

Length of human pregnancies can vary naturally by as much as five weeks

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The length of a human pregnancy can vary naturally by as much as five weeks, according to research published online today (Wednesday) in Europe's leading reproductive medicine journal *Human Reproduction*.

Normally, women are given a date for the likely delivery of their baby that is calculated as 280 days after the onset of their last menstrual period. Yet only four percent of women deliver at 280 days and only 70% deliver within 10 days of their estimated due date, even when the date is calculated with the help of ultrasound.

Now, for the first time, researchers in the USA have been able to pinpoint the precise point at which a woman ovulates and a fertilised embryo implants in the womb during a naturally conceived pregnancy, and follow the pregnancy through to delivery. Using this information, they have been able to calculate the length of 125 pregnancies.

"We found that the average time from ovulation to birth was 268 days – 38 weeks and two days," said Dr Anne Marie Jukic, a postdoctoral fellow in the Epidemiology Branch at the National Institute of Environmental Health Sciences (Durham, USA), part of the National Institutes for Health. "However, even after we had excluded six pre-term births, we found that the length of the pregnancies varied by as much as 37 days.

"We were a bit surprised by this finding. We know that length of gestation varies among women, but some part of that variation has



always been attributed to errors in the assignment of <u>gestational age</u>. Our measure of length of gestation does not include these sources of error, and yet there is still five weeks of variability. It's fascinating."

The possibility that the length of pregnancies can vary naturally has been little researched, as it is impossible to tell the difference between errors in calculations and natural variability without being able to measure correctly the gestational age of a developing foetus. Previous studies conducted as long ago as the 1970s and 1980s had used the slight rise in a woman's body temperature at waking as a way of detecting when ovulation occurred. This is an inexact measurement and cannot be used to detect when the embryo actually implants in the womb.

In the current study, the researchers took information from daily urine samples collected by women taking part in an earlier study, the North Carolina Early Pregnancy Study, which took place between 1982-1985 and followed 130 singleton pregnancies from unassisted conception through to birth. The women had discontinued contraception in order to become pregnant; they were healthy, with no known fertility problems and they were also less likely to smoke or be obese. The women completed daily diaries and collected daily first-morning urine samples for six months or until the end of the eighth week if they became pregnant.

The urine samples were analysed for three hormones connected with the onset of pregnancy: hCG (human chorionic gonadotropin), estrone-3-glucoronide and pregnanediol-3-glucoronide. The day of ovulation was identified by the drop in the ratio between the hormones oestrogen and progesterone. Embryo implantation was identified as the first day of a sustained rise in levels of hCG. "Since the embryo secretes hCG, and mothers generally have little to no hCG in their urine when they are not pregnant, we used the earliest increase in hCG to indicate implantation," explained Dr Jukic.



In 2010, the researchers contacted the women for the current study to obtain information about their labour and whether induction or Caesarean section had been required. Full information was available on 125 pregnancies after excluding those that had been affected by exposure to diethylstilbestrol – an endocrine disrupter that is known to shorten pregnancies.

In addition to the variation in the length of gestation, the study found that embryos that took longer to implant, also took longer from implantation to delivery, and that pregnancies that showed a late progesterone rise were significantly shorter by an average of 12 days than pregnancies with an early rise.

Dr Jukic said: "I am intrigued by the observation that events that occur very early in pregnancy, weeks before a woman even knows she is pregnant, are related to the timing of birth, which occurs months later. I think this suggests that events in early pregnancy may provide a novel pathway for investigating birth outcomes."

Other factors that appeared to influence pregnancy duration included: older women delivered later on average, with each year of age adding roughly one day to their pregnancy; women who had themselves been heavier at birth had longer gestations, with each 100g in the mother's own birthweight corresponding roughly to a one-day longer pregnancy; and if a woman had longer pregnancies previously or subsequently to the pregnancy being investigated in the study, then the study pregnancy was likely to be longer, with a one-week increase in the average length corresponding to about a 2.5-day longer pregnancy in the study. "This last finding suggests that individual women tend to be consistent about when they deliver," said Dr Jukic.

In their paper, the authors conclude: "The length of human gestation varies considerably among healthy pregnancies, even when ovulation is



accurately measured. This variability is greater than suggested by the clinical assignment of a single 'due date'. The duration of previous pregnancies may provide a useful measure of a woman's 'natural' length of pregnancy and may help in predicting an individual woman's due date. We also found that events in the first two weeks after conception were strongly predictive of the total length of pregnancy, suggesting that the trajectory for the timing of delivery may be set in early pregnancy."

They warn that it is too early to make clinical recommendations based on their study and that further research needs to be carried out.

Dr Jukic concluded: "I think the best that can be said is that natural variability may be greater than we have previously thought, and if that is true, clinicians may want to keep that in mind when trying to decide whether to intervene on a <u>pregnancy</u>."

More information: "Length of human pregnancy and contributors to its natural variation", by A.M. Jukic, D.D. Baird, C.R. Weinberg, D.R. McConnaughey, A.J. Wilcox. *Human Reproduction* journal. doi:10.1093/humrep/det297

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