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SURVEY ARTICLE

Various Methods for Computing Risk Factors of Down Syndrome in Fetus

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Abstract
There is a chromosomal defect that significantly affects an individual's life is Down syndrome. Early identification of Down syndrome is crucial for an accurate assessment of the fetus. The process of assess the fetus includes measurement of the crown rump length, fetal heart rate, short arm or thighs bones length, nasal bone present or absent and the thickness of fluid behind neck. And the process are done during first and second trimester of pregnancy. Various invasive and noninvasive screenings are used for Down syndrome diagnosis. Research on diagnosing Down syndrome has been extensively documented. Additionally, this survey includes various techniques using deep learning for detecting the availability of Down Syndrome and does analysis of image processing methods and formulas for its diagnosis.

1 Introduction

The most of chromosomal condition like Down syndrome is common reason of intellectual disability. It's just a noncurable condition to have Down syndrome. It cannot be treated because it is not a sickness. Down syndrome can be identified before a child is born, despite the fact that it cannot be prevented. An embryo that develops with Trisomy-21(extra copy of chromosome-21) or one that is partially or completely extra is what results in Down -Syndrome [10]. Figure 1 [10] Here is a graph tells how age of pregnancy shows impact on child birth with down syndrome. There is one child takes birth with down syndrome out of 900 births at the mother's pregnancy age of 30, out of 400 births at the mother's pregnancy age of 35, out of 300 births at the mother's pregnancy age of 36, out of 230 births at the mother's pregnancy age of 37, out of 180 births at the mother's pregnancy age of 38, out of 135 births at the mother's pregnancy age of 39, out of 105 births at the mother's pregnancy age of 40, out of 60 births at the mother's pregnancy age of 42, out of 35 births at the mother's pregnancy age of 44, out of 20 births at the mother's pregnancy age of 45, out of 16 births at the mother's pregnancy age of 48, out of 12 births at the mother's pregnancy age of 50.

Due to this disorder, 95% of all chromosomal abnormalities take place.

The addition of extra chromosomes in individuals with Down-Syndrome has an impact on both their physical characteristics and development, as depicted in Fig. 2. Detecting Down syndrome can be achieved through prenatal testing, encompassing screening and diagnostic tests, as illustrated in Fig. 3. During the 10–14th to 15–22nd weeks of pregnancy, a combination of a blood test and ultrasound is employed for screening. While the blood test can indicate a high likelihood of Down syndrome, it cannot provide a definitive diagnosis. Non-invasive diagnosis of Down syndrome can be accomplished through ultrasonography. Important features in ultrasonography include the fetal heart rate, nasal bone presence, nuchal translucency, FMF(frontomaxilliary facial) angle, and other factors. Invasive procedure includes cutting or surgery of skin of uterus which can become risk of complications and the miscarriage for fetus. In the early stages of pregnancy, ultrasonography can identify the fluid stored under the fetus-skin around the neck area, known as nuchal translucency [5]. An observation is done as a darkened region beneath the skin and typically occurs during the 11th and 14th weeks of pregnancy. If the nuchal translucency (NT) width exceeds the usual measurement of under 2.5 mms, it could indicate the presence of Down syndrome or another chromosomal abnormality. The fetal nasal bone is another

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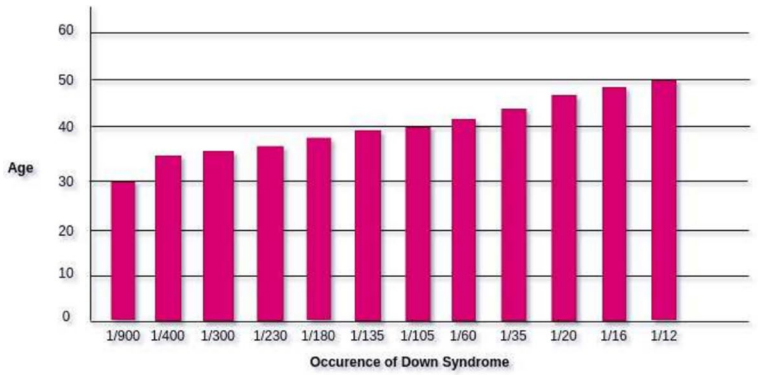


Fig. 1 Occurence of Down Syndrome by age of pregnancy (Source: [10])

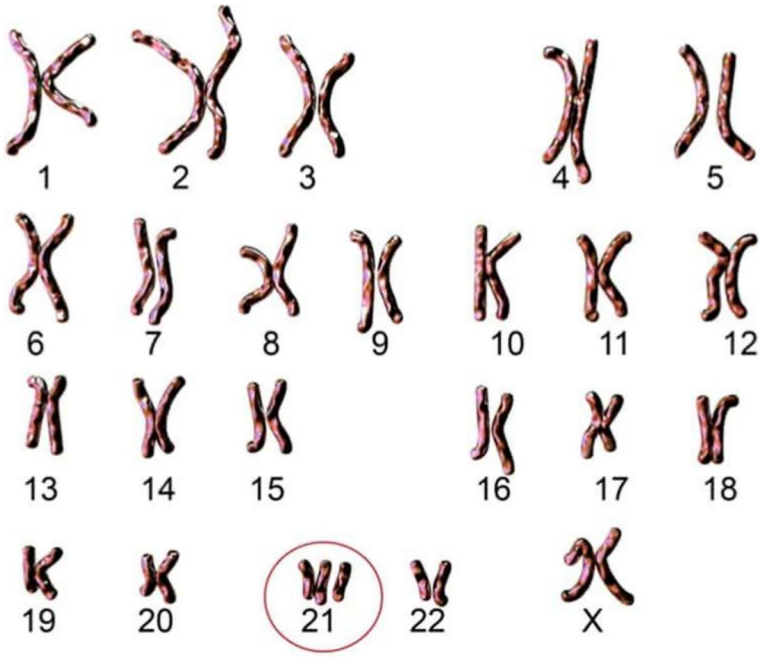


Fig. 2 The view of extra chromosome- T21 for Down Syndrome (Source: [29])

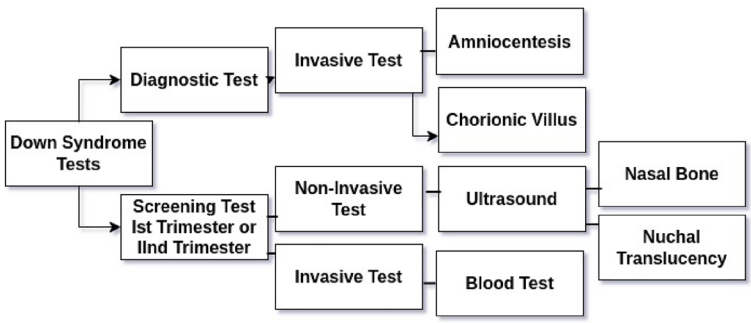


Fig. 3 The prenatal-screening (Source: [28])

prominent indicator of Down syndrome [5]. When examining the nasal bone, you should be able to identify three separate lines. The first line is a thick parallel line located just above the top line, and it appears more echoic than the overlying skin, resembling an equals (=) symbol. The topmopst line represents the skin itself,& the third line indicates tip of nose. A condition is if skin and nasal-tip are present there, but there is no discernible echo indicating the availability of nasal bone, it is treated as absent.

This review's main goal is to:

- Summarize the research that has been done on noninvasive methods for Trisomy 21 detection in the early stages of pregnancy.
- To identify the specific characteristics or features that change with gestational age and are documented in ultrasound images during each trimester.
- To gather the techniques detailed in the research that were employed to develop and evaluate the dependability in ML algorithm.
- To analyse different applications of deep-learning methods for improved Down syndrome detection.

2 Materials and Methodologies

We utilized the databases PubMed, IEEE Xplore, Scopus and Elsevier to access research papers. Our search criteria primarily concentrated on attributes such as NB(nasal bone), DS(down syndrome), NB length and similar terms. We emphasized the advantages and drawbacks to gain a deeper understanding of the techniques employed for Down syndrome detection.

1. In the initial trimester, blood tests are conducted to assess the levels of placental pregnancy-associated plasma protein-A proteins (PAPP-A) and beta human chorionic gonadotropin (HCG). [21] During the second trimester, a set of triple and quadruple measurements is taken, along with an alpha-fetoprotein (AFP) test. These tests help determine the probability of the fetus having chromosomal abnormalities. Importantly, the blood tests do not pose any harm to the fetus.
2. In contrast to X-rays and gamma rays, which involve exposing the body to radiation, diagnostic sonography, or medical ultrasound, is considered the safest imaging technique available.

This review article intends to present non-invasive ultrasonography methods for detection of Down Syndrome.

2.1 Measurement of Nuchal Translucency Fluid (NT) Thickness Through Ultrasonography

The most prevalent autosomal chromosomal anomaly, Down syndrome, affects one in 800–1000 babies. The NT test, as seen in Fig. 3, can be used to diagnose Down syndrome at its earliest stages. Through the assistance of automated techniques and processing, it has been determined that measuring nuchal translucency (NT) serves as the primary indicator for detecting Down syndrome [11] In the first trimester, this test can also detect other chromosomal abnormalities [2]. The research related to the automated assessment of width of NT is summarized in Table 1. This section provides a concise overview of the various techniques used to estimate the width of NT from Ultrasound pictures.

2.1.1 Measuring the NT Width During First-Trimester from Ultrasound

Thickness of amniotic fluid in back of neck is assessed to identify DS in the first trimester(10–14 weeks of pregnancy) in the study published by Nirmala and Palanisamy [2]. Blob analysis is used to carry out this NT measurement. Mean shift analysis is used to segment the nuchal translucency zone, and a clever operator helps to make the fetuses' edges more visible. Median filtering is used to remove the speckle noise that is deteriorating the photos [2]. A normal fetus's NT thickness throughout the gestational period, which ranges from 11 to 14 weeks, cannot be larger than 2.12 mm [2]. Computed-assisted measuring gives doctors and clinicians an accurate reading that they can use to alter the NT thickness. Figure 4 depicts the fundamental phases of image processing.

2.1.2 To Measure the NT Width During First-Trimester from Ultrasound

False detection results from manual examination and NT thickness computation. So, an automated method of NT thickness measurement is suggested. During the first trimester, fetal ultrasound scans are used to precisely assess the NT width. the crown-rump length(CRL);total length of fetus from head to buttack is the foundation for NT measurement. The CRL must range from 45 to 84 mm. The back neck(nuchal translucency) area is extracted or featured by Morphological process and Otsu thresholding, and the back of neck having amniotic fluid seems to be in black-spot. This spot has been extracted by Lee filters. Maternal serum indicators have been employed for aberrant amniotic width in back of neck screening to increase detection rates [11].

2.1.3 Measuring the NT Width Using Neural Network and Wavelet Analysis

Ultrasound imaging is a well-known non-invasive method for detecting chromosomal abnormalities and other disorders connected to the heart, brain, and other organs. A measuring method for determining the thickness of nuchal translucency using an unsupervised approach was presented in the work by Sciortino et al. [5]. A black flap or anechogenic region surrounded by two thin hyperechogenic patches is what the NT ultrasonography region looks like. According to Fig. 5, wavelet analysis and neural network classifiers were recommended as efficient ways to find and measure NT. The 97.4%. accuracy is maintained.

Table 1 Comparative study of different Mthods for Nuchal Translucency

Done by	Procedures Used	Results obtained
Mary Christeena Thomas & Sridhar P. Arjunan [1]	DETECTION OF EDGE - Canny Operator EXTRACTING OF FEATURE - "Nuchal Translucency" FILTERATION - Median Filtering (for de-speckling) THICKNESS OF NT - "Blob Analysis" SEGMENTATION OF IMAGE- "Mean Shift Analysis"	The 14th week of normal fetus must have NT width greater than 2.12mm
Nirmala & Palanisamy [2]	DETECTION OF EDGE - "Canny operator" EXTRACTION OF FEATURE - "Nuchal translucency" FILTERATION - "Median Filtering (de-speckling)" THICKNESS OF NT - "Blob analysis" SEGMENTATION OF IMAGE - "Mean shift analysis"	The 14th week of normal fetus must have NT width greater than 2.12mm
Sciortino et al. [5]	EXTRACTION OF FEATURE - "To measure the thickness of the NT(nuchal translucency)" METHODOLOGY - "Neural Network classifier and Wavelet Analysis"	The obtained error of 0.3mm in NT width was in 97.4%
Sonia & Shanthi [11]	SEGMENTATION OF IMAGE - "Morphological operation with Otsu thresholds" EXTRACTION OF FEATURE - "Nuchal Translucency (NT) thickness measurement" FILTER and ROI - "Lee filter"	"Normal fetus NT width: 1.99 ± 0.62 mm; abnormal fetus NT width: 4.10 ± 0.90 mm during 11 to 13+6 weeks of gestation i.e first trimester"
Sonia & Shanthi [14]	EXTRACTION OF FEATURE - "Nuchal Translucency (NT)" DENOISING METHOD - "Lee and Frost Filter" CLASSIFICATION - "Gray Level Co-occurrence Matrix (GLCM), classifier-Support Vector Machine (SVM) with Polynomial Kernel. "	"Classification rate of 94.4% and Better performance were obtained with Polynomial Kernel function using SVM classifier "
Yinhui Deng et al. [12]	CLASSIFICATION - "SVM applied to represent the NT, head, and body" METHODOLOGY - "for detection of the NT region Hierarchical structural model used " EXTRACTION OF FEATURE - "Automated NT detection"	"An optimal solution for NT detection from tree-structured possibilities of NT can be found by generalized distance transform and Dynamic Programming. "
Siqing Nie et al. [16]	METHODOLOGY - "to detect the width and NT region Dynamic programming is used " EXTRACTION OF FEATURE - "Thickness of NT"	"This technique is able to detect the 1-D(one dimension) marker(NT thickness) and +1-D(higher dimension) markers like volume and area"
Anzalone et al. [20]	PREPROCESSING - "SVM classifier & Anisotropic filtering ROI" METHODOLOGY - "perceptron in multi-layer network. A hierarchical structural predefined model for the automatic detection of the NT region". EXTRACTION OF FEATURE -"NT(Nuchal translucency) width from video."	"The predefined prototype which can measure NT thickness automatically from ultrasound video instantly"
Nina Mahale et al. [23]	EXTRACTION OF FEATURES -"differentiation of NT width along with CRL(crown rump length) and method is (LR)Linear Regression for separation"	"The average or mean of CRL was found 58 ± 9.07 mm; The average or mean of NT width was found 1.5 ± 0.5 mm; the median pregnancy age was found 12.5 weeks"
Shiney et al. [34]	EXTRACTION OF FEATURE - "Nuchal Translucency Thickness, Naso Frontal Angle(NFA), Nasal Bone Length"	"By combining two or more soft markers the diagnostic accuracy is enhanced"
Andreas et al. [19]	CLASSIFICATION - "SVM and k-nearest neighbor models" EXTRACTION OF FEATURE - "Noninvasive estimation" ML TECHNIQUE -"ML techniques- artificial neural network (ANN)"	"ANN predicted best results with Trisomy 21 cases-0% false negative rate, 3.9% false positive rate and 96.1% of euploids"
Nicolaides et al. [25]	EXTRACTION OF FEATURE - "to evaluate the NT thickness at 10–14 weeks' gestation for finding abnormal fetus karyotype"	"Descrepancy in Chromosomes is 3%(28 of 827 cases).51 fetus i.e 6% fetus were reported with 3–8 mm NT width 35% in 18 cases. "

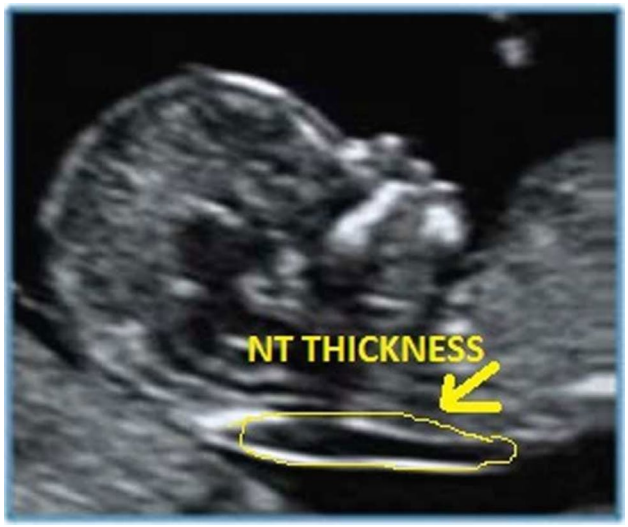


Fig. 4 Nuchal translucency thickness in foetus (Source: [11])

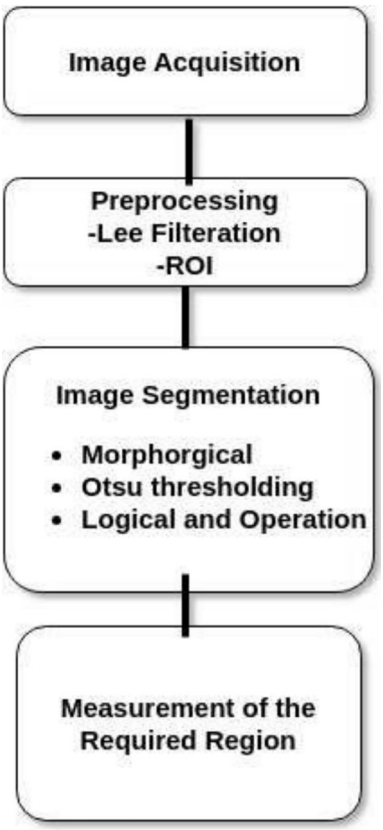


Fig. 5 Basic image processing system - BIPS (Source: [11])

2.1.4 Use of Hierarchical Structure to Find Fetus with Nuchal Translucency [12]

Early gestational stages are when the NT thickness is assessed, necessitating ineffective manual intervention that took more time. The hierarchical structural model automatically detects the NT region to get around this. The SVM classifier is used to depict the fetus's NT, head, and body. For NT detection, distance transform and dynamic programming are used.

2.1.5 Finding NT with 3D Ultrasound Technique

During the early stages of pregnancy, all fetuses display back neck spot (NT), which is a buildup of fluid in the fetal skin around the fetal neck area. Sonographers traditionally evaluate width of amniotic fluid in neck manually in the mid-sagittal view as part of prenatal screening. Based on dynamic programming was published by Nie et al for measuring NT width in mid-sagittal view [16]. As a result, 3D ultrasound data now includes NT volume measurements. With this technique, NT may be detected more accurately (Fig. 6).

2.1.6 Measuring the NT Width Using Ultrasound Video [20]

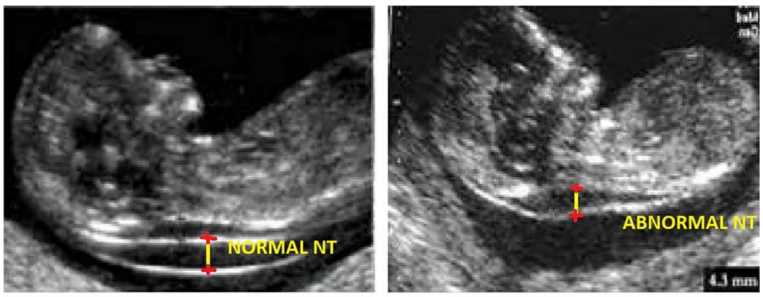
Ultrasound images enable the assessment of the nuchal translucency thickness of the fetus. Presently, this measurement is manually determined by the sonographer, a process that is time-consuming, subject to potential errors, and reliant on the expertise of highly skilled professionals.

2.1.7 Variation in Nuchal Translucency on Inreasing CRL(Crown Rump Length) and Gestation Age of Normal Singleton Pregnancy

To evaluate width of amniotic fluid in back of neck using ultrasound-image in a healthy fetus during 10–14th weeks of pregnancy, the work of Obg et al. [23] was examined. With a 10 mm spacing and the 95th percentile, the NT thickness was calculated using the linear regression approach. To check for any chromosomal abnormalities, one uses this relevant data on fetus back neck spot i.e NT width reference.

2.1.8 Segmentaion of Nuchal Translucency Using SegNet and VGG-16 [1]

There are a lot of difficulties to segment the NT region because of speckle noise and less margins. The study introduces VGG-16 for semantic segmentation of NT area. The NT segmented areas are trained for the identification of DS utilizing a transfer learning approach using AlexNet. The proposed model had sensitivity −85.7%, classification accuracy −91.7% and a receiver operating characteristic (ROC) −0.95. It also had a Jaccard index of 0.96.



(a) Normal NT (b) Abnormal NT

Fig. 6 NT in normal and abnormal fetus (Source: [2])

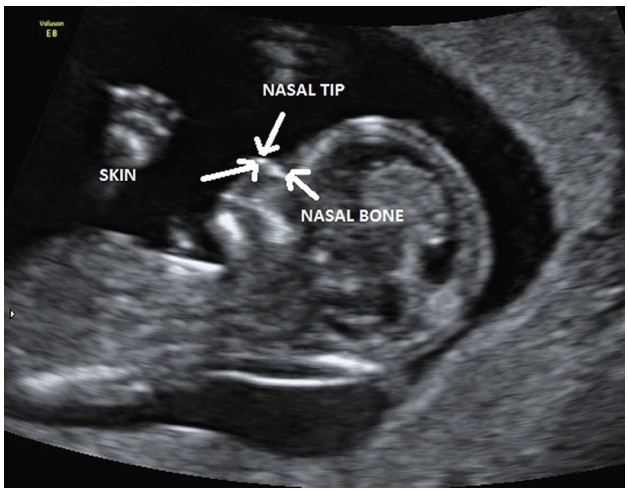


Fig. 7 Nasal bone presence (source: [9])

2.1.9 Disadvantages of NT Measurement

The decision to measure is made by qualified professionals. Since the width of NT is only a few millimeters, even a small discrepancy in the sonographer's estimation of NT thickness could result in a misdiagnosis. Additionally, automatic computerised evaluation has been developed to address this issue. NT width shouldn't be larger than 2.12 mm for a fetus in gestational week 14.

2.2 Nasal Bone Detection

An addition of 21st chromosome in fetus causes Down Syndrome as indicated in Fig. 7, is the most prevalent chromosomal anomaly [2–31]. According to a recent study, the absence of the nasal bone is a crucial sign for identifying Down syndrome at an early stage of pregnancy. The ultrasonic images lose quality due to speckle noise. As a result, NB detection during the first trimester is particularly challenging. The methods described in the literature are outlined in this section (Table 1).

2.2.1 finding NB(Nasal Bone) Using ANN During First Trimester

The detection of Down syndrome using various preprocessing methods of image and BPNN (Backpropagation Neural Network) technique has been described in a work done by Sonia and Shanthi [9]. To extract features in the spatial and transform domain, DCT (Discrete Cosine Transform) and Wavelet Transform were utilized. They claimed that applying a hybrid de-speckling technique improved accuracy.

2.2.2 To Find Trisomy 13, 18,21 Using Various Screening Test

According to the approach described by Maiz et al. [13], "screening for Trisomy 21, 18, 13, and Turner syndrome is done on the fetal nasal bone between 11 and 13 weeks of gestation". Numerous indications are utilized to identify the syndrome, including PAPP-A (Pregnancy-Associated Plasma Protein A), serum-free B human chronic gonadotropin, fetal heart rate (FHR), and nasal bone thickness.

2.2.3 Finding NB for Detecting Down Syndrome in Earlier Age of Fetus

Currently, the presence of nasal bone in the fetus's ultrasonogram image can be used to visually identify someone with Down syndrome. The smaller size of NB in the first trimester makes it difficult for sonographers to visually identify them, which can cause confusion and mistakes. A study discussed by Anjit et al. [4] focuses on different image-preprocessing methods that may reliably identify Down syndrome at an earlier.

1. segment-feature extraction of NB using thresholding of Otsu and
2. Figure 8 illustrates a logical various operation in transforming domains utilizing the BPNN network, DCT, and wavelet-transformation and the spatial image.

As Nasal Bone (NB) examination involves a visual inspection of the fetus through ultrasonography, it is sus-

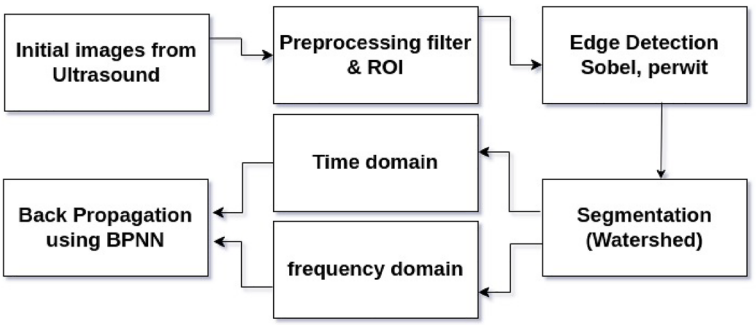


Fig. 8 To find NB(Nasal Bone) reported in Block Diagram. (Source: [3])

ceptible to errors and inefficiencies, which can increase the chances of false detections. To address these issues, a study conducted by Rajesh and Devi [10] proposed a computational approach to detect instances of NB using Backpropagation Neural Networks (BPNN). This method utilizes "Daubechies(D4) Wavelet-transforms and DCT(discrete cosine transform)" [10] to extract nasal spot in both the spatial and transform domains. Furthermore, a median filter is applied to ommit speckle-noise from the ultrasound images.

2.2.4 Using Method of Map Matching

Wee and Supriyanto proposed a computerised method map matching to detect the availability of nasal bone [8]. Prior to map matching based on picture correlation, image pre-processing techniques are used to determine the presence of the nasal bone. These procedures used to be operator-dependent, which led to errors and inaccurate results.

2.2.5 Using Fetal Nasal Bone Length

Nasal Bone Length (NBL) is a method to identify Down syndrome that was published in a study by Sonia and Shanthi [9]. Based on the Euclidean distance, the NBL is determined. To assess NB length at an early stage, a number of techniques are used, including "ROI, NB segmentation, Otsu thresholding, and logical operations" [9].

2.2.6 Using Cross-Correlation Method

In the survey of Wee et al. [15], the nasal bone of the fetus was identified using a normalized grayscale cross technique. The nasal bone's threshold boundary is set at 0.35 mms. We can reliably categorize the nasal bone using this method. Noise is removed from the image, and the nasal bone ROI is segmented. The accuracy is maintained around 96.26%, making it an effective way to locate the NB. Figure 8.

2.2.7 Finding the NB Length in Second Trimester of Pregnancy [24]

Survey on the Indian population, a survey on fetus NB during 16–26 weeks of pregnancy is conducted focusing on the length of NB. The nasal bone of the fetus ranged in angle from 45° to 135° when measured between 2004 and 2009 in 2962 pregnant women. Gestational age should be taken into consideration when defining the hypoplasia of NB (Fig. 9). In the second trimester, ultrasound images are also retrieved, segmented, and calculated to determine the NB length and Front Maxillary-Facial angle (FMF) to look for Down syndrome [6]. Here, the image is processed using canny operators and mean shift analysis. The FMF is determined to be less than 85°, and it is fixed that a good growth rate rather than normal fetuses.

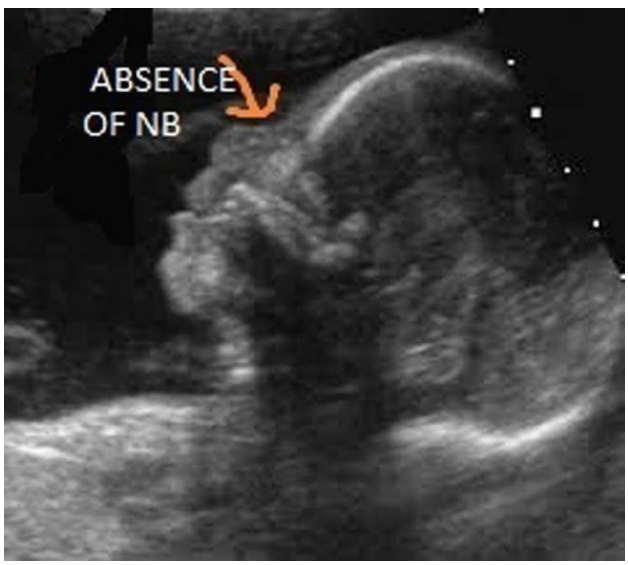


Fig. 9 Absence of nasal bone

2.2.8 Classification of Image Features to Detect Down Syndrome Using Haralick Features

Fetuses with DS have an cognitive defect [13]. Down syndrome is a hereditary conditions. A technique GLCM(Gray-level co-occurence matrix) is used in the research presented by Sonia and Shanthi [14]. They use Haralick features to extract the features for their investigation. In order to eliminate the Speckle noise, Lee and frost filters were utilized. De-noising methods including image processing were performed; ROI extraction, extraction of feature, and SVM classification were utilized for categorize the properties in both casual and pathological NT with Accuracy 94.4%.

2.2.9 Disadvantages of Nasal Bone Measurement

Due to the NB's modest physical size in the first trimester of pregnancy, many approaches are inaccurate. The speckling-spots, which reduces the quality of image, is another significant flaw in the ultrasound image. Only proficient sonographers who have received training can make a reliable diagnosis. To combat this, we employ de-speckle to lessen scattered spots and enhance the qualities for a perfect test. Additionally, 3D ultrasound imaging, which allows for more precise measurements in the 2nd and 3rd trimesters, can be used for the study.

2.3 Facial Features

The research that has been reported on the numerous facial traits that are utilized to identify the presence of Down syndrome are compiled in Table 2.

2.3.1 Using Face-Image to Identify Down Syndrome

Chromosome disorders include Down syndrome [17]. A Down syndrome patient is at risk for a variety of conditions, including epilepsy, mental impairment, and congenital cardiac defects. By looking at the face, one can make a Down syndrome diagnosis. In this study, a novel approach to detecting Down syndrome using machine learning and photography is offered. To discriminate between normal and abnormal fetuses, SVM classifiers are used. The achieved accuracy is 97.92%. Down syndrome affeted Children have distinctive facial features (Table 4).

With the use of facial pictures and computer-aided diagnostics, Down syndrome can be identified and diagnosed. Here, utilizing facial images, we suggest a machine-learning technique to identify Down syndrome. With an accuracy of 94.6%, an SVM classifier using an RBF kernel can distinguish between normal and abnormal fetuses.

According to this study's findings trisomy 21 and other chromosomal diseases, including NB, are strongly linked to identifying a fetus's abnormality. The CRL and NB are measured during the ultrasound to check for the sign of Down syndrome availability.

2.4 Deep Learning

With deep learning, we can feed photos directly into the algorithm, which properly predicts the item without the need for manual feature extraction. Many inputting layer and abstracted layers can be developed and used in deep learning. The approach allows to supervised ML, unsupervised ML and semi-supervised i.e pattern analysis.

2.4.1 Deep Learning Based Model

Although DS cannot be currently fixed, it is detected and avoided in early age of fetus [23]. Deep learning algorithms were employed in a latest survey by Feng et al. [22] to construct chromosomal SNPs based on the recently released illuminate array of genotype.

The availability of some typical face-characteristics (mentioned in Table 3) as well as physical traits such small mouths, noses, and ears can be utilized to diagnose Down syndrome [17]. Karyotype testing is done to verify the diagnosis. These are costly & time-consuming, and many out-of-the-way medical facilities lack easy access to these technologies.

NT is a valuable marker for the chromosomal defects and can be used to detect aberrant fetal karyotype [25] in Nuchal Translucency at 10–14th weeks of gestation. The work done by Wojtowicz et al. [26] described creation of a novel strategy to resolve dermatoglyphic sequence of design identification and to comprehend the classification steps for early Down syndrome prediction. They claimed that by combining literary information discovered through the investigation of dermatoglyphic indices utilizing digital pattern recognition techniques, Down syndrome in neonates can be diagnosed.

3 Additional Survey

1. 90%, 100%, and 37.5% of trisomy, translocation, and mosaic patients in a defined group with an incidence of about 1 in 600 births received an accurate clinical diagnosis. Simian crease, sandal gap, epicanthic folds, hypotonia, upslanting palpebral fissures, and projecting tongue were among the phenotypic abnormalities seen in 49.5% of patients. Parents were unnecessarily stressed and worried because the same six characteristics raised the possibility of Down syndrome in people with normal karyotyping. Mosaic cases frequently lack dysmorphic traits and may be more prevalent than previously thought. As such, it is a diagnostic that should be taken

Table 2 Comparative study of methods for nasal bone

Done by	Procedures used	Results obtained
Rafeek and Gunasundari [3]	PREPROCESSING: "ROI-region of interest and Filtering (Hybrid despeckle filter)", DETECTION OF EDGE: "Prewitt, Sobel", Deep Learning Techniques: "BPNN", SEGMENTATION: "Watershed", EXTRACTION OF FEATURE: "Presence of Nasal Bone", CLASSIFIER: "SVM"	NB along with DWT: "8 (false)& 70 (true detection), Without NB: 4 (false) and 21 (true detection)"
Sonia and Shanthi [7]	SEGMENTATION OF IMAGE: "Segmentation using morphological, Otsu thresholding and logical operations", EXTRACTION OF FEATURE: "Nasal Bone Length", MEASUREMENT OF NB: "NBL is CALCULATED using Euclidean Distance formula"	"NB length of normal fetus should be from 2.27±0.11 during 13 th weeks of fetus to 5.24±0.12 mm during 19th weeks"
Wee and Supriyanto [8]	PREPROCESSING(FILTER): "ROI & Filtering", METHOD: "Map-matching computerized method", EXTRACTION OF FEATURE: "Absence of Nasal Bone"	"A maximum value of the nasal bone threshold is 0.35 to decide present or absence"
Sonia and Shanthi [9]	ACCURACY RATE: "97%", EXTRACTION OF FEATURE: "NBL-nasal bone length during (11–14 and 15–22) in first & Second trimester	"NB length is calculated during first-second trimester of gestation and CRL in percentile of 5,50& 95. The absence & Presence of Hypoplasia is measured with ethnic and race group of peoples."
Kagan et al. [13]	EXTRACTION OF FEATURE: "Calculation of nasal bone of fetus is a set of serum free beta-human chorionic fetus nuchal translucency width, PAPP-A, beta-hCG, fetal heart rate (FHR) and maternal age"	"In 2.6% of Euploid fetus, nasal bone was not present with Trisomy 21 was 59.8%. Rate of detection was 91%"
Laikhin et al. [15]	ACCURACY: "96.26%, METHOD: "For detection of NB absence normalized gray-scale cross-correlation techniques was used"	"0.35 is set as the Threshold value of border that denotes presence or absence of nasal bone. Accuracy got is 96.26%"
Cicero et al. [21]	EXTRACTION OF FEATURE: "Chromosomal defects and nasal bone status present or absent at the 11th–14th week ultrasound scan"	"Total fetus-3788 Nasal bone examined: 6.8% (Asians) 10.4% (Afro-Caribbean) 28% (Caucasians)"
Narayani Bandeppa et al. [24]	EXTRACTION OF FEATURE: "Length of Nasal Bone during 16–26th weeks of gestation, age of pregnancy factor is considered."	"The increasing median of nasal bone length linearly from 3.3mm to 6.65mm corresponding to the 16–26th weeks of gestational age"
Janhvi Manohar [27]	PREPROCESSING OR FILTER: "ROI using hierarchical block matching algorithm (HBM)& Median filtering ", METHODS: "K-means clustering algorithm"	"Soft markers:Small Humerus Length short Femur Length, NT. Nasal hypoplasia is alone itself most important second trimester marker-test of Trisomy 21"
Nirmala and Palanisamy [6]	PREPROCESSING: "Median filter & ROI", SEGMENTATION OF IMAGE: "Mean shift", EDGE DETECTOR: "Canny blob analysis", EXTRACTION OF FEATURE: "front maxillary facial Angle (FMFL) AND Nasal bone length"	"NB length increases poorly and the FMF was got 85° above in trisomy 21"
Vincy Devi and Rajesh [10]	TECHNIQUE: "BPNN", EXTRACTION OF FEATURE: "Nasal bone presence", PREPROCESSING: "Filtering & ROI SEGMENTATION:" Otsu thresholding segmentation using logical operations morphological, in transform& spatial domain using DCT wavelet-transformation","	"The transform domain provides more reliance and consistency in comparison of spatial domain for detecting NB 68% with BPNN and NB 89% with hybridized despeckling-filter and BPNN)"
Anjit and Rishidas [4]	PREPROCESSING: "Despeckling alog with Median filteration", SEGMENTATION: "Watershed transform", FEATURE EXTRACTION: Features extracted in transform and spatial domain by D4 and DCT wavelet transform. "Nasal Bone absent." METHOD: "Back Propagation Neural Network (BPNN)"	"Rate in Transforming Domain: DCT: Without NB = 80%, Nasal Bone = 78%, DWT:Without NB = 88%, Nasal Bone - 86%, Rate in Spatial domain: Without NB = 64%, Nasal Bone = 68%,."
Bunduki et al. [33]	EXTRACTION OF FEATURE: "NB length testing in second trimester Ultrasound sonaography."	"For 5.1% false-positive rate sensitivity of 59.1% were found with cutt-off of 5th percentile of trisomy 21 screening"

Table 2 (continued)

Done by	Procedures used	Results obtained
Altunkeser and Kazım Körez [31]	EXTRACTION OF FEATURE: "to set the normal ranges for, ratio of prenasal thickness to nasal bone length (PNT/NBL) at 18–24 weeks, prenasal skin thickness (PNT), inter-ocular distance (IOD), fetal nasal bone length (NBL)"	"PNT/NBL with gestational age ratio changed nothing. NBL increment:5.5mm-8.3mm. IOD increment: 11.1 mm−14.5 mm. PNT increment: 3.5 mm−5.1 mm."

into consideration in all cases of educationally abnormal people who do not yet have a conclusive diagnosis [36].

2. The kids functional performance varied greatly. Activities requiring fine motor skills tended to be the ones where self-care performance appeared to be most delayed. In terms of fundamental functional mobility skills, children seemed less impaired. The management of bladder and bowel control in relation to starting school was listed by parents as their top worries, along with language functioning in children who have not yet received toilet training. The Norwegian version of the Pediatric Evaluation of Disability Inventory (PEDI) was used to measure functional performance in a cross-sectional study of 43 5-year-old Down syndrome children in Norway. Further descriptive data concerning function, impairments, and health were also acquired [37].
3. The aim of this study was to ascertain whether male adolescents with Down syndrome (DS) exhibit a communication style that is distinct from that of boys in three control groups that were matched for both mental and chronological age. Aerodynamic activities, oral-motor functioning, articulation, and language understanding and production were all taken into account while creating descriptive communication profiles. The relationship between these measurements and speech intelligibility was of special interest. It was discovered that the DS group differed considerably from the other groups in terms of mean speech length, syntax understanding, single word articulation, specific diadochokinetic activities, and some aerodynamic skills. The idea that people with DS struggle with sequential processing led to the development of a theory that affected the communication profile as a whole [38].
4. The clinical disorders that are more frequently seen in these populations need to be known by professionals who work with people who have Down syndrome. Given that some congenital anomalies may be life-threatening, prompt medical intervention is frequently necessary for conditions such congenital cataracts, gastrointestinal system anomalies, and congenital heart problems. Many clinical conditions and disorders, including infectious diseases, increased nutritional intake, periodontitis, sleep apnea, seizure disorders, visual impairment, audiologic deficits, thyroid dysfunction, and skeletal issues, typically occur at a higher prevalence during the following childhood years.

   Particular features of maturation, physical problems (thyroid abnormalities, increased weight gain, skin infections, and others), and mental health issues must all be taken into account during adolescence. Similar worries may also be seen in adulthood, which is additionally frequently characterized by rapid aging and the

Table 3 Studies and comparison in facial features for finding DS (down syndrome)

Done by	Procedures used	Results obtained
Qian Zhao et al. [17]	EXTRACTION OF FEATURES: "some of facial appearance are as indicator using photography" METHOD: "Machine learning-SVM" CLASSIFICATION: "support vector machine" ACCURACY RATE: "97.92%"	Features: "Geometric−0.958 (Accuracy) & 0.958 (precision) Texture−0.771 (Accuracy) & 0.783 (precision) Combined−0.979 (Accuracy) & 1.000 (precision)"
Qian Zhao et al. [18]	METHODS: "SVM-support vector machine" CLASSIFICATION: "A machine learning algorithm name as SVM with radial basis function kernel(RBF)". EXTRACTION OF FEATURES: "different facial features using Digital-Photograph"	"94.6% accuracy, 93.3% precision and 95.5% recall by using SVM with RBF kernel"
Saraydemir et al. [35]	EXTRACTION OF FEATURES: "facial difference METHODS: GWT(Gabor wevelet transform)" CLASSIFICATION: "SVM and KNN"	"The classification-accuracy is 96% and 97.34% with kNN and SVM methods"

possibility of Alzheimer's disease in certain Down syndrome individuals.

A person with Down syndrome needs to get extra care throughout their lifetime for these illnesses and ailments. A person with Down syndrome should not get appropriate medical care that would be offered without hesitation to someone without this chromosomal condition [39].

5. Down syndrome (DS) is a congenital condition that carries significant medical and societal burdens, and currently, there is no medical remedy available for it. Therefore, it is crucial to conduct screening for DS in all expectant mothers. Non-invasive prenatal screening (NIPS) for fetal aneuploidy, which became a part of clinical practice in November 2011, is not yet considered a definitive diagnostic test due to the potential occurrence of false-positive(FP) and false-negative (FN) results. As a result, it is recommended to pursue invasive diagnostic procedures such as chorionic villus sampling (CVS) or amniocentesis in cases where a "positive cell-free DNA (cfDNA)" [40] fetus aneuploidy screening test is obtained.

Table 4 Facial features of a fetus for diagnosing down syndrome [29]

List of features	List of characteristics
Upper lip	Thin
Ears	Short
Nose	Short
Head	Short
Finger	Short
Mouth	Short
Eyes	Upward slanting
Hands	Wide Short
Physical development	Slow
Behavior	Impulsive
Learning	Learning

The performance of trisomy 21 screening through cell-free fetal DNA (cffDNA) testing, with an accuracy exceeding 99% and an extremely low false positive rate below 0.1%, is more favorable than alternative screening approaches. However, while the test is gaining widespread acceptance, its widespread use is constrained by the substantial cost. As a result, it is typically recommended for patients already identified as high-risk through a traditional primary screening method. In the context of cffDNA testing, the nuchal scan is regarded as the most suitable initial screening method [40].

6. In the past 25 years, there has been a notable increase in the proportion of women aged 35 and older giving birth, rising from 4.8% to 18.6%. This shift has been accompanied by a rise in the overall occurrence of Down syndrome (DS) from 1.1 to 2.9 cases per 1000 births. The study identified four distinct life stages in individuals with DS: prenatal, childhood, early adulthood, adulthood, and senescence. Throughout these life stages, pneumonia and various respiratory infections were the most common causes of death, accounting for a significant proportion of mortality, ranging from 23% in adulthood to 40% in senescence. However, each life stage exhibited its unique set of comorbidities. Congenital heart defects were prevalent causes of mortality during childhood (13%) and adulthood (23%), whereas in senescence, coronary artery disease (10%) and cardiac, renal, and respiratory failure (9%) became the leading causes of death [41].
7. Down syndrome, also known as Trisomy 21, stands as the most prevalent chromosomal abnormality among newborns and is linked to various congenital deformities. Multiple theories have been proposed to enhance our comprehension of the relationship between the observable characteristics (phenotype) and genetic makeup (genotype) associated with Down syndrome. It was believed that a specific "critical region" within chromosome 21 at 21q22 played a significant role in various Down syn-

drome manifestations, including craniofacial anomalies, congenital heart defects in the endocardial cushions, clinodactyly of the fifth finger, mental retardation, and other features. The primary objective of this review is to elucidate the common genes implicated in phenotypes linked to Down syndrome, which encompass genes like APP(Amyloid Precursor Protein), BACE2(Beta Secretase 2), PICALM(Phosphatidylinositol Binding Clathrin Assembly Protein), APOE(Apolipoprotein), GATA 1(GATA binding protein), JAK 2(Janus Kinase2), CRELD 1(Cystein rich with EGF like domains1), and DSCAM(Down syndrome cell adhesion Molecules). This review also provides a comprehensive description of techniques employed in prenatal diagnosis for Down syndrome. Rapid aneuploidy testing was introduced in the mid-1990s, initially in the form of FISH (Fluorescence In Situ Hybridization), allowing testing on uncultured amniocytes. Within a few years, MLPA (Multiplex Ligation-dependent Probe Amplification) and QF-PCR (Quantitative Fluorescent Polymerase Chain Reaction) were added to the list of rapid aneuploidy testing methods. Another approach involves using Next-Generation Sequencing (NGS) for cell-free fetal DNA screening, which can be extracted from maternal plasma. It's worth noting that, except for FISH, MLPA, and QF-PCR, the other methods are not widely commercialized for aneuploidy diagnosis due to their high operational costs, labor-intensive protocols, and complex data analysis. Given the range of clinical conditions associated with Down syndrome, the management of individuals with this condition necessitates a well-structured, multidisciplinary approach and continuous monitoring [42].

8. In the majority of instances, Down syndrome (DS) arises from an additional copy of human chromosome 21, leading to disrupted gene expression in the brain, which in turn results in impaired intellectual functioning. The understanding of the repercussions of this dosage imbalance associated with trisomy 21 (T21) has been significantly advanced thanks to recent progress in genome sequencing, comparative genome analysis, the exploration of functional genomics, and the utilization of model organisms. This progress has paved the way for novel, evidence-based therapeutic strategies aimed at either preventing or mitigating the effects of T21 on brain structure and cognitive function. Furthermore, these developments hold considerable significance for other domains of research focusing on the neurogenomics of cognition and behavior. They determined and worked in "Gene expression and trisomy 21", "Pathways to intellectual disability in Down syndrome" and "Modeling Down syndrome in mice" [43].
9. The challenges of and life-path of individuals along with Down syndrome (DS) are intricate, encompassing a wide array of medical, psychological, and social issues from early childhood to adulthood. Individuals with DS and their families typically maintain a positive outlook and aspire to achieve a high quality of life, one that capitalizes on the strengths and abilities of the affected child or adult. There are established guidelines in place, offering recommendations and standards to enable individuals with DS to realize their maximum potential [44].

Future work: In order to mitigate the accuracy and false detection challenges in DS diagnosis, it is advisable to identify and delineate whole relevant screenings. These screenings or markers encompass the FMF, dilated brain ventricles, FHR, shining spots on the heart, bowels-shine, little bit kidney damage or swelling, crow's feet, and an augmented nuchal translucency (NT) thickness.

4 Conclusion

To detect Down Syndrome during pregnancy is possible with non-invasive methods. It's important to highlight that, given the diminutive size of the fetus, sonographers are susceptible to inaccuracies and may struggle to consistently ascertain the existence of the nasal bone and other indicators. In the medical arena, computerised system has developed to be a boon that significantly delivers useful information about pregnancy. During the first and second trimesters, the ultrasonography markers, namely the absence of NB or hypoplasia, and NT width, is extremely important in identifying aneuploid fetuses. It is crucial to use precise imaging methods to eliminate ultrasonic speckle noise and to create better segmentation algorithms to increase the detection rate.

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