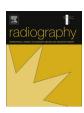


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# Ultrasound biometry of normal human amniotic fluid index in a Nigerian population



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#### ABSTRACT

*Background:* The amniotic fluid index (AFI) closely represents the actual amniotic fluid volume (AFV) with measurements below and above the 5th and 95th percentiles describing oligohydramnios and polyhydramnios respectively.

*Objective*: To create a sonographic reference range nomogram of the AFI for a Nigerian population using polynomial regression, and to test for reproducibility of AFI measurements.

Methods: Five hundred and sixty patients between 16 and 40 weeks fetal gestational age (FGA) were sampled for the study. The FGA was estimated sonographically by combining the fetal biparietal diameter, abdominal circumference, and femoral length measurements. The AFI was obtained by measuring and summing up the deepest pool of amniotic fluid devoid of fetal parts and umbilical cord in each quadrant of the maternal abdomen. To test for reproducibility of AFI measurements, two sonographers with more than 8 years of obstetric clinical experience independently measured the AFI of 40 patients. Polynomial regression, Pearson's correlation, and intra class correlations were used for data analysis. Results: The mean  $\pm$  SD of the AFI obtained in the second and third trimester respectively is  $15.2 \pm 4.0$  cm, and  $16.0 \pm 5.8$  cm. There was a steady but insignificant decrease in the AFI at all the FGA studied. A log transformed linear model adequately fitted the relationship between the AFI and FGA, given as:  $AFI_{cm} = 1.1461 + 0.00091 \times FGA$  ( $R^2 = 0.002$ ). Our normal AFI range is from 8.6 cm to 27.0 cm. Conclusion: Oligohydramnios and polyhydramnios can be satisfactorily diagnosed in the study population when AFI measurement is below or above 8.6 cm and 27.0 cm respectively.

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#### Introduction

Prior to the introduction of ultrasound as a modality for fetal assessment, the evaluation of the fetal heart both in non-stress conditions and induced uterine contractions (contraction stress test) served as a marker for assessment of fetal wellbeing.<sup>1</sup> The advent of real time sonography provided better fetal monitoring as well as extra biomarkers for predicting perinatal outcome, one of such markers being the amniotic fluid volume (AFV). The amniotic fluid (AF) originates mainly from fetal urine and lung fluid, each of which contributes about 8 ml/kg/h and 100 ml per day respectively.<sup>2</sup> Lesser contributors include the transmembrane route prior

to keratinization of fetal skin and transfers across the chorionic plate. Its functions as described by Hamann<sup>2</sup> are homeostatic (e.g. bacteriostaticity, maintenance of amniotic sac integrity, preventing contractions and maintaining cervical consistency), physical (e.g. temperature regulation, prevention of fetal injury and acting as a shock absorber), and functional (e.g. providing room for muscle exercise via fetal movement, breathing, and swallowing). Amniotic fluid recycling, primarily by fetal swallowing and reabsorption via the lungs, maintains the AFV with disruptions leading to oligohydramnios and polyhydramnios, both of which are directly correlated with perinatal mortality and morbidity.<sup>3,4</sup> Earliest attempts at measuring the AFV involved the dye dilution method, where a known volume of a dye that cannot be metabolized by the fetus is injected during amniocentesis. After about 40 min post injection, a sample of the AF was aspirated and the dilution of the dye calculated.<sup>5</sup> The first large scale study to determine the AFV using this method was by Brace and Wolf<sup>6</sup> in a cross-sectional study involving

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705 patients, and subsequently by Magann et al. who measured the AFV of 144 singleton pregnancies from 15 to 40 weeks gestation. The study by Magann et al. revealed that the AFV increased gradually to peak at 34–38 weeks, a maximum AFV of between 400 and 1200 ml, after which it decreased rapidly to about 800 ml after 40 weeks gestation. The dve dilution technique enjoys high precision but is invasive and impractical to use in everyday obstetrics management. In 1980 Manning et al.<sup>8</sup> introduced a 5 parameter method of assessing the fetal biophysical profile (BPP), one parameter being the single deepest vertical pocket (SDVP) of amniotic fluid. They established normal values of SDVP as 2-8 cm, below 2 cm as oligohydramnios, and above 8 cm as polyhydramnios. Williams et al.<sup>9</sup> however demonstrated that SDVP measurements had poor interobserver reproducibility. Phelan et al.<sup>10</sup> first introduced a method of estimating AFV known as the amniotic fluid index (AFI), which consisted of dividing the maternal abdomen into four quadrants using the linear nigra and an imaginary line running across the maternal umbilicus and perpendicular to the linear nigra as landmarks. Four measurements in centimeters of the deepest pool of amniotic fluid devoid of fetal parts or the umbilical cord are taken at each quadrant and the values summed to give the AFI. They suggested 5 cm as the threshold value below which oligohydramnios may be diagnosed. Moore and Cayle<sup>11</sup> also studied 750 patients using the methods described by Phelan et al. 10 and defined oligohydramnios as an AFI less than 8 cm or below the 5th percentile. Their definition was confirmed by Magann et al. 12 who performed a weekly AFI measurement on 50 patients from 14 to 41 weeks gestation.

Since then, several works have been carried out to create reference range nomograms of the AFI. Variations in values are dependent on the studied population, which suggests that AFI nomograms should be specific to a given population. 11,13-16 Some fetal and maternal biometric parameters could equally affect AFI measurements. A previous study has demonstrated a significant relationship between AFI and abdominal circumference (AC), estimated fetal weight (EFW), and head circumference to abdominal circumference ratio, <sup>17</sup> even though recent findings tend to disagree with this. 18,19 In Nigeria, three attempts have been made to our knowledge to create a reference range nomogram of AFI. 16,20,21 Of importance is the work of Chama et al. 16 in their longitudinal study 14 years ago involving 90 singleton pregnant subjects, who were scanned from 20 to 42 weeks of fetal gestational age (FGA). Their results demonstrated a gradual rise in AFI up to 26 weeks followed by a fall towards term. They defined a narrow range with lower and upper limit of AFI as 7.7 cm and 14.7 cm respectively and advocated for gestational-age specific values to be applied to populations from which they were obtained for better clinical use of the AFI. Though their methodology provides a fair assessment of the AFI of the population under study, we feel that the sample size would not be representative of the population under study. Also, Hofmeyr and Gülmezoglu's<sup>22</sup> systematic review concluded that factors such as maternal hydration significantly affected longitudinal AFI measurements, which could have affected the AFI centile values. Furthermore, polynomial regression would provide better centile charts of the AFI. We, therefore, conducted this study using a larger sample from a Nigerian population to construct a nomogram of the AFI. We also assessed the influence of inter and intra observer variation on reproducibility of AFI measurements, taking into consideration the operator dependency of ultrasound measurements,<sup>23</sup> and finally, investigated if a significant relationship existed between the AFI and fetal maternal parameters such as EFW, maternal body mass index (BMI), AC, biparietal diameter (BPD), and femur length (FL).

#### Material and methods

This was a cross-sectional study conducted at a university medical center between October 2014 and July 2015. Exclusion criteria included patients with a history of premature rupture of membrane, congenital anomalies, intrauterine growth restriction as previously defined, 13 subjects whose last menstrual period did not agree within 7 days with the sonographically determined gestational age, and multiple gestations. Out of the 583 patients that presented for the study within the time frame, 560 (aged between 17 and 45 years) met the inclusion criteria and were recruited. The equipment used was DP-50 Mindray, Shenzhen, manufactured in 2011, with a variable frequency probe (3.5–5.0 MHz). Ethical clearance was obtained from the Research and Ethics Committee (approval number: NHREC/05/01/2008B-FWA00002458-1RB00002323), and informed consent of patients were sought and acquired. The sonographic gestational age was determined by an average of the completed weeks obtained from the BPD, AC, and FL. Following methods previously described, <sup>24</sup> the BPD was measured as a cross-sectional view of fetal head, showing symmetrical cerebral hemispheres, cerebral falx, thalami, cavum septum pellucidi, and the insula. The caliper was placed at the outer and inner edge of the cranium. The AC was measured on a transverse section of the upper fetal abdomen, showing a circular section of the abdomen, the stomach bubble, intrahepatic portion of the umbilical vein, and a cross-section of one vertebra seen as three triangular echogenic foci. The calipers were placed on the outer surface of the skin line and adjusted till it overlaid the skin contour. An image of the femur closer to the transducer, perpendicular to the angle of insonation, and clearly showing both ends of the diaphysis was obtained. The calipers were placed at both ossified ends and care was taken not to include the epiphysis. Each of these parameters were obtained and measured three times and the average taken as the final value.

The AFI was obtained by dividing the maternal abdomen into four quadrants using as landmarks the linear nigra and an imaginary line perpendicular to the linear nigra passing through the maternal umbilicus. 10 Measurements were taken at the deepest pool of amniotic fluid, excluding areas containing fetal parts and the umbilical cord. Measurement of some pockets of amniotic fluid presenting unavoidably with either fetal parts or umbilical cord were taken at the clear amniotic fluid pool anterior to the structure of interest.<sup>14</sup> All measurements were obtained by a sonographer with more than 8 years of clinical experience in obstetric sonography. Ancillary data obtained were maternal weight, height, gravidity, parity, and number of miscarriages. To assess for interobserver and intraobserver variability, a pilot study was conducted involving the first 40 patients selected. They were scanned by two different sonographers with more than 8 years' experience in obstetric ultrasound. The principal investigator took the AFI at the beginning and end of each scan, while the second took measurements 5 min afterward.

#### Statistical analysis

The results were recorded in a data sheet specifically designed for the purpose and transferred to Statistical Package for the Social Sciences (IBM Corp v.21.0.0.0, 2012) and R (The R foundation for statistical computing v.2.14.2, 2012) for analysis. As was previously described by Royston and Wright, <sup>25</sup> and Silverwood, <sup>26</sup> polynomial regression was applied to construct normal ranges for the 5th, 50th, and 95th percentiles. The polynomial regression curve was tested for consistency by calculating the z scores, plotting the QQ normality curve, and performing the Shapiro—Wilk test. Line charts

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