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3D Display of Stillbirth in Indonesian Obstetrics Part 6: Fetal Sex as Maternal Morbidity Determinant?

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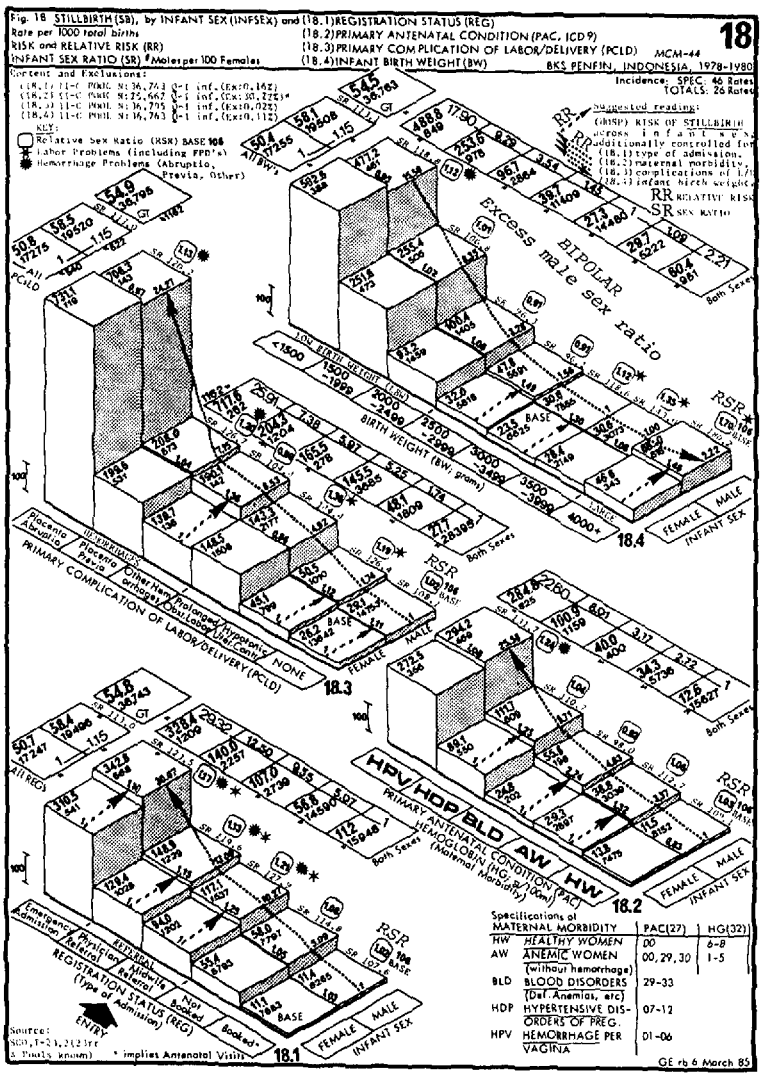
Introduction

In five previous reports in this journal, the risk of stillbirth (SB) in Indonesian university obstetrics for 36,802 singleton-birth deliveries from 1978-1980 was selectively controlled for 8 factors (birth weight, complications, morbidity, registration, antenatal visits, contraceptive use, parity and residence). This report is to introduce as ninth control variable: infant sex.

Material and Method

The material and method remains unchanged. In addition to infant sex, the stillbirth risk is cocontrolled for registration status (Fig. 18.1), maternal morbidity (Fig. 18.2), complications of labor a/o delivery (Fig. 18.3), and birth weight (Fig. 18.4). For each control category, one may calculate the male/female relative risk of stillbirth (RR), the sex ratio of the cells (SR), and the SR relative to 106/100 (RSR), the latter being a measure of the 'excess male sex ratio'. These indices are given in Fig. 18. The *bipolar RSR* in Fig. 18.4 then triggers the display of three complication categories as a function of both infant sex and birth weight (Fig. 19): an informative 'prevalence display'.



Results

Stillbirth by infant sex & four cocontrols

Fig. 18.1 shows *excess male SB risks (EMSB)* for referrals and emergency admissions as well as *excess male SEX ratios (EMSR)*. Fig. 18.2 shows EMSB risks for various *morbidity categories* and an important EMSR (1.24)* for hemorrhage per vaginam (HPV). Fig. 18.3 shows EMSB *risks for unspecified hemorrhage* (1.36) & *notable* EMSR for placenta previa and placenta abruptio (1.20, 1.13).* Fig. 18.4, which controls SB risk for infant sex & *birth* weight, shows EMSB risks for *non-LBW* categories and notable EMSR *at the two extremes of the birth weight distribution* (*1.70*- 1.35*- 1.12*- 0.91 - 0.91 - 1.01 - 1.12*).* This bipolar EMSR points to the existence of two different problems. At higher birth weights, the excess male sex ratio (EMSR) pertains to the known higher birth weight of males over females which in turn links with more complications of labor/delivery - explaining higher SB risks. By contrast, the noted excess male sex ratio (EMSR) at very low birth weight (<1500g) is an interesting observation that may be linked with placenta abruptio, placenta previa, hemorrhage per vaginam, etc. A hypothesis thus emerges: such pathologies during pregnancy are more frequent for women carrying a male infant. This may be instantly examined by displaying the *sex-specific prevalence* of these pathologies for specific birth weight classes.

Three specific complications by SEX and BW

Fig. 19.1 gives the prevalence of placenta previa by SEX and BW. Overall, 3.27% of all deliveries had a placenta previa, the peak prevalence being 14.01% for women whose infant weighs 1500-1999g - the base prevalence being 1.15% for *women carrying a large baby*. Note the 'excess male prevalence' of placenta previa for birth *weights* 1500-1999g (1.20).

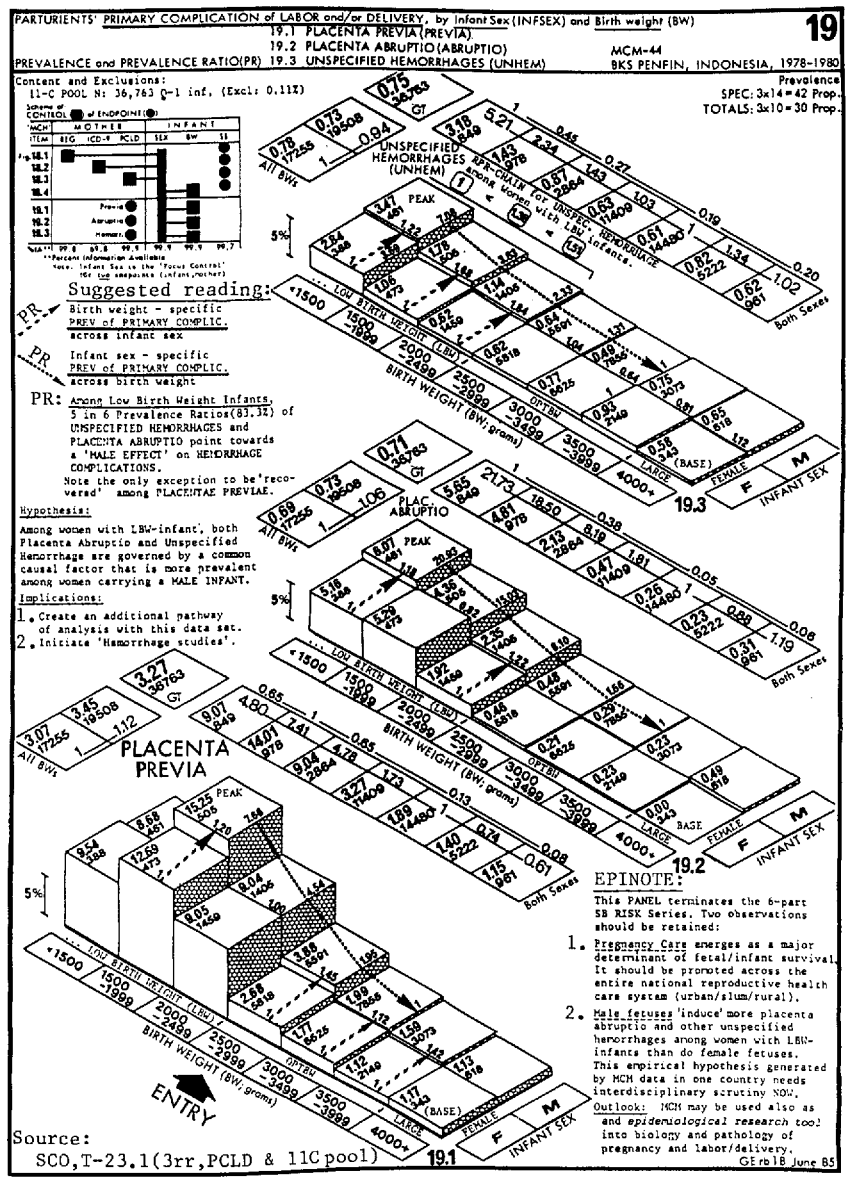
Fig. 19.2 gives the prevalence of placenta abruptio by SEX and BW. Overall, 0.71% of all deliveries had a placenta abruptio. A strong inverse relationship emerges between birth weight and placenta abruptio (over 20-fold variation). In addition, 'excess male prevalence' of placenta abruptio (1.22; 1.18) *is noted for two of* the three low birth weight categories. Hypothesis: A bleeding placenta *previa may mask* placenta abruptio. Concomitant study of Figs. 19.1 and 19.2 suggests placenta abruptio to be *more* prevalent among women with male fetuses for *all three LBW categories*. Male infant - LBW - placenta abruptio would thus appear to be somehow related.

Fig. 19.3 gives the prevalence of unspecified hemorrhage by SEX and BW. Overall, 0.75% of all deliveries were accompanied by unspecified bleeding. Again, a strong inverse relationship with birth weight emerges. In addition, for *all three LBW categories* there is a notable 'excess male prevalence' of unspecified hemorrhage (1.84 - 1.68 - 1.22). The empirical hypothesis thus is: male fetuses 'induce' more placenta abruptio and unspecified hemorrhage than do female infants.

Discussion

The *BIPOLAR* excess male sex ratio noted in Fig. 18.4 points to two different causes operational at opposite ends of the birth weight distribution. At the upper BW-end, prolonged/obstructed labor dominates the EMSR (not given here). At the lower BW-end, the three complication groups displayed in Fig. 19 are operational (placenta previa, placenta abruptio, and other hemorrhages). The synthesis of Fig. 19 is that placenta abruptio & unspecified hemorrhages may have a common factor operating not only during the *third* trimester, but possibly during the *second* or even the *first*. And that this factor is more prevalent among male fetuses. This leads to the hypothesis that male conceptuses produce/carry a factor to a greater extent than female conceptuses that may be responsible for 'excess male *first* trimester hemorrhages', excess male *first* trimester spontaneous abortions, etc. In other words, excess male hemorrhage of placenta previa, excess male placenta abruptio, and excess male unspecified hemorrhages *at the end of the second* trimester or the beginning of the *third* trimester – as picked up in Fig. 19 – may be caused by a factor also responsible for *spontaneous abortion*.

Two publications in the mid-sixties by Rhodes (1) and Hibbard (2) from British hospitals are in line with the Indonesian findings. Hibbard's line of reasoning is particularly worthy of consideration when analyzing important data sets from developing countries (2). The findings make now mandatory a new pathway of analysis for the frozen data set.



Summary and Outlook

Part 6 of the 'SB risk series' is a transition paper from stillbirth to comlications & morbidities. Higher prevalences of *placenta abruptio* & *unspecified hemorrhages* among mothers with male LBW infants, amounts to the empirical hypothesis: the fetus per se may induce such pathologies and the causal factor is more prevalent among male fetuses. Since selection bias may be excluded and referral centers serve as loci of accumulation of rare pathologies, these rare events become amenable to analytical epidemiology. The Indonesian findings from 11 university hospitals confirm two observations in British hospitals (1,2) while the current data set allowed to control for birth weight and thus narrow down the pregnancy period with excess male sex ratios. A new analytical pathway is now needed that would take into account such variables as maternal antenatal condition, previous spontaneous abortion, infant sex, gest. age, birth weight, and infant outcome.

Zusammenfassung und Ausblick

Teil 6 dieser Totgeburtenstudie ist ein Uebergang zur Studie von Komplikationen und Morbiditäten im letzten Schwangerschaftsdrittel. Höhere Prävalenzen von *Plazenta abruptio* und *Blutungen* unter den Frauen mit männlichen Foeten und niedrigem Geburtsgewicht kommt folgender empirischen Hypothese gleich: der Foetus selbst induziert solche Pathologien und der Kausalfaktor ist bei den männlichen Foeten reicher vertreten. Da Fehlerquellen der Selektion ausgeschlossen werden können, und die Zentren seltene Pathologien anhäufen, werden diese der epidemiologischen Differentialanalyse zugänglich. Das indonesische Ergebnis an den elf Universitätsfrauenkliniken bestärkt zwei englische Spitalbeobachtungen von 1965 (1,2), die jedoch ohne Kontrolle des Geburtsgegewichts gemacht wurden. Der nächste analytische Schritt muss die folgenden Variablen einbeziehen: Morbidität der Frau, Spontanabortus, Geschlecht des Kindes, Schwangerschaftsdauer, Geburtsgewicht, und Totgeburtenziffer.

Résumé et Perspective

La partie 6 de l'analyse de la mortinatalité en Indonésie marque une transition vers l'étude des complications et des morbidités de grossesse & de l'accouchement. Une prédominance plus élevée des *hémorragies rétroplacentaires* et des *hémorragies indéterminées* parmi les patientes porteuses d'un foetus mâle de faible poids à la naissance, par rapport au foetus du sexe opposé à faible poids, équivaut à l'hypothèse empirique suivante: c'est bien le foetus qui induit ces pathologies de type hémorragique et le facteur causal est plus abondant parmi les foetus mâles. Puisqu'on peut exclure les biais de sélection en ce qui concerne le sexe de l'enfant, et que les centres universitaires accumulent ces pathologies rares, l'analyse épidemiologique différentielle s'avère prometteuse. Les observations apportées par 11 universités en Indonésie confirment celles faites par deux hôpitaux en Angleterre en 1965, bien que l'étude selon le poids à la naissance fut omise (1,2). Il s'agit maintenant d'étudier la morbidité maternelle et ses liens aux avortements spontanés, au sexe du foetus, à l'âge gestationnel, au poids à la naissance et à la mortinatalité.

References

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