As ultrasound technology has improved our ability to visualize anomalies in the first trimester has grown. The nuchal translucency observed in the first trimester is believed to be mesenchymal edema. Nicolaides and others correlated widening nuchal translucency with increasing risk of Down’s Syndrome. There is a continuum of widening nuchal translucency extending into Cystic Hygroma. In the first trimester scan, diagnosis of cystic hygroma occurs at a frequency of about 1% of fetuses. Larger, septated cystic hygroma occurs at a rate of 1 in 285 fetuses. Markedly thickened nuchal translucency or Cystic Hygroma may be simple or septated on close inspection.

Much of what we have learned about Nuchal Translucency has come out of studies on First Trimester Down Syndrome Screening. In the BUN Study, the first American validation of Nicolaides, Fetal Medicine Foundation, pioneering work, did not attempt to differentiate between nuchal translucency and cystic hygroma and, instead, kept all fetuses in the study irrespective of nuchal translucency thickness. The second major American study, the FASTER trial excluded Cystic Hygromas from the genetic analysis assuming a high rate of Down’s Syndrome in these fetuses.

Differential diagnosis of cystic hygroma includes neural tube defects, such as a posterior encephalocele, or cervical meningocele, and cystic teratoma or hemangioma.

As a marker, Cystic Hygroma is associated certain abnormal conditions—

ANEUPLOIDY: Thickened Nuchal Translucency is most commonly associated with various chromosomal defects including Trisomy 21 (Down Syndrome), Trisomy 13 (Patou Syndrome), Trisomy 18 (Edward Syndrome), Monosomy X (Turner Syndrome) and Triploidy. In non-septated Cystic Hygroma the likelihood of chromosomal abnormalities is 21% while septated Cystic Hygromas the chance is 57%. The most common chromosomal disorder in Septated Cystic Hygroma is Down’s Syndrome followed by Turner’s Syndrome.

The nuchal translucency measurement has been related to probability for chromosomal abnormality as it thickens. The overall likelihood of abnormal katotype increases with increasing nuchal translucency, but the distribution of abnormalities changes. Down’s is more likely with minor enlargement while Turner’s Syndrome increases in frequency with increasing nuchal translucency.

HYDROPS—

The presence of hydrops associated with a cystic hygroma is another independent predictor of compromised outcomes.
ANATOMIC MALFORMATIONS—

About 33% of first trimester fetuses with Cystic Hygroma have associated anatomic, structural malformations. Cardiac defects are the most common anomaly associated with increased nuchal translucency. Other associated malformations include diaphragmatic hernia, renal anomalies, body stalk disruption, and abdominal wall defects.

The prevalence of congenital heart disease increases with increasing nuchal translucency thickness, but there is no clear difference in the distribution of nuchal translucency with different types of cardiac defects.

Depending upon the cut-off used, the overall risk of having a cardiac defect in an euploid fetus with increased nuchal translucency is about 3 to 5 percent (the baseline risk of moderate and severe forms of congenital heart disease in the general population is 6 per 1000 live births).
Abnormalities of Ductus Venosus Doppler studies are also related to thickened nuchal translucency measurements in fetuses with congenital heart disease\(^\text{10}\). During late diastole, velocity is decreased and pulsatility index index increased in fetuses with nuchal translucency >95\(^{\text{th}}\) percentile and heart defects.

**DIAGNOSTIC EVALUATION**

Work-up of a first trimester thickened Nuchal Translucency includes careful ultrasound and cardiac evaluation, chorionic villus sampling or amniocentesis for chromosomal analysis. Fetal testing in the late second trimester and repeat sonography to evaluate for heart and other structural anomalies is warranted.

Using a threshold of ≥3 mm to trigger invasive genetic testing results in 0.4 percent of patients being offered karyotype analysis, with a 1 in 6 chance of detecting aneuploidy, and detection of 19 percent of Down syndrome fetuses\(^\text{11}\). Using a threshold of ≥4 mm would result in 0.09 percent of patients being offered karyotype analysis, with a 1 in 3 chance of detecting aneuploidy, and detection of 7 percent of Down syndrome fetuses.

When an increased Nuchal Translucency is discovered during the course of 1\(^{\text{st}}\) Trimester Down Syndrome Screening, management is guided by risk factor assessment and presence of other consequential anomalies.

**LONG TERM OUTCOME FROM 1\(^{\text{ST}}\) TRIMESTER EVALUATION**

Neonatal outcome is principally dependent on size of the fetal nuchal translucency, presence of abnormal karotype and existence of congenital anomaly.

Cystic Hygroma—

First trimester cystic hygroma is associated with 50% likelihood of karotypic abnormality, 33% chance of major congenital anomaly (CV most likely at 25 / 33 anomalies), 55% chance of any anomaly, 25% chance of fetal or neonatal death and just a 20% likelihood of a normal pediatric course\(^\text{12}\).

Outcome in cases with karotypic abnormality or congenital anomaly relates directly to the genetic or structural disorder.

Neonatal outcome in first trimester cystic hygroma without karotypic or structural anomalies, is directly related to increasing size of the cystic hygroma.

Over 80 percent of simple cystic hygromas with normal karyotype are expected to resolve within four weeks of diagnosis and the vast majority of these patients deliver phenotypically normal infants\(^\text{12}\). Fetuses with diffuse hydrops, however, are often not as fortunate. Fetus’s with hydrops have an 80% likelihood of bad outcome.
Nuchal Translucency—

Less extreme cases, those with enlarged Nuchal Transslucency, have only a 15% overall chance of abnormal karyotype, a 5% chance of structural anomaly and a 90% chance of a normal pediatric outcome\(^\text{13}\).

SECOND TRIMESTER

Thickened Nuchal Translucency commonly resolves spontaneously. Cases without spontaneous resolution by the second trimester have a higher likelihood of chromosomal abnormality\(^\text{14}\).

Invasive genetic testing is offered in all second trimester cases of thickened nuchal translucency or cystic hygroma.
References