



Original Research Article

Study of absent/unossified or hypoplastic nasal bone on ultrasound and its association with aneuploidies

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ABSTRACT

Introduction: Down syndrome is the most common chromosomal abnormality in neonates. Nasal bones are easily identifiable markers on genetic sonograms. AHNb in children with Aneuploidy has been detected by first and second trimester ultrasonography. Evaluation of nasal bone may constitute an additional marker to increase the efficacy of screening for trisomy 21 and can result in major reduction in the need for invasive testing.

Aim & Objectives: To study pregnancy outcome wherein fetuses are diagnosed with absent/unossified or hypoplastic nasal bone (AHNB) on ultrasound in first or second trimester of pregnancy and its association with aneuploidies.

Material and Methods: The retrospective study mainly aimed to evaluate the clinical value of AHNb alone or in combination with other soft markers or structural abnormalities for detection of aneuploidy. Total number of 92 patients with AHNb diagnosed on ultrasound over a period of 9 years were included and their outcome studied.

Results: Of 92 cases studied with AHNb 66.3% had normal pregnancy outcome. Isolated absent nasal bone was associated with abnormal karyotype in only 5% cases and those with soft markers or structural abnormalities were associated with abnormal karyotype in 56.25% cases. So, use of isolated AHNb in ultrasonography may not be an effective screening tool for Aneuploidy.

Conclusion: In case of finding of isolated absent nasal bone, counseling needs to be done, to assure the couple against pregnancy termination and if termination desired, not before karyotyping.

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1. Introduction

Prenatal diagnosis is the science of discovering structural or functional anomalies and birth defects in the developing fetus. It is the testing for a disease or a condition in the fetus prior to birth.

In a publication authored by Langdon Down: Observation of an ethnic classification of the idiots, he described a small nasal bone as one of the several phenotypic characteristics of Trisomy 21.¹ Flattened facial profile and small nose are common in newborns with Trisomy 21.² I studied the second instance of Langdon

Down nasal hypoplasia in prenatal screening for trisomy 21.

Down syndrome is the prevailing chromosomal anomaly among newborns. Approximately 6000 infants are born with Down syndrome in a year, with a prevalence of approximately 1 in every 700 births. Nasal bone hypoplasia is characterized by a nasal bone length that falls below the 2.5th percentile for the duration of gestation. Nasal bones provide as distinct and recognizable indicators on genetic sonograms. Incidence of AHNb is 6.8% in Asian population.³

Absent/unossified or hypoplastic fetal nasal bone (AHNB) in foetuses with Down syndrome can be seen using

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sonography during the first and second trimesters. This has become a recognised indicator in prenatal ultrasonography. The assessment of the nasal bone can serve as an additional indicator to enhance the effectiveness of screening for trisomy 21, can lead to a significant decrease in the requirement for invasive testing and Noninvasive prenatal testing (NIPT).

Ultrasound detection of foetal structural defects is associated with an increased chance of aneuploidy such as Trisomy 21, Trisomy 13, Trisomy 18, Trisomy sex chromosomes and partial Trisomy etc. Roughly 33% of fetuses with trisomy 21 have significant abnormalities, however not all of them can be detected using sonography and only a portion of these abnormalities may be identified during the early stages of pregnancy. Soft markers are ultrasound findings that are not classified as malformations but signal an increased chance of foetal aneuploidy.⁴ Some of the soft markers observed include nasal bone hypoplasia, thickening of the nuchal fold, presence of an echogenic intracardiac focus, choroid plexus cyst, minimal ventriculomegaly, presence of a single umbilical artery, mild pyelectasis, echogenic kidneys, echogenic bowel, short long bones and bilateral sandal gap.

Trisomy 21 (Down syndrome) is frequently identified chromosomal abnormality during prenatal diagnosis. Aneuploidy is the primary factor behind prenatal or neonatal illness and mortality, resulting in significant financial burden on pregnant women, their families and society at large.⁵

There have been different studies conducted all over world on the pregnancy outcome of AHNb and its correlation with aneuploidies, still there is limited data available in Indian literature. Using criteria based on Indian women may result in a higher incidence of chromosomal abnormalities. Research suggests that the length of the nasal bone is shorter in Indian fetuses as compared with other ethnicity.⁶

Studies have shown that between 0.5% and 2.8% of fetuses with a normal number of chromosomes exhibit a delay in the formation of the nasal bone during ultrasound examinations conducted in either the first or second trimester of pregnancy. Limited information is available on the significance of this after aneuploidy has been ruled out. A counseling challenge arises due to the lack of formal research addressing the results in these circumstances. Prevalence of this condition is higher in specific ethnic groups. However, further evidence is required to establish appropriate guidance for advising women of the potential risk of foetal anomalies when an AHNb is detected and invasive testing reveals a normal karyotype.⁷

The aim of this study is to analyze the results of pregnancies with ultrasonography showing an AHNb in the first or second trimester and to determine its association with aneuploidies. In this study, we examined

the potential enhancement in trisomy 21 screening using the ultrasonography to assess the foetal nasal bone. The primary objective of the study was to assess the clinical significance of foetal absent nasal bone, alone or in combination with other soft markers or structural abnormalities, biochemical screening for identifying fetal chromosomal abnormalities.

2. Materials and Methods

A retrospective study was conducted. Ethical committee approval was obtained for the study. Total number of 92 patients with absent/unossified or hypoplastic fetal nasal bone (AHNB) diagnosed on ultrasound were included at Deenanath Mangeshkar Hospital and Research centre, Pune. Patients were identified through a computer search of the database maintained by the foetal medicine unit (sonocare software). All scans were performed by specialist accredited by Fetal Medicine Foundation (FMF), London for evaluating nasal bone, nuchal translucency and any other sonographic anomaly.

2.1. Inclusion Criteria

Patients who attended antenatal opd and genetics opd, which includes all women who had come diagnosed AHNb or diagnosis done in first or second trimester ultrasound showing fetus with AHNb over a period of 9 years.

2.2. Exclusion criteria

Patients with absent/unossified or hypoplastic fetal nasal bone with incomplete records, Patients who are lost to follow up.

Proformas were completed, all the gathered data was entered into SPSS and analyzed with descriptive statistics. Whether AHNb is an isolated finding or associated with other structural abnormalities on ultrasonography NT scan or anomaly scan were studied. Maternal medical records were examined to assess for fetal karyotype results and pregnancy outcomes like spontaneous abortion, termination, intrauterine death (IUD), preterm delivery and term pregnancy. For those who did not undergo prenatal invasive diagnostic procedures or in fetuses in whom any anomalies were present on ultrasound, newborn medical records were examined for physical examination results at birth and neonatal complications.

3. Results

During the study period, there were total 92 cases of absent/unossified or hypoplastic fetal nasal bone (AHNB) that were diagnosed in the hospital.(Table 1)

Of 92 cases studied, 56.5% had isolated AHNb, 18.5% had AHNb with associated soft markers, 9.8% had AHNb with associated structural anomalies and 15.2% had AHNb with associated both soft markers and structural anomalies



Figure 1: Normal nasal bone on ultrasound

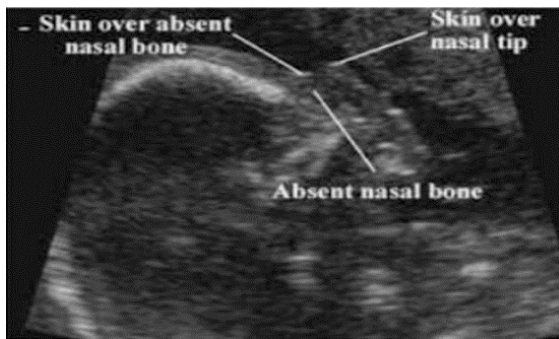


Figure 2: Absent nasal bone on ultrasound

Table 1: Age wise distribution of cases studied.

Age Group (years)	No. of cases	% of cases
<35	82	89.1
≥35	10	10.9
Total	92	100.0

Table 2: Percentage Distribution of absent/unossified or hypoplastic fetal nasal bone (AHNB) with or without soft markers and/or any structural anomaly.

Diagnosis of AHNB	No. of cases	% of cases
Isolated AHNB	52	56.5
AHNB with soft markers	17	18.5
AHNB with structural anomalies	9	9.8
AHNB with both soft markers and structural anomalies	14	15.2
Total	92	100.0

in the study group.(Table 2)

Of the 92 cases, 20 did not undergo karyotyping, leaving 72 cases for further analysis. Of 72 cases studied (on whom karyotyping was done), 20 (27.8%) had abnormal karyotype and 52 (72.2%) had normal karyotype in the study group.(Figure 3)

Of 92 cases studied, 61 had normal pregnancy outcome i.e., term / preterm delivery and remaining 31 had abnormal pregnancy outcome i.e., Termination of pregnancy, IUD,

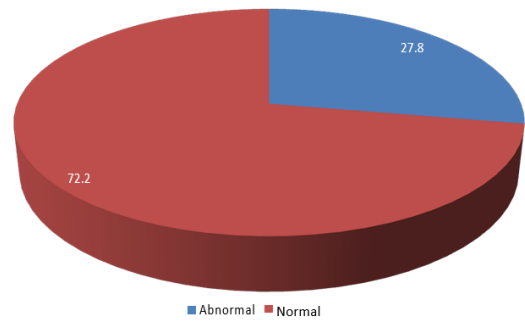


Figure 3: Distribution of karyotype status in the study group

Table 3: Distribution of pregnancy outcome in the study group.

Pregnancy outco	Karyotype		Total	% of cases
	Done	Not done		
Term / Preterm Delivery	46	15	61	66.3
Termination of Pregnancy	24	2	26	28.3
IUD	2	1	3	3.2
Still Birth	0	1	1	1.1
Spontaneous Birth	0	1	1	1.1
Total	72	20	92	100

still birth and spontaneous abortion.

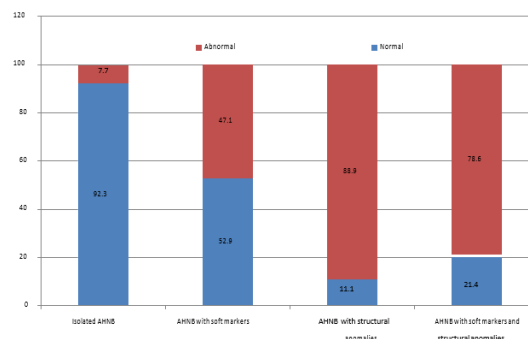


Figure 4: Distribution of pregnancy outcome according to the diagnosis of AHNB along with isolated or associated with soft markers and/or structural anomalies

Of 52 cases with isolated AHNB, 48 had normal pregnancy outcome, 4 had abnormal pregnancy outcome.

Amniocentesis was done on 59 cases, out of which 45 had normal karyotype and 14 had abnormal karyotype. Post-delivery karyotype performed on one baby, it was normal karyotype. Abortus karyotyping was done in 12 cases.

P-value by Chi-Square test <0.05 is considered to be statistically significant. The distribution of incidence of abnormal karyotype is significantly higher among the group of cases with AHNB associated soft markers or structural abnormality compared to group of cases with isolated AHNB in the study group (P-value<0.001).

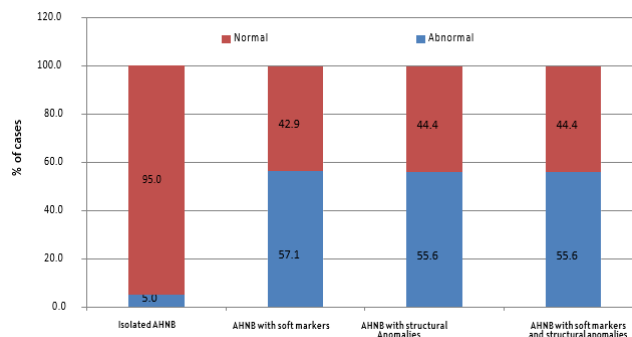


Figure 5: Distribution of incidence of abnormal karyotype according to the diagnosis of AHNb along with isolated or associated with soft markers and/or structural anomalies

Table 4: Distribution of combined screening or 2nd trimester biochemical screening in the study group.

Screening	No. of cases	% of cases
Not done	12	13.1
Screen Negative or low risk	48	52.2
Screen Positive or high risk	32	34.7
Total	92	100.0

Out of 32 with screen positive, 28 patients underwent karyotyping and 36 out of 48 patients with screen negative underwent karyotyping. Out of those, 15/28 (53.6) and 4/36 (11.1%) had abnormal karyotype.

4. Discussion

Of 92 cases studied with AHNb, 61 (66.3%) had normal pregnancy outcome. Of the 92 cases, 20 did not undergo karyotyping, leaving 72 cases for further analysis.

The mean of age in the group was 29.1 ± 4.4 years and the minimum – maximum age range was 19 – 43 years. Of 92 cases studied, 89.1% were of age less than 35 years and 10.9% were of age more than or equal to 35 years. Of the 10 cases of more than or equal to 35 years age, 6 had abnormal karyotype. That means 30% patients with abnormal karyotype were more than or equal to 35 years age. This is comparable to studies of Hirak D et al.⁸ 23.68 % and with Zournatzi V et al.⁹ 30% of trisomy 21 occurred in mothers over the age of 35. Advanced maternal age is associated with an increased chance of aneuploidies, by non-disjunction of the chromosomes at the time of maternal oogenesis. This makes it a significant factor in the likelihood of fetuses having chromosomal abnormalities.¹⁰

Among those who underwent karyotyping, 27.8% had abnormal karyotype which is comparable to Li H et al.¹¹ 27.8% and Yan du et al.¹² 22.54%.

Isolated AHNb was associated with abnormal karyotype in only 5 % cases. Our study rate is comparable with Lin R

et al i.e, 4.5%,⁵ Yan du et al i.e, 7.14%¹² and Desai P et al i.e, 8.4%.¹³

Isolated AHNb was associated with 92.3% had normal pregnancy outcome. This was comparable to Prasad CS et al. (86.7%).¹⁴

So, use of isolated AHNb in ultrasonography may not be a reliable method for screening Down's syndrome. When seen along with soft markers or structural abnormalities were associated with abnormal karyotype in 56.25% cases is comparable with Dash et al.¹⁵ 41.4% and Yan du et al.¹² 44.83%. The distribution of incidence of abnormal karyotype is significantly higher among the group of cases with AHNb associated soft markers or structural abnormality compared to group of cases with isolated AHNb in the study group (P-value=0.001). This can be used for appropriate counseling of couples.

Amniocentesis is recommended for fetuses that have a structural abnormality or additional soft marker, which should be thoroughly examined by a skilled sonologist.

Of the patients with positive biochemical screening, 53.6% had abnormal karyotype. We found significant difference in abnormal karyotype status between group of cases with positive and negative biochemical screening. My study had sensitivity of 79% and specificity of 71%.

Out of 20 abnormal karyotype, 15 were Trisomy 21 (most common aneuploidy), one Trisomy 13, one Trisomy 18, one Trisomy sex chromosomes, one partial trisomy 18q21 and one partial trisomy 5p+.

Limitations of this study is that the nasal bone assessment is an observer dependent variable. So specialist with appropriate training is necessary to use this parameter for aneuploidy screening.

Incidence calculation of AHNb limited as the study population was selected on the bias of AHNb.

All 92 patients did not undergo karyotyping, so karyotype status of all patients was not known.

5. Conclusion

All pregnant women irrespective of maternal age should undergo prenatal screening.

Isolated nasal bone was associated with abnormal karyotype in only 5 % cases and in majority of cases this is a normal variation. In case of finding of isolated AHNb, counseling needs to be done, to assure the couple against pregnancy termination and if termination desired, not before karyotyping. Positive biochemical screening is strongly associated with abnormal karyotype. So, these cases should always be offered karyotyping/ noninvasive Prenatal Testing. The first-trimester anomaly scan does not serve as a substitute for the second-trimester anatomic survey, which continues to be the most complete fetal structural evaluation. But the first trimester screening offers the option for earlier diagnosis of major anomalies.

Clinical interpretation of various soft markers should be done judiciously prior to opting for invasive test and termination of pregnancy.

6. Abbreviation

AHNB- Absent/unossified or hypoplastic nasal bone, NIPT- Non-invasive prenatal testing.

7. Source of Funding

None

8. Conflict of Interest

None


9. Acknowledgments

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