR) [13,15]. It provides information on fetal and placental cardiovascular function on the basis of the blood flow dynamics measured in uterine, umbilical and fetal arteries [80]. A Cochrane review by Alfirevic et al. comprising of 16 studies and involving 10, 225 babies had shown that fetal and umbilical artery Doppler ultrasound in high

[29 % (95 % CI 2% to 48 %)] as a proxy for reduction in stillbirths in high risk pregnancies. It is important to take into account that Doppler ultrasound is a screening test and cannot influence clinically important outcomes



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