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# Abnormal Nuchal Translucency and Outcomes of Singleton Pregnancies (Antop) Study: An 8 -year Retrospective Cohort Analysis

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**Research Article**

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## Abstract

**Background:** An abnormal nuchal translucency (NT) at 11-13+6 weeks scan is associated with chromosomal abnormalities; foetal structural anomalies and adverse pregnancy outcomes.

**Aims and Objectives:** To study the clinical characteristics and perinatal outcomes of foetuses with abnormal NT (>95$^{th}$ centile for GA)

To compare the foetal outcomes, good versus poor, with worsening NT. To compare the characteristics and outcomes of foetuses with NT 95$^{th}$-99$^{th}$ centile and ≥99$^{th}$ centile. To study the long-term outcomes of liveborns among these foetuses.

**Methodology:** This is a retrospective cohort study of all pregnant women attending antenatal clinics, who had abnormal NT measurement at 11-13+6 weeks scan, during the study period (2017-2024).

**Results:** There were 135 pregnant women in our cohort. Mean age of women was 28.1± 5.37yrs. Nearly one third (28%) had NT between >95th-99th centile while rest had NT ≥99$^{th}$ centile. One third foetuses had NT ≥6.5 mm

Hydrops and structural anomalies were detected in 40% and 70% respectively. The number of foetuses with good and poor outcomes was comparable till NT ≥6 mm. In this subgroup, poor perinatal outcomes were 18 times more than good outcomes.

Of the 67.4% women undergoing invasive foetal testing, 40.7% had abnormal results, most being chromosomal abnormalities (92%). Of the euploid foetuses (N=54), poor outcomes were seen in 53.7% of them. Half of those who underwent further genetic evaluation (N=4, 57.1%), were found to have single gene disorders.

A significant portion of pregnancies was terminated (N=77, 57.0%). One fifth of cases (N=27) were lost to follow up. Overall liveborn rates was 22.9%. Among the liveborns, majority, 77.4% were normal. Seven babies had structural or genetic abnormality requiring long term follow up.

**Conclusion:** In our cohort overall liveborn rates were low. In carefully selected cases of ongoing pregnancies, good outcomes were observed. Long term follow up of liveborns, however, is warranted as some of them may develop problems later on.


## BACKGROUND

Nuchal translucency (NT) is the ultrasonographic measurement of the subcutaneous fluid collection at the back of foetal neck and it is an important component of first-trimester screening for aneuploidy. It is routinely measured between 11 to 13 + 6 weeks of gestation (1, 2). While some consider NT > 95th centile as abnormal, other have used a cutoff ≥ 99th centile for abnormality (2–4).

Multiple studies have shown associations between increased NT and common aneuploidies such as trisomy 21, trisomy 18, and monosomy X (5, 6) with chromosomal abnormalities identified in 20–50% of foetuses with enlarged NT (7). The risk of chromosomal abnormalities increases as the NT measurement increases, from about 20% when the NT is 4.0 mm to nearly 65% when it measures 6.5 mm or more (8).

Enlarged NT was also found to be associated with structural defects, especially cardiac defects, even in the presence of normal karyotype (9–11). Advanced genetic technologies such as chromosomal microarray (CMA) and next-generation sequencing (NGS) have helped in detecting submicroscopic chromosomal changes such as microdeletions /microduplications and single gene disorders associated with enlarged NT (4, 12–14) and an NT measurement ≥ 99th is a clear indication for invasive testing (4, 8). Moreover, studies have also shown correlation between increased NT and adverse pregnancy outcomes such as miscarriage, intrauterine foetal demise (IUFD), preterm birth and neonatal complications (2, 15, 16).

Although many studies have looked at association of increased NT with aneuploidies and /or chromosomal aberrations (5, 14, 16, 17), very few studies have looked at the obstetric, perinatal, and neonatal outcomes in pregnancies with increased NT. In addition, many of these studies have specifically focused only on certain outcome like chromosomal abnormalities or structural anomalies or neonatal outcomes. Studies by Buffin et al and Kalem et al have shown that foetuses with increased NT may have a higher likelihood of neonatal morbidity compared with those with normal NT measurements (18, 19).None of them have studied long term outcomes of liveborns with abnormal NT.

The majority of available literature on increased NT are from the Western world and the Middle East. While these studies have provided valuable information regarding the association between NT thickness and pregnancy outcomes, differences in population characteristics may influence the outcomes. For example, consanguineous marriages are relatively common in many Middle Eastern populations, so the rate of inherited genetic disorders may be higher leading to increased prevalence of certain foetal abnormalities. Hence, the outcomes observed from these studies cannot be extrapolated to LMIC (low and middle income countries) or to countries where consanguinity rates are variable like India (20).

Studies from the Indian subcontinent are very few, most being case reports or case series (7, 21) with only two prospective cohort studies which focussed more on perinatal outcomes with no much focus on long term outcomes (22, 23).

The present study looked at maternal and foetal characteristics, perinatal; neonatal and long-term outcomes among liveborns (up to 2 years) in singleton pregnancies with abnormal NT in an LMIC setting. We stratified abnormal NT measurements into eight groups and studied the overall trends of foetal outcomes in relation to worsening NT measurement.

We also compared outcomes of foetuses with NT ≥ 99th centile and those with NT 95th -99th centile. A subgroup analysis of euploid foetuses was done to study their outcomes and presence of other genetic abnormalities.

We wanted the information we obtained from this study to be used for counselling pregnant women with abnormal foetal NT.

# METHODOLOGY

**Research design**

This was a retrospective cohort study of prospectively collected data of women with singleton pregnancies with abnormal foetal NT, diagnosed on first trimester scans, between Jan 2017- December 2024 at a tertiary care perinatal centre in India. The study was approved by the Institutional review board (IRB no 15645(OBSERVE)) and was conducted in accordance with the principles of the Declaration of Helsinki.

**Study setting**

This study was carried out in the Foetal Medicine Unit, Departments of Obstetrics and Gynaecology, Neonatology; Cytogenetics; Clinical genetics and biostatistics at Christian Medical College and Hospital, Vellore, a tertiary care perinatal centre in South India.

**Methods**

NT was measured between 11–13 + 6 weeks (CRL 45-84mm) using standard protocol determined by the Foetal Medicine Foundation, UK (24) using Voluson E10 (GE Healthcare Systems) by two experienced operators. An abnormal NT was diagnosed when NT > 95th centile for the gestational age (GA).

All women with singleton pregnancies, whose foetuses were diagnosed to have abnormal NT were included in the study. Patients with multiple gestations and NT measurement beyond 13 + 6 weeks were excluded. Patient consent was not obtained prior to enrolling in study as this was a retrospective study. However, prior to doing invasive foetal testing a signed informed written consent was obtained from all women as per the hospital policy.

The pregnancy details were obtained from maternal antenatal records, stored at the Medical Records Department, of the hospital for a period of 10 years. Details of the invasive testing done and genetic tests ordered were obtained from the prospectively maintained registers in the Scan room. Genetic tests used for detection of chromosomal abnormalities included karyotyping, QF-PCR (Quantitative fluorescent polymerase chain reaction) and CMA whereas single gene disorder was assessed by exome sequencing. Results of the genetic tests were obtained from the electronic records maintained by the department of cytogenetics and Clinical Genetics. Labour and delivery details were obtained from the electronic birth registry in the labour ward Neonatal details were obtained from the neonatal database and follow up of liveborns was obtained from outpatient records of babies from High-Risk Infant clinic.

All this information were entered in the excel sheet.

**Statistical methods**: All study variables were summarized using descriptive statistical methods. Quantitative variables studied, included: parity, previous obstetric history; mode of conception; method of invasive foetal testing; presence or absence of genetic abnormality; type of genetic abnormality and outcomes of pregnancies.

Foetal/Neonatal quantitative variables included; presence of associated anomalies or hydrops, types of congenital anomalies; percentage of cases with resolution or progression, perinatal outcomes of ongoing pregnancies, percentage of live borns, still borns and early neonatal death among ongoing pregnancies. We also recorded the long-term outcomes of the liveborn in our cohort.

We compared clinical characteristics of foetuses with good versus poor outcomes. Poor outcomes were defined as termination of pregnancy /intrauterine foetal demise or neonatal death. Good outcomes were defined as liveborn. Moreover, we compared outcomes of foetuses with NT > 95-99th centiles versus NT ≥ 99th centile. We also stratified abnormal NT measurement into groups in the ascending order of values and compared the overall trend of good versus poor perinatal outcomes with worsening NT. Subgroup analysis of euploid foetuses with abnormal NT and their outcomes was also carried out.

Categorical variables were summarized using frequencies and percentages whereas continuous variables such as such as maternal age; gestational age at delivery; birth weight and NT measurement were expressed as means with standard deviations. The proportion of women with adverse maternal/foetal outcomes were calculated with 95% confidence interval (CI). Chi-square tests were used to examine association between categorical variables and adverse outcomes. All analyses were performed using SPSS 29 software.

## RESULTS

Based on the chart review, we had 153 women who were eligible, out of which 18 were excluded as 1 had twin gestation and the rest (N = 17) had NT done at > 13 + 6 weeks (Fig. 1). Hence, 135 women were included in the study.

The mean maternal age was 28.1 ± 5.37 years. The majority of women (60.7%) were in the age group of 21–30 years, followed by women aged 31–40 years (29.6%). Only 1.5% of the patients were over 41 years of age (Table 1).

Table 1
THE MATERNAL CHARACTERISTICS OF THE STUDY COHORT

| MATERNAL CHARACTERISTICS | NUMBER (PERCENTAGE) |
|---|---|
| **AGE: (range) (N = 135)** | |
| 1. < 20 yrs | 11 (8.1%) |
| 2. 21–30 yrs | 82 (60.7%) |
| 3. 31–40 yrs | 40 (29.6%) |
| 4. > 41 yrs | 2 (1.5%) |
| **AGE in number** | |
| N (Missing) | 135 (0) |
| Mean (SD) | 28.1 (5.37) |
| Median (Range) | 28.0 (18.0, 43.0) |
| **OBSTETRIC SCORE**: (N = 135) | |
| 1. Primigravida | 54 (40.0%) |
| 2. Multigravida | 78 (57.8%) |
| 3. Not available | 3 (2.2%) |
| **GESTATIONAL AGE at NT scan**: (N = 135) | |
| 1. 11 Weeks | 6 (4.4%) |
| 2. 12 Weeks | 56 (41.5%) |
| 3. 13 Weeks | 73 (54.1%) |
| **TYPE OF CONCEPTION**: (N = 135) | |
| 1. Spontaneous | 128 (94.8%) |
| 2. Artificial | 3 (2.2%) |
| 3. Not available | 4 (3.0%) |
| SD: Standard deviation, NT: Nuchal Translucency | |

Most women (57.8%) were multigravidae. Obstetric history was unavailable in 2.2% of cases. Majority (94.8%) had spontaneous conception whereas only 2.2% were conceived through assisted reproductive techniques. Information regarding mode of conception was not available for 35 women (Table 1).

Majority of women (54.1%) had NT scan done at 13 weeks followed by 12 weeks (41.5%) (Table 1).

The overall mean NT, in our cohort, was 5.0 ± 2.25 mm. Nearly, one-third (31.1%) had NT ≥ 6 mm. More than two third foetuses (71.9%) had NT ≥ 99th centile, while 28.1% had NT between the 95th and 99th centiles, (Table 2).

Table 2
FETAL AND NT CHARACTERISTICS OF THE STUDY COHORT

| FETAL CHARACTERISTICS | NUMBER (PERCENTAGE) |
|---|---|
| **MEASUREMENT of NT scan in mm: (RANGE), n (%) (N = 135)** | |
| 1. 2.5 -2.9mm | 16 (11.9%) |
| 2. 3.0-3.4mm | 22 (16.3%) |
| 3. 3.5-3.9mm | 18 (13.3%) |
| 4. 4.0-4.4mm | 16 (11.9%) |
| 5. 4.5-4.9mm | 10 (7.4%) |
| 6. 5.0-5.4mm | 4 (3.0%) |
| 7. 5.5-5.9mm | 7 (5.2%) |
| 8. > 6mm | 42 (31.1%) |
| **NT VALUE** | |
| N (Missing) | 135 (0) |
| Mean (SD) | 5.0 (2.25) |
| Median (Range) | 4.2 (2.5, 15.0) |
| **NT CENTILE** (N = 135) | |
| 1. 95–99 Centile (2.5-3.4mm) | 38 (28.1%) |
| 2. ≥ 99 Centile (> 3.5mm) | 97 (71.9%) |
| **COMBINED FIRST TRIMESTER SCREENING**: (N = 135) | |
| 1. Done | 20 (14.8%) |
| 2. Not done | 115 (85.2%) |
| **RISK OF T21 ON CFTS**: (N = 135) | |
| 1. Low risk | 8 (40.0%) |
| 2. Intermediate risk | 2 (10.0%) |
| 3. High risk | 10 (50.0%) |
| Missing | 115 |
| **NONINVASIVE PRENATAL TESTING (N = 135)** | |
| 1. Done | 2 (1.5%) |
| 2. Not done | 133 (98.5%) |
| **PRESENCE OF STRUCTURAL ANOMALIES**: (N = 135) | |
| 1. Yes | 95 (70.4%) |
| NOTE: Perinatal outcome: Missing values were replaced using information from other variables (termination as bad outcome and coded as 2) and the remaining values were left as missing | |
| [a] Termination of pregnancy includes all termination i.e. at time of diagnosis as well as mid-trimester termination | |
| CNS: Central Nervous System, CVS: Chorionic Villous Sampling, DNA: Deoxyribonucleic acid, | |
| IUD/IUFD: Intra uterine death/ fetal death, OPD: Outpatient department, TOP: Termination of pregnancy | |

| FETAL CHARACTERISTICS | NUMBER (PERCENTAGE) |
|---|---|
| **MEASUREMENT of NT scan in mm: (RANGE), n (%) (N = 135)** | |
| 2. No | 40 (29.6%) |
| **PRESENCE OF HYDROPS** (N = 135) | |
| 1. Yes | 54 (40.0%) |
| 2. No | 81 (60.0%) |
| **TYPE OF STRUCTURAL ANOMALIES**: | |
| N (Missing) | 94 (41) |
| Mean (SD) | 4.5 (2.69) |
| Median (Range) | 6.0 (1.0, 8.0) |
| 1. Cystic Hygroma | 25 (26.6%) |
| 2. Skeletal Dysplasia | 9 (9.6%) |
| 3. Congenital Heart Defect | 6 (6.4%) |
| 4. Gastrointestinal Anomalies | 2 (2.1%) |
| 5. CNS Anomalies | 3 (3.2%) |
| 6. Soft Markers | 4 (4.3%) |
| 7. Multiple Anomalies | 45 (47.8%) |
| **INVASIVE TESTING** :(N = 135) | |
| 1. Done | 91 (67.4%) |
| 2. Not done | 44 (32.6%) |
| **TYPE OF INVASIVE TESTING**: (N = 135) | |
| 1. CVS (Chorionic Villous Sampling) | 84 (92.3%) |
| 2. Amniocentesis | 7 (7.7%) |
| Missing | 44 |
| **GENETIC TEST ORDERED**: (N = 135) | |
| 1. Chromosomal tests | 25 (27.8%) |
| 2. Chromosomal tests +/- Single gene testing (DNA banking) | 65 (72.2%) |
| Missing | 45 |
| **RESULT OF INVASIVE TEST**: (N = 135) | |
| 1. Normal | 54 (59.3%) |
| 2. Abnormal | 37 (40.7%) |
| Missing | 44 |
| NOTE: Perinatal outcome: Missing values were replaced using information from other variables (termination as bad outcome and coded as 2) and the remaining values were left as missing | |
| [a] Termination of pregnancy includes all termination i.e. at time of diagnosis as well as mid-trimester termination | |
| CNS: Central Nervous System, CVS: Chorionic Villous Sampling, DNA: Deoxyribonucleic acid, | |
| IUD/IUFD: Intra uterine death/ fetal death, OPD: Outpatient department, TOP: Termination of pregnancy | |

| FETAL CHARACTERISTICS | NUMBER (PERCENTAGE) |
|---|---|
| **MEASUREMENT of NT scan in mm: (RANGE), n (%) (N = 135)** | |
| **TYPE OF ABNORMALITY**: (N = 135) | |
| 1. Chromosomal Abnormality | 34 (91.9%) |
| 2. Single Gene Disorder | 3 (8.1%) |
| Missing | 98 |
| **TYPE OF CHROMOSOMAL ABNORMALITY**: (N = 135) | |
| 1. T21 | 12 (35.3%) |
| 2. T13 | 2 (5.9%) |
| 3. T18 | 5 (14.7%) |
| 4. Turners Syndrome | 12 (35.3%) |
| 5. Others | 3 (8.8%) |
| Missing | 101 |
| **If Others specify**: (N = 3) | |
| 1. Chr17p13.3 microduplication | 1 (33.3%) |
| 2. Derivative chromosome 6 abnormality | 1 (33.3%) |
| 3. Mosaic Turners Syndrome | 1 (33.3%) |
| Missing | 132 |
| **FURTHER PREGNANCY MANAGEMENT**: (N = 135) | |
| 1. Termination of Pregnancy (Termination of pregnancy at time of diagnosis + Mid trimester termination)[a] | 77 (57.0%) |
| 2. Ongoing Pregnancy | 31 (22.9%) |
| 3. Lost to follow up | 27 (20.0%) |
| **REASON FOR TERMINATION OF PREGNANCY AT DIAGNOSIS**: (N = 135) | |
| 1. Genetic Abnormality | 33 (44.0%) |
| 2. Multiple associated anomalies | 39 (52.0%) |
| 3. Miscarriage | 3 (4.0%) |
| Missing | 60 |
| **ONGOING PREGNANCIES**: (N = 135) | |
| 1. Ongoing pregnancy till term | 31 (77.5%) |
| 2. Ongoing pregnancy till preterm (Mid trimester termination)[a] | 9 (22.5%) |
| Missing | 95 |
| NOTE: Perinatal outcome: Missing values were replaced using information from other variables (termination as bad outcome and coded as 2) and the remaining values were left as missing | |
| [a] Termination of pregnancy includes all termination i.e. at time of diagnosis as well as mid-trimester termination | |
| CNS: Central Nervous System, CVS: Chorionic Villous Sampling, DNA: Deoxyribonucleic acid, | |
| IUD/IUFD: Intra uterine death/ fetal death, OPD: Outpatient department, TOP: Termination of pregnancy | |

| FETAL CHARACTERISTICS | NUMBER (PERCENTAGE) |
|---|---|
| **MEASUREMENT of NT scan in mm: (RANGE), n (%) (N = 135)** | |
| **GESTATIONAL AGE AT SUBSEQUENT SCAN**: | |
| N (Missing) | 39 (96) |
| Mean (SD) | 19.6 (2.06) |
| Median (Range) | 20.0 (14.0, 24.0) |
| **SUBSEQUENT SCAN FINDINGS**: (N = 135) | |
| 1. Normal | 30 (75.0%) |
| 2. Abnormal | 9 (22.5%) |
| 3. Not available | 1 (2.5%) |
| Missing | 95 |
| **FETAL ANOMALIES/IUFD ON SUBSEQUENT SCANS (MID TRIMESTER SCANS)**: (N = 135) | |
| 1. Major congenital anomalies | 7 (77.8%) |
| 2. IUD | 2 (22.2%) |
| Missing | 126 |
| **PERINATAL OUTCOME**: (N = 135) | |
| 1. Live born | 31 (28.7%) |
| 2. Mid trimester termination | 77 (71.3%) |
| Missing | 27 |
| **INDICATION FOR MIDTRIMESTER TERMINATION (Bad Outcome)**: n (%) | |
| 1. Evolving anomalies | 7 (77.8%) |
| 2. IUD | 2 (22.2%) |
| Missing | 126 |
| **GESTATIONAL AGE AT DELIVERY**: | |
| N (Missing) | 31 (104) |
| Mean (SD) | 38.5 (1.18) |
| Median (Range) | 39.0 (36.0, 40.0) |
| **POST NATAL FOLLOW UP**: (N = 135) | |
| 1. Normal outcome | 24 (77.4%) |
| 2. Outcome requiring follow up in OPD | 7 (22.6%) |
| Missing | 104 |
| NOTE: Perinatal outcome: Missing values were replaced using information from other variables (termination as bad outcome and coded as 2) and the remaining values were left as missing | |
| [a] Termination of pregnancy includes all termination i.e. at time of diagnosis as well as mid-trimester termination | |
| CNS: Central Nervous System, CVS: Chorionic Villous Sampling, DNA: Deoxyribonucleic acid, | |
| IUD/IUFD: Intra uterine death/ fetal death, OPD: Outpatient department, TOP: Termination of pregnancy | |

Combined first-trimester screening was performed in only 14.8% of cases. Among those, 50% were reported as high risk for Trisomy 21, 10% as intermediate risk, and 40% as low risk and NIPT (Non-invasive prenatal testing) was done only in 1.5% (N = 2) of the cohort (Table 2).

Structural anomalies were detected in 70.4% of cases. Foetal hydrops was present in 40% of the foetuses (Table 2). These included anomalies involving multisystem were the most common (47.8%), followed by isolated cystic hygroma (26.6%). Other structural abnormalities included skeletal dysplasia (9.6%), congenital heart defects (6.4%), central nervous system anomalies (3.2%), and gastrointestinal anomalies (2.1%). Soft markers were seen in 4.3% (Table 2).

Invasive testing was performed in 67.4% (N = 91) of cases. Of these, CVS (chorionic villus sampling) was the most commonly performed (N = 84, 92.3%), followed by amniocentesis performed in 7.7% (N = 7) of cases (Table 2). Of those who underwent genetic testing, 40.7% (N = 37) had abnormal results. Among these, chromosomal abnormalities and single gene disorders were diagnosed in 91.9% and 8.1% respectively. The most frequent aneuploidies were Trisomy 21 (35.3%) and Turner syndrome (35.3%) (Table 2).

More than half (57%) of pregnancies were terminated, 22.9% continued, and 20% were lost to follow-up. The most common reasons for termination of pregnancy were, presence of multiple anomalies (52%), and presence of abnormal genetic results (44%) (Table 2).

Among the ongoing pregnancies (N = 31, 22.9%), 77.5% reached term, and rest resulted in preterm births. Pregnancies were allowed to continue in cases of isolated abnormal NT showing spontaneous resolution; absence of structural anomalies/hydrops and/or absence of aneuploidies/ structural chromosomal abnormalities or copy number variants. The mean gestational age at delivery was 38.5 ± 1.18 weeks. Postnatal follow-up revealed normal outcomes in 77.4% of live-born infants, while a small proportion required follow-up or had confirmed/suspected genetic abnormalities (22.6%) (Table 2).

Perinatal outcomes were not available for 27 women, accounting for the 20% attrition following diagnosis (Table 3). These mostly included women who had come for a second opinion, to our centre, following abnormal NT scan done elsewhere.

Table 3
COMPARISON OF PERINATAL OUTCOMES (LIVE BIRTH VS TERMINATION OF PREGNANCY) IN THE STUDY COHORT

| | **Perinatal OUTCOME:** | | | | |
|---|---|---|---|---|---|
| | **Lost to follow up (N = 27)** | **Live born (N = 31)** | **Termination of Pregnancy (N = 77)** | **Total (N = 135)** | **P-value** |
| **MEASUREMENT of NT scan in mm: (RANGE)**, n (%) | | | | | 0.006 |
| 1. 2.5 -2.9mm | 3 (11.1%) | 7 (22.6%) | 6 (7.8%) | 16 (11.9%) | |
| 2. 3.0-3.4mm | 5 (18.5%) | 6 (19.4%) | 11 (14.3%) | 22 (16.3%) | |
| 3. 3.5-3.9mm | 5 (18.5%) | 5 (16.1%) | 8 (10.4%) | 18 (13.3%) | |
| 4. 4.0-4.4mm | 6 (22.2%) | 4 (12.9%) | 6 (7.8%) | 16 (11.9%) | |
| 5. 4.5-4.9mm | 2 (7.4%) | 5 (16.1%) | 3 (3.9%) | 10 (7.4%) | |
| 6. 5.0-5.4mm | 1 (3.7%) | 1 (3.2%) | 2 (2.6%) | 4 (3.0%) | |
| 7. 5.5-5.9mm | 2 (7.4%) | 1 (3.2%) | 4 (5.2%) | 7 (5.2%) | |
| 8. > 6mm | 3 (11.1%) | 2 (6.5%) | 37 (48.1%) | 42 (31.1%) | |
| **PRESENCE OF STRUCTURAL ANOMALIES**: n (%) | | | | | < .001 |
| 1. Yes | 17 (63.0%) | 10 (32.3%) | 68 (88.3%) | 95 (70.4%) | |
| 2. No | 10 (37.0%) | 21 (67.7%) | 9 (11.7%) | 40 (29.6%) | |
| **PRESENCE OF HYDROPS**, n (%) | | | | | < .001 |
| 1. Yes | 5 (18.5%) | 7 (22.6%) | 42 (54.5%) | 54 (40.0%) | |
| 2. No | 22 (81.5%) | 24 (77.4%) | 35 (45.5%) | 81 (60.0%) | |
| **INVASIVE TESTING**: n (%) | | | | | < .001 |
| 1. Done | 7 (25.9%) | 22 (71.0%) | 62 (80.5%) | 91 (67.4%) | |
| 2. Not done | 20 (74.1%) | 9 (29.0%) | 15 (19.5%) | 44 (32.6%) | |
| **RESULT OF INVASIVE TEST**: n (%) | | | | | < .001 |
| 1. Normal | 4 (57.1%) | 21 (95.5%) | 29 (46.8%) | 54 (59.3%) | |
| 2. Abnormal | 3 (42.9%) | 1 (4.5%) | 33 (53.2%) | 37 (40.7%) | |
| Missing | 20 | 9 | 15 | 44 | |

NT: Nuchal Translucency

Overall, live birth rates showed a declining trend with increasing NT, while termination rates showed rising trend. Higher NT values, particularly ≥ 6 mm, were associated with termination of pregnancy in almost half (48.1%) as compared to lower NT 2.5–2.9 mm

where termination rates were less than one third. (14.3%) (Table 3).

Moreover, within this subgroup, poor perinatal outcomes were seen nearly 18 times more than good outcomes, 88% versus 5% respectively. Outcomes were not available for 7% foetuses. Moreover, among the liveborn in our cohort, only 2 (6.5%) had NT > 6 mm (Table 3).

On comparing foetuses with NT 95th -99th centile versus those with ≥ 99th centile, presence of structural anomalies was comparable in the two groups, 60.5% versus 74.2% (p = 0.117) (Table 4). Foetal hydrops was detected significantly more in cases with NT ≥ 99th centile (45.4% versus 26.3%, p = 0.042) (Table 4). Invasive testing was performed more frequently in the ≥ 99th centile group (71.1%) compared to the 95–99th centile group (57.9%). However, this was not statistically significant (p = 0.140). Comparing perinatal outcomes of both groups, liveborn were seen almost twice more in the NT 95-99th centile group than the 99th centile (43% versus 23%, p value 0.037) (Table 4)

Table 4
COMPARISON OF FETUSES WITH NT 95TH–99TH CENTILE AND ≥ 99TH CENTILE

| | **NT CENTILE** | | | |
|---|---|---|---|---|
| | **95–99 Centile (N = 38)** | **> 99 Centile (N = 97)** | **Total (N = 135)** | **P-value** |
| **PRESENCE OF STRUCTURAL ANOMALIES**: n (%) | | | | 0.117 |
| 1. Yes | 23 (60.5%) | 72 (74.2%) | 95 (70.4%) | |
| 2. No | 15 (39.5%) | 25 (25.8%) | 40 (29.6%) | |
| **PRESENCE OF HYDROPS**: n (%) | | | | 0.042 |
| 1. Yes | 10 (26.3%) | 44 (45.4%) | 54 (40.0%) | |
| 2. No | 28 (73.7%) | 53 (54.6%) | 81 (60.0%) | |
| **INVASIVE TESTING**: n (%) | | | | 0.140 |
| 1. Done | 22 (57.9%) | 69 (71.1%) | 91 (67.4%) | |
| 2. Not done | 16 (42.1%) | 28 (28.9%) | 44 (32.6%) | |
| **PERINATAL OUTCOME**: n (%) | | | | 0.037 |
| 1. Live born | 13 (43.3%) | 18 (23.1%) | 31 (28.7%) | |
| 2. Mid trimester termination | 17 (56.7%) | 60 (76.9%) | 77 (71.3%) | |
| Missing | 8 | 19 | 27 | |
| NT: Nuchal Translucency | | | | |

Mean gestational age at birth was 38.5 ± 1.16 weeks (Table 5). One infant (3.4%) was depressed at birth whereas rest 28 infants (96.6%) had normal APGAR score. Data was not available for 2 infants who delivered outside (Table 5).

Table 5
NEONATAL CHARACTERISTICS OF THE STUDY COHORT

| NEONATAL CHARACTERISTICS | NUMBER (PERCENTAGE) |
|---|---|
| **Neonatal Follow up (N = 31)** | |
| 1. Yes | 7 (22.6%) |
| 2. No | 24 (77.4%) |
| **Indication for neonatal follow up (N = 7)** | |
| 1. Structural anomaly | 2 (28.6%) |
| 2. Genetic disorder (Chromosomal + SGD) | 3 (42.9%) |
| 3. Autism Spectrum disorder | 2 (28.6%) |
| **Mean Gestational age at birth (in weeks ± 2SD)** | 38.5 ± 1.16 |
| **APGAR (Depressed at birth) (N = 29)** | |
| 1. Yes | 1 (3.4%) (APGAR 7,9) |
| 2. No | 28 (96.6%) |
| Missing (Delivered outside) | 2 |
| **Birth weight (N = 29)** | |
| 1. Mean birth weight (in Kg ± 2SD) | 2.9 ± 0.41 |
| 2. Small for gestational age (N) | 3 (10.3%) |
| 3. Appropriate for the gestational age (N) | 26 (89.7%) |
| Missing (Delivered outside) | 2 |
| **Nursery admission requirement (N = 29)** | |
| 1. Yes | 11 (37.9%) |
| 2. No | 18 (62.1%) |
| Missing (Delivered outside) | 2 |
| **END/LND** | 0 |
| **Post Natal long term follow up (N = 31)** | |
| 1. Yes | 7 (22.6%) |
| 2. No | 24 (77.4%) |
| SGD: Single gene disorder, END: Early neonatal death, LND: Late neonatal death | |

Mean birth weight, in our cohort, was 2.9 ± 0.41 Kg. Three babies (10.3%) were small for gestational age while rest (26 infants, 89.7%) were appropriate for gestational age. Birth weight was not available for babies who delivered outside (Table 5).

Nursery admission was required in 37.9% (N = 11) of neonates. There were no cases of early or late neonatal deaths in our study. Postnatal long-term follow-up was required in 22.6% (N = 7) of the infants, while the majority (77.4%) did not require ongoing follow-up and had good developmental outcomes (Table 5).

Among those requiring follow up, the main indications were suspected genetic abnormalities (N = 3, 42.9%); structural anomalies (N = 2; 28.6%), and neurodevelopmental disorders (autism spectrum disorder) (N = 2, 28.6%) (Table 5).

On doing subgroup analysis of euploid foetuses in our cohort (N = 54, 40%), majority had NT>99th centile (N = 39 cases, 72.2%). Nearly one third had hydrops and two thirds had associated structural anomalies. Among the foetuses with structural anomalies (N

= 35), 83% resulted in termination of pregnancy (Table 6).

Table 6
CHARACTERISTICS AND OUTCOMES OF EUPLOID FETUSES WITH ABNORMAL NT (N = 54)

| CHARACTERISTICS | NUMBER (PERCENTAGE) |
|---|---|
| **NT Measurement (N = 54)** | |
| 1. 95-99th centile | 15 (27.8%) |
| 2. > 99th centile | 39 (72.2%) |
| **Associated Hydrops (N = 54)** | |
| 1. Yes | 18 (33.3%) |
| 2. No | 36 (66.7%) |
| **Associated Structural Anomalies (N = 54)** | |
| 1. Yes | 35 (64.8%) |
| 2. No | 19 (35.2%) |
| **Further Genetic Evaluation WES/CES (N = 54)** | |
| 1. Done | 7 (13%) |
| 2. Note done | 47 (87%) |
| **Results Of Genetic Testing (N = 7)** | |
| 1. Normal | 3 (42.9%) |
| 2. Abnormal | 4 (57.1%) |
| **Perinatal Outcomes (N = 54)** | |
| 1. TOP | 27 (50%) |
| 2. IUFD | 2 (3.7%) |
| 3. Liveborn | 21 (38.9%) |
| 4. END | 0 |
| 5. Lost to follow up | 4 |
| **Long Term Outcomes (N = 21)** | |
| 1. Normal | 18 (85.7%) |
| 2. Abnormal | 3 (14.3%) |
| **Spontaneous Resolution (of structural anomalies) (N = 35)** | |
| 1. Yes | 6 (17.1%) |
| 2. No | 29 (82.9%) |
| TOP: Termination of pregnancy, IUFD: Intrauterine fetal death, END: Early neonatal death, NT: Nuchal Translucency | |

Seven of these had further genetic testing, following a normal karyotype, out of which more than half were found to have single gene disorders including pathogenic/likely pathogenic variants in *PDHA1, COL11A1, COL5A2* genes. Half of these foetuses were aborted. Liveborn were seen in approximately 40% cases. Among the liveborn, 1 had undescended testis (Table 6).

Figure 2 is an alluvial plot depicting the relationship between NT centiles; presence of structural anomalies and/or abnormal invasive testing results and perinatal outcome.

## DISCUSSION

In our cohort of 135 pregnancies, most women were between 21–30 years of age (60.7%), followed by those between 31–40 years (29.6%). Only a small proportion were above 40 years (1.5%). This age distribution is consistent with previous studies, which have shown that abnormal NT is frequently detected in women younger than 35 years, despite advanced maternal age being a known risk factor for chromosomal abnormalities (25–27). These findings corroborate recommendations by American College of Obstetricians and Gynaecologists, that all pregnant women, irrespective of age, should be offered first-trimester screening.

In our cohort, structural anomalies and hydrops were present in 70.4% and 40%, respectively, leading to pregnancy terminations in 57% cases. This was also responsible for the low livebirth rates in our cohort (22.9%). These findings show that increasing NT thickness is directly related to adverse pregnancy outcome. Foetuses with NT ≥ 99th centile had significantly higher termination rates and lower live birth rates compared to those between the 95th–99th centile (1, 3, 15).

Studies by Bagci et al (2024) reported an overall live birth rate of 74.1% (N = 63/85) and whereas Adnan et al (2025) reported that only 38% (N = 109/290) of pregnancies resulted in delivery beyond 24 weeks. The cutoff for abnormal NT in the study by Bagci et al was > 95th centile for GA. There is no information on how many had NT ≥ 99th centile. This is in contrast to Adnan et al who categorized NT measurements into five groups like us, indicating similar study design like ours.

Our study demonstrated a significant association between increased NT and chromosomal abnormalities, with 40.7% of those who underwent invasive testing showing abnormal genetic results mostly chromosomal abnormalities (91.9%). Trisomy 21 and Turner syndrome were the most commonly identified conditions. These findings were consistent with studies by Bellai-Dussault K et al (2024) and Bianchi et al (2025) both of which reported trisomy 21 as the most identified chromosomal abnormality (6, 8).

Adverse outcomes were also observed in some foetuses with normal genetic testing, indicating that increased NT may reflect risk of structural or perinatal complications. A study by Gadsbøll K et al. showed that even with a normal chromosomal microarray, foetuses with increased NT remain at higher risk for adverse outcomes. A Similar study by Stuurman KE et al. reported that even with normal chromosomal microarray foetuses with an isolated increased NT had a 28.8% risk of either pregnancy loss or an affected child (28, 29).

In subgroup analysis of euploid foetuses with NT ≥ 99th centile, one third had associated hydrops and two thirds had structural anomalies, resulting in 50% pregnancies being terminated and 4% had IUFD. These findings validate the fact that elevated NT is a strong indicator of poor perinatal outcome even in presence of a normal chromosomal testing.

Moreover, these foetuses also need further genetic evaluation as they have a high chance of having SGDs (Single gene disorders). In our cohort of 54 euploid foetuses, only seven underwent further testing due to financial constraints, out of which > 50% had pathogenic variants on WES (Whole exome sequencing). A study by Cao et al (2023) reported a diagnostic yield of 4.8% for WES in foetuses with increased NT alone, and 37.5% in foetus with presence of additional structural abnormalities (30). Together, these findings suggest the need to consider prenatal WES in all foetuses with increased NT and structural anomalies.

Among those who were liveborn few had abnormal outcomes. Thus, in euploid foetuses, NT being ≥ 99th centile was a predictor of poor foetal outcomes.

Table 7 presents an overview of the studies on abnormal NT in the medical literature in last 10 years or so.

Table 7
SUMMARY OF STUDIES ON ABNORMAL NT IN THE LAST DECADE

| Study | Country | Study Design | NT Value/ Centile | Chromosomal Abnormalities | Structural Anomalies | Adverse outcomes (TOP) | Key Findings |
|---|---|---|---|---|---|---|---|
| Present Study<br><br>(N = 135) | India | Retrospective | 95th – 99th vs ≥ 99th centile | 40.7% overall abnormal invasive tests (91.9% chromosomal abnormality) | 70.4% (Hydrops 40%) | 57% (TOP) | NT centile > 99th centile is associated with adverse outcomes, even in presence of normal chromosomes. Long term follow up is required to look for evolving problems in the early childhood stage |
| Sahin et al (2019)(5) (N = 78) | Turkey | Retrospective | > 1.5mm | | 21.1%<br><br>(Cardiac anomalies = 9.6%) | | Higher NT associated with poor outcome |
| Tekesin et al (2020) (31) (N = 393) | Germany | Retrospective | ≥ 95th centile | 72.7% (NT > 6.5mm group) | | TOP = 42.9% (NT ≥ 6.5mm category) | Mildly increased NT, increased risk of an adverse pregnancy outcome |
| Nakamura et al., (2020) (32)(N = 162) | Japan | Retrospective | ≥ 99th centile<br><br>(> 5.5-6.5mm vs ≥ 6.5mm) | 71% (NT ≥ 6.5mm)<br><br>57% (NT ≥ 5.5- 6.5mm) | 16.7% multiple congenital anomalies seen in NT ≥ 6.5mm | 25% IUFD in NT ≥ 6.5mm | Larger NT associated with chromosomal abnormalities |
| Ozyuncu et al., (2021) (33)(N = 158) | Turkey | Retrospective | ≥ 99th centile<br><br>(2.6–<3.5 mm vs 3.5–4.5 mm vs > 4.5 mm | 55.4% in NT > 4.5mm | 85.7% in NT > 4.5mm | 66% in NT > 4.5mm | Higher NT values directly proportional to increased rates of chromosomal, structural abnormalities and adverse outcomes |
| Narava et al., (2022) (34) (N = 132) | UAE | Retrospective | NT >95th centile vs NT ≥ 3 mm vs cystic hygroma. | 7.6% NT > 95th centile<br><br>29.2% NT ≥ 3 mm<br><br>40% in foetus with cystic hygroma | 14.6% NT ≥ 3 mm<br><br>20% in foetus with cystic hygroma | 13.4% miscarriage, 7.8% TOP, 5.6% IUFD in NT ≥ 3 mm<br><br>20% miscarriage, 13.3% TOP, 13.3% IUFD in foetus with cystic hygroma | Risk of chromosomal abnormalities and adverse outcomes increased with NT thickness |

| Study | Country | Study Design | NT Value/ Centile | Chromosomal Abnormalities | Structural Anomalies | Adverse outcomes (TOP) | Key Findings |
|---|---|---|---|---|---|---|---|
| Fantasia et al. (2023) (4) (N = 306) | Italy | Retrospective | 95th – 99th centile | 10.1% | 13.7% | 13% miscarriage or TOP | Mildly increased NT associated with increased risk |
| Niroomanesh et al., (2023) (35)(N = 720) | Iran | Retrospective | NT > 3 mm and normal karyotype | 27.3%<br><br>normal karyotype | 9.6% cardiac abnormalities and 6% other anomalies in foetuses with normal karyotype | 11.9% IUFD<br><br>Abortion 19.9% | Foetuses with increased NT but normal karyotype require follow-up for anomalies |
| Khair et al., (2023) (1)(N = 479, 370 with normal NT and 109 with increased NT) | UAE | Retrospective | NT, ≥ 95th percentile; with normal karyotype vs Normal NT | Normal karyotype | 21% (vs. 3.3%) | Miscarriage 9.2% (vs. 1.1%)<br><br>IUFD 2.8%<br><br>TOP 3.7% | Even when karyotype is normal increased NT is associated with adverse pregnancy outcomes |
| Bet et al., (2024) (36) (N = 109) | Netherlands | Prospective | NT > 2.5mm | 22.9% | 64.0% | 35.8% | Risk increases with increased NT |
| Guo et al., (2025) (37) (N = 4200) | China | Retrospective | NT ≥ 3.0 mm | 17.7% | 13.6% | 31.5% | Increased NT strongly associated with foetal abnormalities |

Our cohort showed that despite normal genetic testing 22% of the liveborn required long term follow up. Three had genetic abnormalities whereas 2 were diagnosed to have autism spectrum disorder. These findings indicate that normal prenatal workup does not completely exclude the possibility of underlying disorder thereby emphasizing the need for long term follow up.

The strengths of this study include being a single centre study ensured that the follow up and protocol for clinical management in these pregnancies was uniform. Secondly this study provided a detailed evaluation of maternal, perinatal and neonatal outcomes, along with long term follow up of live born infants which was lacking in many previous studies.

Moreover, our study was done over a period of eight years from 2017 to 2024. This long duration allowed for the inclusion of a larger number of cases which provided a clearer assessment of the outcome patterns

Limitations of this study were its retrospective design and loss to follow up which was up to 27%. Moreover, there may have been a referral bias since ours is tertiary care perinatal centre, more critical cases were likely to present. Hence the findings may not be extrapolated to the general population.

**Clinical implications**

Points for counselling in pregnancies with abnormal NT.

Invasive prenatal testing should be offered in all women with abnormal NT due to association with aneuploidies, most commonly Trisomy 21. In euploid foetuses with NT ≥ 99th centile, further genetic testing should be carried out to rule out monogenic disorders.

Significantly more foetuses tend to have associated hydrops/structural anomalies when NT ≥ 99th centile in comparison to those with NT 95th -99th centile.

There was an overall decreasing trend of liveborn with worsening NT measurement. The chances of poor perinatal outcomes were 18 times more than good ones when NT ≥ 6 mm.

Among euploid foetuses, NT ≥ 99th centile was associated with poor outcomes.

Carefully selected cases such as those with isolated abnormal NT showing spontaneous resolution on subsequent scans; absence of associated foetal structural anomalies/hydrops and /or normal foetal genetic evaluation may lead to good outcomes in nearly 80% cases. However, these babies may still require long term follow up as some of them may develop issues later on.

## CONCLUSION

In our cohort of 135 pregnancies, 72% (N = 97) had NT ≥ 99th centile and 31.1% (N = 42) had NT ≥6mm. Overall liveborn rates were low, probably due to significant number of foetuses with associated congenital anomalies and or hydrops. Moreover, 40.7% (N = 37) had abnormal genetic results, most common being Trisomy 21.

In the NT ≥6mm, poor perinatal outcomes were 18 times more than good outcomes.

Of the euploid foetuses, who had NT ≥ 99th centile poor outcomes were seen in 53.7%.

In carefully selected cases of ongoing pregnancies with close monitoring, good outcomes are achievable. Long term follow up of liveborns is warranted as some of them may develop problems later on. However, large prospective multicentric trials are needed to look at the long-term outcomes among the liveborns.

## Abbreviations

NT
Nuchal translucency
CMA
Chromosomal microarray and NGS:Next-generation sequencing
IUFD
Intrauterine foetal demise (IUFD)
LMIC
Low middle income countries
GA
Gestational age
QF-PCR
Quantitative fluorescent polymerase chain reaction
SGD
Single gene disorders
WES
Whole exome sequencing

## Declarations

**Ethics approval and consent to participate:** Institutional Review Board (IRB), IRB Min No: 15645 dated 16.08.2023. It was conducted in accordance with the principles of the Declaration of Helsinki.

Consent was not obtained for enrolling in the study as this is a retrospective study.

**Consent for publication:** Not applicable

**Availability of data and materials:**The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Competing interests:** Authors have no conflicts of interest to disclose

**Funding:**No funding was required for this study

**Authors' contributions:**

Concept or design of the article: NSG, MMB and PS;

Acquisition of data: NSG, LSJ, PRN, VK, MT, MPC, MMB;

Analysis or interpretation of data: NSG, LSJ, PS, VK, MMB

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## Figures

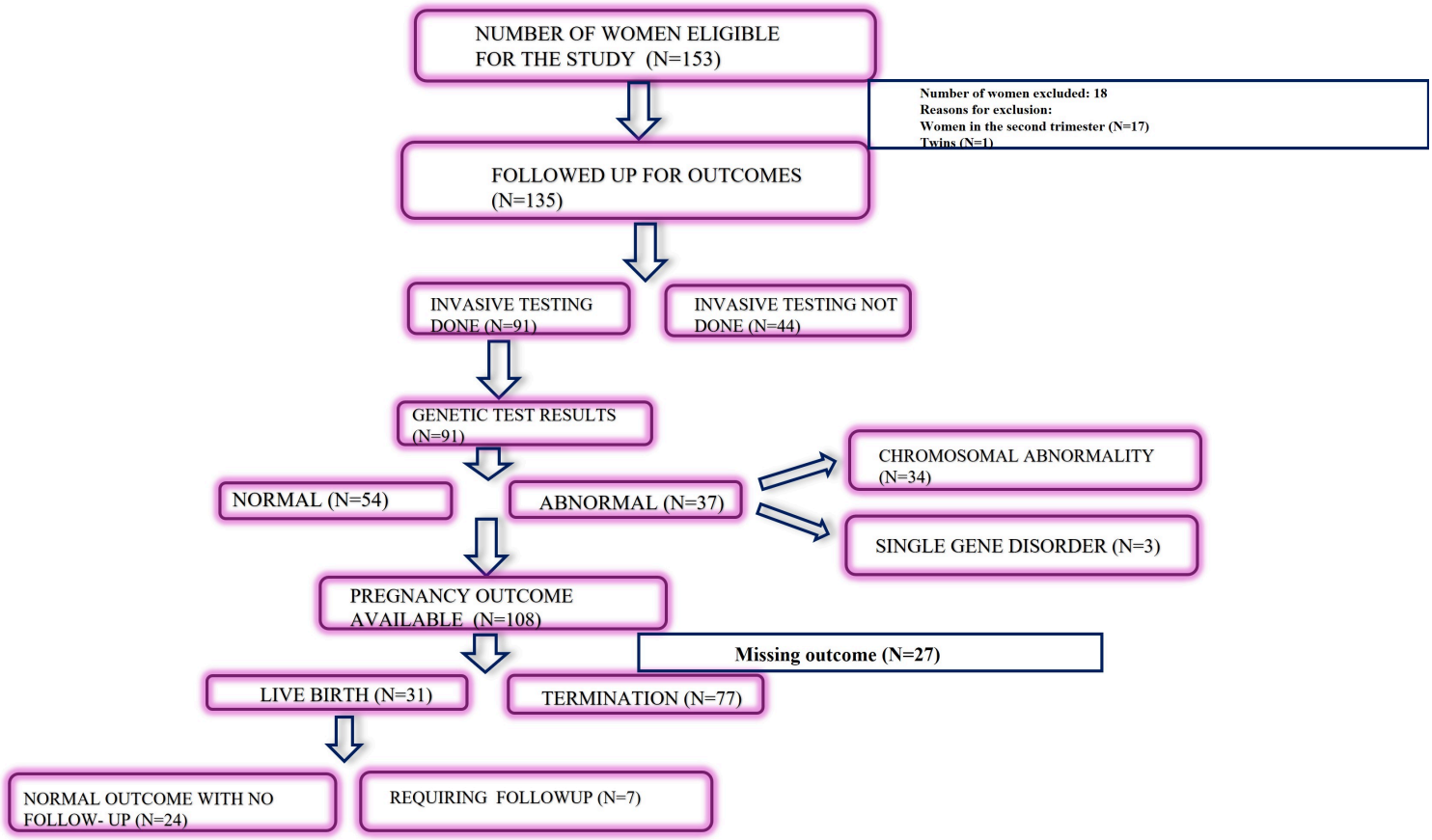



**Figure 1**

**CONSORT DIAGRAM**

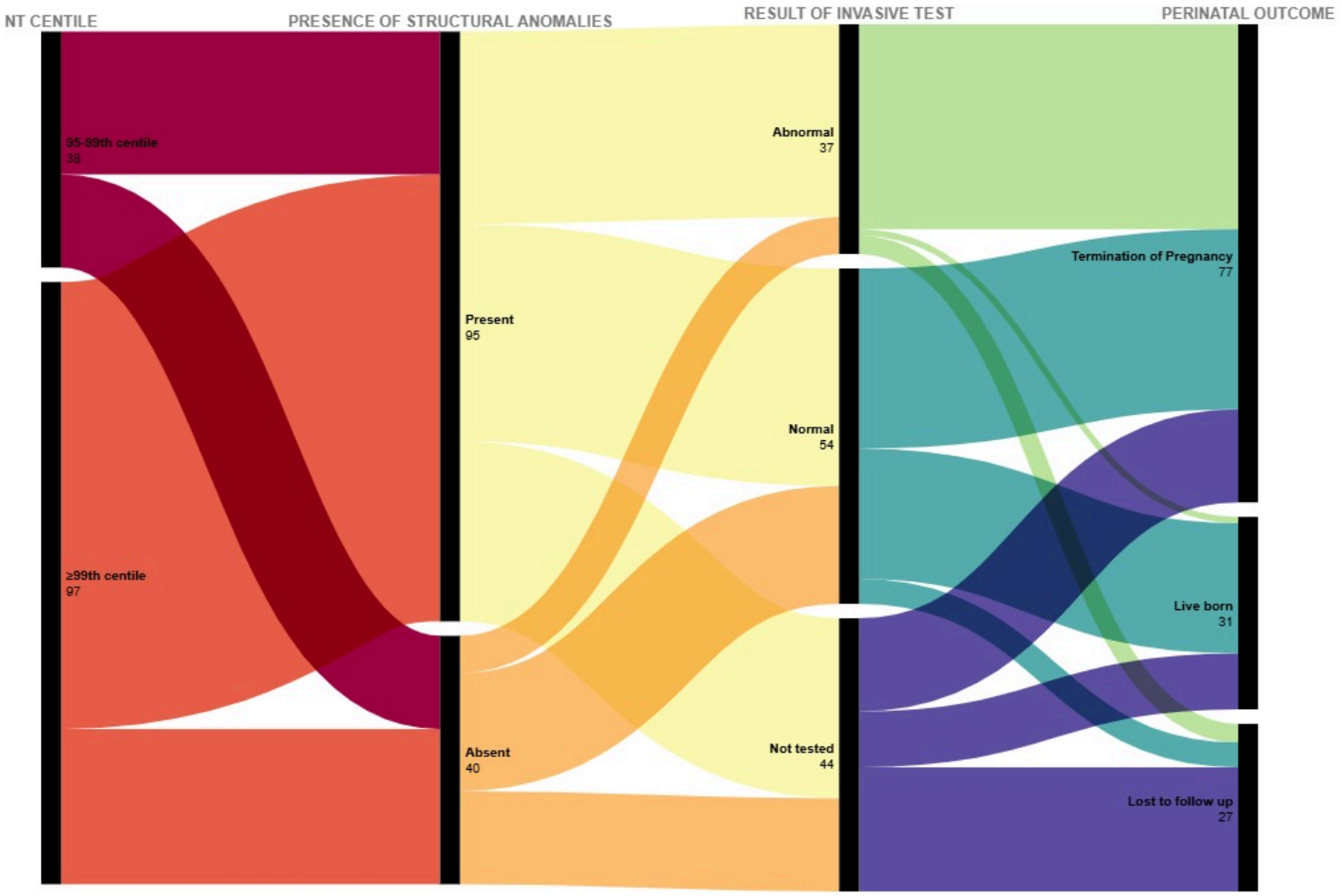



**Figure 2**

**ALLUVIAL PLOT (Legend)**

An alluvial plot or flow diagram was used to demonstrate how our two groups (NT 95th -99$^{th}$ centile and NT ≥ 99$^{th}$ centile) changed; flow across different variables.

The variables included presence or absence of structural anomalies; presence or absence of abnormal genetic evaluation and outcomes of pregnancies (liveborns or terminations).

The ribbons or the flows connect the two groups across the variables mentioned above. The thicker the ribbon the greater the proportion of cases following that pathway.

In the first stratum, the majority of foetuses belonged to the **NT ≥ 99th centile group (N=97),** while a smaller proportion had NT between the **95th–99th centile (N=38).** A larger flow from the ≥99th centile group towards presence of structural anomalies category, suggest that elevated NT is most often associated with congenital anomalies.

In the second stratum, **structural anomalies were present in 95 foetuses,** whereas **40 foetuses had no detectable anomalies** at initial evaluation. Among foetuses with structural anomalies, a large proportion demonstrated **abnormal invasive test results (N=37),** indicating a strong association between structural abnormalities and underlying genetic defects.

In the third stratum, invasive testing outcomes were categorized as **abnormal (N=37), normal (N=54), and not tested (N=44)**. Foetuses with abnormal genetic results predominantly progressed toward **termination of pregnancy**, reflecting the severity of associated chromosomal or genetic abnormalities. However, some foetuses with normal genetic results also resulted in termination or loss to follow-up, emphasizing that a normal genetic report alone does not guarantee a favourable outcome.

In the final stratum**, 31 pregnancies resulted in live births, 77 underwent termination**, and **27 were lost to follow-up**. Live births were more commonly observed among foetuses with normal genetic results and absent structural anomalies.

A small number of foetuses without structural anomalies or with normal genetic testing still had adverse outcomes, emphasizing the evolving nature of pregnancies with increased NT.