MATERNAL, NEONATAL, AND CHILD HEALTH DIGEST

UNIVERSITY OF WASHINGTON STRATEGIC ANALYSIS, RESEARCH & TRAINING (START) CENTER

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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PRODUCED BY: BURKE, B; SLYKER, J

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3. **Performance of QuantiFERON-TB Gold Plus for detection of latent tuberculosis infection in pregnant women living in a tuberculosis- and HIV-endemic setting.** {Abstract & START Commentary} {Full article}
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6. **Neurodevelopmental outcomes of infants with very low birth weights are associated with the severity of their extra-uterine growth retardation.** {Abstract & START Commentary} {Full article}
   - This study aimed to explore the relationship between neurodevelopmental outcomes at the corrected age of 24 months and severity and duration of EUGR among very low birth weight infants.

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7. **Dynamics of paediatric urogenital schistosome infection, morbidity and treatment: a longitudinal study among preschool children in Zimbabwe.** {Abstract & START Commentary} {Full article}
   - Authors estimated the prevalence of and incidence of disease among this population, showed that treatment can reduce microhematuria, and that incident infections may affect growth and morbidity.

8. **National and regional under-5 mortality rate by economic status for low-income and middle-income countries: a systematic assessment.** {Abstract & START Commentary} {Full article}

- Authors evaluated disparities in under-5 mortality rates by household economic status in LMICs.

OPTIMIZE PREVENTION AND TREATMENT OF ACUTE ILLNESS

9. **Integration of postpartum healthcare services for HIV-infected women and their infants in South Africa: A randomised controlled trial.** {Abstract & START Commentary} {Full article}
   - In this study, authors evaluated the impact of integrated postpartum ART MCH intervention on ART adherence and viral suppression.

CROSS-CUTTING

10. **Status and drivers of maternal, newborn, child and adolescent health in the Islamic world: a comparative analysis.** {Abstract & START Commentary} {Full article}
    - Authors conducted an ecological study to understand maternal, newborn, child, and adolescent health in countries that are majority Muslim.

DETAILS OF ARTICLES

OPTIMIZING BIRTH OUTCOMES FOR MOTHERS AND NEWBORNS

1. [Prospective cohort study comparing outcomes between vacuum extraction and second-stage cesarean delivery at a Ugandan tertiary referral hospital.](#)
   Nolens B, Namiiro F, Lule J, van den Akker T, van Roosmalen J, Byamugisha J
   Int J Gynaecol Obstet. 2018 April. [Epub ahead of print]
   PubMed ID. 29630724

ABSTRACT
OBJECTIVE: To compare maternal and perinatal outcomes between vacuum extraction and second-stage cesarean delivery (SSCD).
METHODS: The present observational cohort study was conducted among women with term vertex singleton pregnancies who underwent vacuum extraction or SSCD at Mulago National Referral Hospital, Kampala, Uganda, between November 25, 2014, and July 8, 2015. Severe maternal outcomes (mortality, uterine rupture, hysterectomy, re-laparotomy) and perinatal outcomes (mortality, trauma, low Apgar score, convulsions) were compared between initial delivery mode.
RESULTS: Among 13 152 deliveries, 358 women who underwent vacuum extraction and 425 women who underwent SSCD were enrolled in the study. No maternal deaths occurred after vacuum extraction versus five deaths from complications of SSCD. Vacuum extraction was associated with less severe maternal outcomes compared with SSCD (3 [0.8%] vs 18 [4.2%]; adjusted odds ratio [aOR] 0.24, 95% confidence interval [CI] 0.07-0.84). Fetal death during the decision-to-delivery interval was also less common in the vacuum extraction group (3 [0.9%] vs 18 [4.4%]; aOR 0.24, 95% CI 0.07-0.84); however, the perinatal mortality rate did not differ between the vacuum extraction and SSCD groups (29 [8.4%] vs 45 [11.0%], respectively; aOR 0.83, 95% CI 0.49-1.41). One infant in each group exhibited neurodevelopmental anomalies at 6 months.
CONCLUSION: Vacuum extraction had better maternal outcomes and equivalent perinatal outcomes compared with SSCD. These findings encourage re-introduction of vacuum extraction.

START COMMENTARY: Two interventions to address prolonged second stage labor are vacuum extraction and cesarean section. While both of these approaches have risks, vacuum extraction is less invasive and less expensive than cesarean, but has a high failure rate. Due to this fear of failure and the need to delivery quickly, providers often default to cesarean delivery, although the risks may be greater. This study compared birth outcomes for each of these for both mother and infant. As delivery mode was not randomized, and there are different indications for caesarean and vacuum extraction, there is confounding by indication in this study and results must be interpreted cautiously. The women who received vacuum extraction were significantly different than the women who underwent a cesarean delivery in the proportion of the sample who are nulliparous, experienced a previous cesarean delivery, delivered an infant weighing more than 4000 grams, in the second stage of labor at hospital admission, indications (specifically, delay, fetal distress, other), and impending uterine rupture, as shown in Table 1.

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2. [Infection-Induced Thrombin Production: A Potential Novel Mechanism for Preterm Premature Rupture of Membranes (PPROM).](#)
   Feng L, Allen TK, Marinello WP, Murtha AP
   Am J Obstet Gynecol. 2018 April. [Epub ahead of print]
   PubMed ID. 29660299

ABSTRACT

BACKGROUND: Preterm premature rupture of membranes (PPROM) is a leading contributor to maternal and neonatal morbidity and mortality. Epidemiologic and experimental studies have demonstrated that thrombin causes fetal membrane weakening and subsequently PPROM. Although blood is suspected as the likely source of thrombin in fetal membranes and amniotic fluid of patients with PPROM, this has not been proven. Ureaplasma Parvum (U. parvum) is emerging as a pathogen involved in prematurity, including PPROM, but until now, prothrombin production directly induced by bacteria in fetal membranes has not been described.

OBJECTIVES: This study was designed to investigate whether U. parvum exposure can induce prothrombin production in fetal membranes cells.

STUDY DESIGN: Primary fetal membrane cells (amnion epithelial, chorion trophoblast, and decidua stromal) or full-thickness fetal membrane tissue explants from elective, term, uncomplicated cesarean deliveries were harvested. Cells or tissue explants were infected with live U. parvum (1 x 105, 1 x 106, or 1 x 107 colony forming units (cfu)/ml) or lipopolysaccharide (Escherichia coli J5, L-5014, Sigma, 100 ng/ml or 1000 ng/ml) for 24 hours. Tissue explants were fixed for immunohistochemistry staining of thrombin/prothrombin. Fetal membrane cells were fixed for confocal immunofluorescent staining of the biomarkers of fetal membrane cell types and thrombin/prothrombin. Protein and mRNA were harvested from the cells and tissue explants for Western blot or qRT-PCR to quantify thrombin/prothrombin protein or mRNA production, respectively. Data are presented as mean values ± standard errors of mean. Data were analyzed using one-way ANOVA with post hoc Dunnett's test.

RESULTS: Prothrombin production and localization was confirmed by Western blot and immunostainings in all primary fetal membrane cells and tissue explants. Immunofluorescence observations revealed a perinuclear localization of prothrombin in amnion epithelial cells. Localization of prothrombin in chorion and decidua cells was perinuclear and cytoplasmic. Prothrombin mRNA and protein expression in fetal membranes was significantly increased by U. parvum, but not lipopolysaccharide, treatments in a dose-dependent manner. Specifically, U. parvum at a dose of 1x107 cfu/ml significantly increased both prothrombin mRNA (fold changes in amnion: 4.1±1.9; chorion: 5.7±4.2; decidua: 10.0±5.4; FM: 9.2±3.0) and protein expression (fold changes in amnion: 138.0±44.0; chorion: 139.6±15.1; decidua: 56.9±29.1; fetal membrane: 133.1±40.0) compared to untreated controls. U. parvum at a dose of 1x106 cfu/ml significantly upregulated prothrombin protein expression in chorion cells (fold change: 54.9±5.3) and prothrombin mRNA expression in decidua cells (fold change: 4.4±1.9).

CONCLUSIONS: Our results demonstrate that prothrombin can be directly produced by fetal membrane amnion, chorion, and decidua cells. Further, prothrombin production can be stimulated by U. parvum exposure in fetal membranes. These findings represent a potential novel underlying mechanism of U. parvum-induced rupture of fetal membranes.

START COMMENTARY: Before this study, it was known that Ureaplasma infection and prothombin were each independently associated with preterm birth; this report advances our mechanistic understanding

of preterm birth by drawing links between maternal infection with the organism, increased fetal prothrombin production, and PROM. This study shows that *U. parvum* exposure to fetal membrane tissues leads to increased prothrombin production in a dose-dependent manner, which in turn, leads to changes in characteristics of PROM. One limitation is the use of gram-negative bacterial lipopolysaccharide (LPS) as the comparison, instead of live *E. coli*. Authors used LPS as live *E. coli* has challenges with overgrowth but, acknowledge that they cannot conclude that live *E. coli* does not also stimulate prothrombin production through another endotoxin.

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3. [Performance of QuantiFERON-TB Gold Plus for detection of latent tuberculosis infection in pregnant women living in a tuberculosis- and HIV-endemic setting](#)
König Walles J, Tesfaye F, Jansson M, Tolera Balcha T, Winqvist N, Kefeni M, et al.
*PLoS One.*13(4). 2018 April.
PubMed ID. 29617458

ABSTRACT

We evaluated the performance of QuantiFERON-TB Gold Plus (QFT-Plus), which includes two Mycobacterium tuberculosis antigen formulations (TB1 and TB2), for detection of latent tuberculosis infection during pregnancy. Eight-hundred-twenty-nine Ethiopian pregnant women (5.9% HIV-positive) were tested with QFT-Plus, with bacteriological sputum analysis performed for women with clinically suspected tuberculosis and HIV-positive women irrespective of clinical presentation. QFT-Plus read-out was categorized according to the conventional cut-off (0.35 IU/ml) for both antigen formulations. In addition, we analyzed the distribution of QFT-Plus results within a borderline zone (0.20-0.70 IU/ml), and interferon-γ response in relation to HIV infection and gestational age. Two-hundred-seventy-seven women (33%) were QFT-Plus-positive (HIV-positive 16/49 [33%]; HIV-negative 261/780 [33%]). There was a strong agreement between the two antigen formulations (κ = 0.92), with discordant results in 29 cases (3.5%). Whereas discordant QFT-Plus results were rare in pregnancy, several results with both TB1 and TB2 within the borderline range were observed (11/49 [22%] vs. 43/780 [5.5%] in HIV-positive and HIV-negative women, respectively; p<0.0001). HIV-positive women had lower absolute interferon-γ levels (TB1: 0.47 vs. 2.16 IU/ml; p<0.001, TB2: 0.49 vs. 2.24 IU/ml, p<0.001, considering results ≥0.20 IU/ml) compared to HIV-negative women. QFT-Plus-positive women who submitted samples at later stages of pregnancy had lower mitogen- (p<0.001) but higher TB-antigen-specific (p = 0.031 for TB1, p = 0.061 for TB2) interferon-γ response. Considering their lower capacity to produce TB-specific interferon-γ, a lower cut-off level for defining QFT-Plus-positivity may be considered in HIV-positive pregnant women.

START COMMENTARY: It is well-known that immunoassays to detect LTBI have reduced sensitivity in pregnant women and individuals with HIV. This study is the first evaluation of the QFT-Plus assay for diagnosis of LTBI in pregnancy. Authors evaluated the performance of QFT-Plus among a cohort of pregnant women in Ethiopia, with about 6% of the sample also being HIV-positive. Figure 1 shows lower IFN-γ responses to TB1 and TB2 stimulation in HIV positive compared to negative women. In addition, they found that HIV positive women were more likely to have responses that which were below the assay's stated limit of detection (Figure 2). As there is not a gold standard for LTBI, the optimal cutoff for defining LTBI with this test is unknown, although these findings suggest that a lower limit of detection may be appropriate for use of this assay in HIV-infected women. A limitation of the study is the lack of a control group of non-pregnant women.

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4. [Utility of serum resistin in the diagnosis of neonatal sepsis and prediction of disease severity in term and late preterm infants](#)
Khattab AA, El-Mekkawy MS, Helwa MA, Omar ES

ABSTRACT

INTRODUCTION: Resistin is a proinflammatory hormone recently proposed as a sepsis biomarker. Our aim was to evaluate the diagnostic and prognostic values of this marker in neonatal sepsis.
METHODS: This is a prospective observational study that includes 60 term and late preterm neonates with proven and possible sepsis besides 30 healthy controls. Resistin and other biomarkers, like C-reactive protein (CRP), were measured within 2 h of neonatal intensive care unit (NICU) admission. Infants were monitored and the primary outcome was 30-day mortality.
RESULTS: Resistin was higher among septic neonates compared with controls ($P<0.001$). Resistin had an area under the receiver operating characteristic (ROC) curve of 0.994 for differentiating septic infants from controls. The area under the curve (AUC) for differentiating infants with culture-proven sepsis from controls was 0.999 compared with an AUC of 1 for CRP. The other markers, like platelet count, were inferior to resistin and CRP. Resistin was positively correlated with CRP [Spearman's correlation coefficient $(rs)=0.55$, $P<0.001$]. No significant differences in resistin levels were noted between survivors and non-survivors but resistin was higher among infants with severe sepsis ($P=0.015$) and among those who needed mechanical ventilation ($P<0.001$).
CONCLUSION: Resistin is useful for the diagnosis of neonatal sepsis. Resistin failed to predict mortality but was associated with indicators of disease severity.

START COMMENTARY: This study shows that resistin was a very accurate biomarker for neonatal sepsis, which has not been previously reported. Controls are healthy neonates without exposure to prolonged rupture of membranes. Cases were term or late term preterm infant from age 0-30 days with proven or possible sepsis. Authors excluded infants born less than 34 weeks or more than 42 weeks, those with postnatal age more than 30 days, those who failed to get a blood sample within 2 hours of admission, and those with any of the following: genetic syndromes, major congenital abnormalities, surgical conditions, meconium aspiration syndrome, perinatal asphyxia, and/or birth injury. Proven sepsis was diagnosed when pathogen isolated from blood, urine, cerebrospinal fluid, or normally sterile sites associated with clinical features of sepsis. Possible sepsis was diagnosed in the presence of clinical features indicating sepsis and raised CRP (>5mg/dL). When using a resistin level cut off of 22.8 ng/ml, the sensitivity is 98.3% and specificity is 99.97% for sepsis. A limitation of the study is possible and proven sepsis cases were grouped together, with some potential misclassification of the possible group. Limitations also include small sample size and a sample that excluded preterm infants under 34 weeks, limiting generalizability. In addition, it is still not known if resistin has the same challenges as other sepsis biomarkers for neonates where the levels can rise in septic and non-septic conditions.

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ABSTRACT
BACKGROUND: Anemia affects as many as half of all pregnant women in low-income and middle-income countries, but the burden of disease and associated maternal mortality are not robustly quantified. We aimed to assess the association between severe anemia and maternal death with data from the WHO Multicountry Survey on maternal and newborn health.
METHODS: We used multilevel and propensity score regression analyses to establish the relation between severe anemia and maternal death in 359 health facilities in 29 countries across Latin America, Africa, the Western Pacific, eastern Mediterranean, and southeast Asia. Severe anemia was defined as antenatal or postnatal hemoglobin concentrations of less than 70 g/L in a blood sample obtained before death. Maternal death was defined as death any time after admission until the seventh day post partum or discharge. In regression analyses, we adjusted for post-partum hemorrhage, general anesthesia, admission to intensive care, sepsis, pre-eclampsia or eclampsia, thrombocytopenia, shock, massive transfusion, severe oliguria, failure to form clots, and severe acidosis as confounding variables. These variables were used to develop the propensity score.
FINDINGS: 312 281 women admitted in labor or with ectopic pregnancies were included in the adjusted multilevel logistic analysis, and 12 470 were included in the propensity score regression analysis. The adjusted odds ratio for maternal death in women with severe anemia compared with those without severe anemia was 2·36 (95% CI 1·60-3·48). In the propensity score analysis, severe anemia was also associated with maternal death (adjusted odds ratio 1·86 [95% CI 1·39-2·49]).
INTERPRETATION: Prevention and treatment of anemia during pregnancy and post partum should remain a global public health and research priority.

START COMMENTARY: Authors used multilevel logistic regression and propensity score regression analysis to explore the relationship between maternal mortality and severe anemia. They did propensity score analysis to mitigate confounding bias due to differences in women with and without anemia, as shown in Table 1. The authors conducted sensitivity analysis to explore the effect of post-partum hemorrhage on this association. When they removed it from the multilevel regression model, the strength of the association increased. Some strengths of the study are the large dataset and use of two analysis approaches. Some limitations are the limited number of variables available for adjustment, anemia treated as a binary variable in the dataset, and missing data. Note that the definition for maternal mortality for this study is not the standard definition used for maternal mortality; the standard definition according to the WHO is death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of duration and site of pregnancy, from any cause related to or aggravated by pregnancy, but not from an accident or incidental cause.

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6. [Neurodevelopmental outcomes of infants with very low birth weights are associated with the severity of their extra-uterine growth retardation](#)
Chien HC, Chen CH, Wang TM, Hsu YC, Lin MC
*Pediatr Neonatol.*52(2). 2018 April.
PubMed ID. 28866004

ABSTRACT

BACKGROUND: For infants with very low birth weights (VLBW), their neurodevelopmental outcomes are thought to be associated with extra-uterine growth retardation (EUGR). In this study, based on a single institute, we analyzed the association between different levels or severity of EUGR of VLBW infants and their neurodevelopmental outcomes later at a corrected age of 24 months.

METHODS: This is a hospital-based retrospective cohort study. The severity of EUGR was classified into three categories according to the z-score of discharge weight: z < -2.0, <-2.5, and <-3.0. The outcomes were assessed using the Bayley Scales of Infant Development-II (BSID-II) at a corrected age of 24 months. We then estimated the association of EUGR with low mental developmental index (MDI) or low psychomotor developmental index (PDI). Multiple logistic regression and stratified analyses were used to adjust for the possible confounding factors.

RESULTS: In total, 224 VLBW infants were enrolled in this study from 1997 to 2006. In the univariate analysis, EUGR for weight at discharge from hospital was associated with MDI <85 at the corrected age of 24 months, and this association was related to the severity of EUGR (z < -2.5, OR: 1.92 (1.04-3.53); z < -3.0, OR: 2.83 (1.26-6.36)). In addition, the relationship was not confounded by gender nor small for gestational age. The stratified analysis against hemodynamic significant patent ductus arteriosus also revealed that EUGR was an independent predictor for neurodevelopmental outcomes.

CONCLUSION: In VLBW preterm infants, EUGR was significantly associated with low MDI scores assessed at a corrected age of 24 months. Early evaluation and recognition of EUGR should be emphasized when caring for preterm infants.

START COMMENTARY: This study aimed to explore the relationship between neurodevelopmental outcomes and severity and duration of EUGR among very low birth weight infants. The inclusion criteria were preterm infants with birth weight less than 1500 g who were treated in the neonatal intensive care units of Taichung Veterans General Hospital. Authors used the following exclusion criteria: infants with chromosome anomalies, hydrocephalus, neonatal seizures, congenital brain malformations, cystic PVL or severe IVH during hospitalization, and those infants who missed the last follow up. The odds ratios for low MDI by EUGR weight z-score are presented in Figure 1, showing a clear increase in odds of low MDI score with negatively increasing z-scores for EUGR weight. Some limitations of this study are the small sample size, retrospective chart reviews, one hospital provided all the data, and missing data.

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7. [Dynamics of paediatric urogenital schistosome infection, morbidity and treatment: a longitudinal study among preschool children in Zimbabwe](#)
   Osakunor DNM, Mduluza T, Midzi N, Chase-Topping M, Mutsaka-Makuvaza MJ, Chimponda T, et al.
   *BMJ Glob Health.*3(2). 2018 March.
   PubMed ID. 29616147

ABSTRACT
BACKGROUND: Recent research has shown that in schistosome-endemic areas preschool-aged children (PSAC), that is, ≤5 years, are at risk of infection. However, there exists a knowledge gap on the dynamics of infection and morbidity in this age group. In this study, we determined the incidence and dynamics of the first urogenital schistosome infections, morbidity and treatment in PSAC.
METHODS: Children (6 months to 5 years) were recruited and followed up for 12 months. Baseline demographics, anthropometric and parasitology data were collected from 1502 children. Urinary morbidity was assessed by hematuria and growth-related morbidity was assessed using standard WHO anthropometric indices. Children negative for Schistosoma haematobium infection were followed up quarterly to determine infection and morbidity incidence.
RESULTS: At baseline, the prevalence of S haematobium infection and microhematuria was 8.5% and 8.6%, respectively. Based on different anthropometric indices, 2.2%-8.2% of children were malnourished, 10.1% underweight and 18.0% stunted. The fraction of morbidity attributable to schistosome infection was 92% for microhematuria, 38% for stunting and malnutrition at 9%-34%, depending on indices used. S haematobium-positive children were at greater odds of presenting with microhematuria (adjusted OR (AOR)=25.6; 95% CI 14.5 to 45.1) and stunting (AOR=1.7; 95% CI 1.1 to 2.7). Annual incidence of S haematobium infection and microhematuria was 17.4% and 20.4%, respectively. Microhematuria occurred within 3 months of first infection and resolved in a significant number of children, 12 weeks post-praziquantel treatment, from 42.3% to 10.3%; P<0.001.
CONCLUSION: We demonstrated for the first time the incidence of schistosome infection in PSAC, along with microhematuria, which appears within 3 months of first infection and resolves after praziquantel treatment. A proportion of stunting and malnutrition is attributable to S haematobium infection. The study adds scientific evidence to the calls for inclusion of PSAC in schistosome control programs.

START COMMENTARY: While previous longitudinal studies on schistosome incidence and pathogenesis have primarily focused on children > 5 years old, there are fewer data available in younger children. Authors of this study followed a sample of uninfected children at baseline for a year. Authors estimated the prevalence of and incidence of disease among this population, showed that treatment can reduce microhematuria, and that incident infections may affect growth and morbidity. Children were recruited for the study from creches, early child development centers, and preschools. The study inclusion criteria for enrollment were children aged 6 months to 5 years who were lifelong residents of the study area, have no previous antihelminthic treatment, were negative for *S. mansoni*, consented to participate, and were diagnosed negative for *S. haematobium* by egg count at baseline. This region was selected for the study because it has a high prevalence of *S. haematobium* and low prevalence of *S. mansoini* (which could confound growth and morbidity results). To determine infection, authors collected urine samples

for haematuria and stool for parasite eggs. Authors found more intense infections with greater age, as shown in Figure 1. Figure 2 shows the proportion with morbidity among those infected, compared to the total population. Figure 4 shows how infection impacts morbidity among 18 individuals in the study. A limitation is that investigators did not collect data on diet, coinfection, or socioeconomic status, which could have confounded results.

8. [National and regional under-5 mortality rate by economic status for low-income and middle-income countries: a systematic assessment](#)
Chao F, You D, Pedersen J, Hug L, Alkema L
*Lancet Glob Health.*6(5). 2018 May.
PubMed ID. 29653627

ABSTRACT
BACKGROUND: The progress to achieve the fourth Millennium Development Goal in reducing mortality rate in children younger than 5 years since 1990 has been remarkable. However, work remains to be done in the Sustainable Development Goal era. Estimates of under-5 mortality rates at the national level can hide disparities within countries. We assessed disparities in under-5 mortality rates by household economic status in low-income and middle-income countries (LMICs).
METHOD: We estimated country-year-specific under-5 mortality rates by wealth quintile on the basis of household wealth indices for 137 LMICs from 1990 to 2016, using a Bayesian statistical model. We estimated the association between quintile-specific and national-level under-5 mortality rates. We assessed the levels and trends of absolute and relative disparity in under-5 mortality rate between the poorest and richest quintiles, and among all quintiles.
FINDINGS: In 2016, for all LMICs (excluding China), the aggregated under-5 mortality rate was 64·6 (90% uncertainty interval [UI] 61·1-70·1) deaths per 1000 livebirths in the poorest households (first quintile), 31·3 (29·5-34·2) deaths per 1000 livebirths in the richest households (fifth quintile), and in between those outcomes for the middle quintiles. Between 1990 and 2016, the largest absolute decline in under-5 mortality rate occurred in the two poorest quintiles: 77·6 (90% UI 71·2-82·6) deaths per 1000 livebirths in the poorest quintile and 77·9 (72·0-82·2) deaths per 1000 livebirths in the second poorest quintile. The difference in under-5 mortality rate between the poorest and richest quintiles decreased significantly by 38·8 (90% UI 32·9-43·8) deaths per 1000 livebirths between 1990 and 2016. The poorest to richest under-5 mortality rate ratio, however, remained similar (2·03 [90% UI 1·94-2·11] in 1990, 1·99 [1·91-2·08] in 2000, and 2·06 [1·92-2·20] in 2016). During 1990-2016, around half of the total under-5 deaths occurred in the poorest two quintiles (48·5% in 1990 and 2000, 49·5% in 2016) and less than a third were in the richest two quintiles (30·4% in 1990, 30·5% in 2000, 29·9% in 2016). For all regions, differences in the under-5 mortality rate between the first and fifth quintiles decreased significantly, ranging from 20·6 (90% UI 15·9-25·1) deaths per 1000 livebirths in eastern Europe and central Asia to 59·5 (48·5-70·4) deaths per 1000 livebirths in south Asia. In 2016, the ratios of under-5 mortality rate in the first quintile to under-5 mortality rate in the fifth quintile were significantly above 2·00 in two regions, with 2·49 (90% UI 2·15-2·87) in east Asia and Pacific (excluding China) and 2·41 (2·05-2·80) in south Asia. Eastern and southern Africa had the smallest ratio in 2016 at 1·62 (90% UI 1·48-1·76). Our model suggested that the expected ratio of under-5 mortality rate in the first quintile to under-5 mortality rate in the fifth quintile increases as national-level under-5 mortality rate decreases.
INTERPRETATION: For all LMICs (excluding China) combined, the absolute disparities in under-5 mortality rate between the poorest and richest households have narrowed significantly since 1990, whereas the relative differences have remained stable. To further narrow the rich-and-poor gap in under-5 mortality rate on the relative scale, targeted interventions that focus on the poorest populations are needed.

START COMMENTARY:

This is the first study to model the association between the ratio of the poorest to richest under-5 mortality rates, the national-level under-5 mortality rates, and to estimate under-5 mortality rates for all wealth quintile groups. All data comes from the Demographic Health Surveys (DHS) and Multiple Indicator Cluster Surveys (MICS) completed between 1990 and 2016 in 99 LMICs. The wealth index from the DHS is used as a proxy for household wealth. Authors treated the middle wealth group (quintile 3) as the reference group. The main finding is that disparities in under 5 mortality have narrowed on the additive scale (under-5 mortality rate) but have stayed constant on the multiplicative scale (under-5 mortality rate ratio), as shown in Table 1 and Figure 2. In addition, as the national under-5 mortality rate decreases, generally, the ratio of first to fifth quintile morality rate increases, as shown in Figure 5. So, the disparity continues and grows as countries reduce their under-5 mortality rates. Some limitations of this analysis are that authors did not have data for 38 of the 137 LMICs and sometimes the available data was old.

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OPTIMIZE PREVENTION AND TREATMENT OF ACUTE ILLNESS

9. Integration of postpartum healthcare services for HIV-infected women and their infants in South Africa: A randomised controlled trial
Myer L, Phillips TK, Zerbe A, Brittain K, Lesosky M, Hsiao NY, et al.
*PLoS Med.*15(3). 2018 March.
PubMed ID. 29601570

ABSTRACT

BACKGROUND: As the number of HIV-infected women initiating lifelong antiretroviral therapy (ART) during pregnancy increases globally, concerns have emerged regarding low levels of retention in HIV services and suboptimal adherence to ART during the postpartum period. We examined the impact of integrating postpartum ART for HIV+ mothers alongside infant follow-up within maternal and child health (MCH) services in Cape Town, South Africa.

METHODS AND FINDINGS: We conducted a randomized trial among HIV+ postpartum women aged ≥18 years who initiated ART during pregnancy in the local antenatal care clinic and were breastfeeding when screened before 6 weeks postpartum. We compared an integrated postnatal service among mothers and their infants (the MCH-ART intervention) to the local standard of care (control)-immediate postnatal referral of HIV+ women on ART to general adult ART services and their infants to separate routine infant follow-up. Evaluation data were collected through medical records and trial measurement visits scheduled and located separately from healthcare services involved in either arm. The primary trial outcome was a composite endpoint of women's retention in ART care and viral suppression (VS) (viral load < 50 copies/ml) at 12 months postpartum; secondary outcomes included duration of any and exclusive breastfeeding, mother-to-child HIV transmission, and infant mortality. Between 5 June 2013 and 10 December 2014, a total of 471 mother-infant pairs were enrolled and randomized (mean age, 28.6 years; 18% nulliparous; 57% newly diagnosed with HIV in pregnancy; median duration of ART use at randomization, 18 weeks). Among 411 women (87%) with primary endpoint data available, 77% of women (n = 155) randomized to the MCH-ART intervention achieved the primary composite outcome of retention in ART services with VS at 12 months postpartum, compared to 56% of women (n = 117) randomized to the control arm (absolute risk difference, 0.21; 95% CI: 0.12-0.30; p < 0.001). The findings for improved retention in care and VS among women in the MCH-ART intervention arm were consistent across subgroups of participants according to demographic and clinical characteristics. The median durations of any breastfeeding and exclusive breastfeeding were longer in women randomized to the intervention versus control arm (6.9 versus 3.0 months, p = 0.006, and 3.0 versus 1.4 months, p < 0.001, respectively). For the infants, overall HIV-free survival through 12 months of age was 97%: mother-to-child HIV transmission was 1.2% overall (n = 4 and n = 1 transmissions in the intervention and control arms, respectively), and infant mortality was 1.9% (n = 6 and n = 3 deaths in the intervention and control arms, respectively), and these outcomes were similar by trial arm. Interpretation of these findings should be qualified by the location of this study in a single urban area as well as the self-reported nature of breastfeeding outcomes.

CONCLUSIONS: In this study, we found that integrating ART services into the MCH platform during the postnatal period was a simple and effective intervention, and this should be considered for improving maternal and child outcomes in the context of HIV.

START COMMENTARY: Integration of ART with MCH services is an approach to increase retention in care and adherence/viral suppression of postpartum HIV-infected women. In this study, authors evaluated the impact of this intervention adherence to ART services and viral suppression. Authors found the intervention to lead to improved retention in care and viral suppression among women in the intervention arm, as well as increasing breastfeeding duration. The study eligibility criteria were: >18 years old, <6 weeks postpartum, initiated ART during a recently-completed pregnancy, and breastfeeding their infant at time of screening. Note that the eligibility for ART initiation changed during the study enrollment period to reflect a change in WHO recommendations. To understand the effect of the change in eligibility, authors conducted sensitivity analysis to see if findings differed by enrollment requirements but found findings to be consistent across eligibility criteria. The effect of the intervention was related to the amount of exposure, in a graded manner. Women were referred out once they stopped breastfeeding. Women who were referred out within 3 months had similar results to the control group, while women with at least 9 months of exposure to the intervention had the best HIV viral load and ART retention outcomes. The effect of the intervention was consistent across subgroups, including across CD4 counts at first antenatal visit and education level, as shown in Figure 3. The time to cessation of breastfeeding was longer for women in the intervention group, as shown in the survival analysis in Figure 4. Some limitations of the study are that authors did not have power to detect associations with outcomes that were extremely common, such as contraceptive initiation, or very rare, such as mother-to-child HIV transmission. In addition, all the study data comes from one location, limiting generalizability, and breastfeeding data were self-reported.

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10. [Status and drivers of maternal, newborn, child and adolescent health in the Islamic world: a comparative analysis](#)
    Akseer N, Kamali M, Bakhache N, Mirza M, Mehta S, Al-Gashm S, et al.
    *Lancet.*391(10129). 2018 April.
    PubMed ID. 29395272

ABSTRACT
BACKGROUND: The Millennium Development Goal (MDG) period saw dramatic gains in health goals MDG 4 and MDG 5 for improving child and maternal health. However, many Muslim countries in the south Asian, Middle Eastern, and African regions lagged behind. In this study, we aimed to evaluate the status of, progress in, and key determinants of reproductive, maternal, newborn, child, and adolescent health in Muslim majority countries (MMCs). The specific objectives were to understand the current status and progress in reproductive, maternal, newborn, child, and adolescent health in MMCs, and the determinants of child survival among the least developed countries among the MMCs; to explore differences in outcomes and the key contextual determinants of health between MMCs and non-MMCs; and to understand the health service coverage and contextual determinants that differ between best and poor or moderate performing MMCs.
METHODS: In this country-level ecological study, we examined data from between 1990 and 2015 from multiple publicly available data repositories. We examined 47 MMCs, of which 26 were among the 75 high-burden Countdown to 2015 countries. These 26 MMCs were compared with 48 non-Muslim Countdown countries. We also examined characteristics of the eight best performing MMCs that had accelerated improvement in child survival (ie, that reached their MDG 4 targets). We estimated adolescent, maternal, under-5, and newborn mortality, and stillbirths, and the causes of death, essential interventions coverage, and contextual determinants for all MMCs and comparative groups using standardized methods. We also did a hierarchical multivariable analysis of determinants of under-5 mortality and newborn mortality in low-income and middle-income MMCs.
FINDINGS: Despite notable reductions between 1990 and 2015, MMCs compared with a global estimate of all countries including MMCs had higher mortality rates, and MMCs relative to non-MMCs within Countdown countries also performed worse. Coverage of essential interventions across the continuum of care was on average lower among MMCs, especially for indicators of reproductive health, prenatal care, delivery, and labor, and childhood vaccines. Outcomes within MMCs for mortality and many reproductive, maternal, newborn, child, and adolescent health indicators varied considerably. Structural and contextual factors, especially state governance, conflict, and women and girl's empowerment indicators, were significantly worse in MMCs compared with non-MMCs within the high-burden Countdown countries, and were shown to be strongly associated with child and newborn mortality within low-income and middle-income MMCs. In adjusted hierarchical models, among other factors, under-5 mortality in MMCs increased with more refugees originating from a country (β=23·67, p=0·0116), and decreased with better political stability or absence of terrorism (β=-0·99, p=0·0285), greater political rights or government effectiveness (β=-1·17, p<0·0001), improvements in log gross national income per capita (β=-4·44, p<0·0001), higher total adult literacy (β=-1·69, p<0·0001), higher female adult literacy (β=-0·97, p<0·0001), and greater female to male enrolment in secondary school (β=-16·1, p<0·0001). The best performing MMCs were Azerbaijan, Bangladesh, Egypt, Indonesia, Kyrgyzstan, Morocco, Niger, and Senegal, which had higher coverage of family planning interventions and newborn or child vaccinations, and excelled in many of the above contextual determinants when compared with moderate or poorly performing MMCs.

INTERPRETATION: The status and progress in reproductive, maternal, newborn, child, and adolescent health is heterogeneous among MMCs, with little indication that religion and its practice affects outcomes systemically. Some Islamic countries such as Niger and Bangladesh have made great progress, despite poverty. Key findings from this study have policy and programmatic implications that could be prioritized by national heads of state and policy makers, development partners, funders, and the Organization of the Islamic Cooperation to scale up and improve these health outcomes in Muslim countries in the post-2015 era.

START COMMENTARY: Authors conducted an ecological study to understand maternal, newborn, child, and adolescent health in countries that are more than 50% Muslim (referred to as Muslim-majority countries or MMC). The authors examined indicators within MMC and compared MMC to non-MMC within the 75 high-burden Countdown to 2015 countries. Authors used many different data sources for their analysis. The data sources predominately came from the United Nations, the Institute for Health Metrics and Evaluation, the World Bank, UNICEF, and WHO, as shown in Table 1. As this is an ecological study, the results should be interpreted with caution and cannot be used to infer causation.

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