

Original Research Article

Diagnostic Impact of Fine Needle Aspiration Cytology in Pediatric Abdominal Mass in a Tertiary Care Hospital

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Abstract: Paediatric abdominal tumours include a variety of neoplasm having characteristic incidence, pathology and clinical behaviour. Pathologists play a very important role in the management of paediatric abdominal masses by giving an accurate diagnosis for these potentially curable tumours. Fine-needle aspiration cytology (FNAC) is a rapid and valuable tool in this regard. The aim of the present study is to correlate FNAC findings with histopathological features, with special emphasis on diagnostic efficacy of FNAC. 50 patients presenting with abdominal masses were selected using prospective non-randomized method followed by clinical & radiological examination and ultrasonography guided FNAC were done. Patients with severe coagulopathy, history of acute hypertensive crisis and already diagnosed cases were excluded. Out of 50 cases, we found 5 benign lesions and 45 malignant lesions. FNAC was inconclusive in only two cases. Out of 50 cases, the majority of cases (82%) were seen in the 0-5 years of age group. Concordance with final histopathology was subsequently obtained in 48/50 (96%) of cases. FNAC is a simple technique with minimal trauma without any major complication. This study shows that FNAC is both sensitive (98%) and specific (80%). It has a high positive predictive value (98%) and a negative predictive value of 80% for diagnosing paediatric malignancies. Overall diagnostic accuracy was found to be of 96%. Thus we can conclude FNAC is a valuable diagnostic aid as it is easily done with reliable results.

Keywords: FNAC, Histopathology, Paediatric abdominal tumour

INTRODUCTION

Pediatric malignancies are the second leading cause of death (following accidents) in children [1-3]. Worldwide, the total number of new cases of paediatric tumours exceeds 200,000 annually and more than 80% of these are from the developing countries [4]. The incidence and biological behaviour of paediatric tumours is distinctive compared to those in adults [15]. In India, cancer related death in this age group constitutes 2% of all deaths [6]. In contrast with this data from England and Wales where cancer is second most common cause of disease-related death (20%) [7]. The data on standardized incidence rate of childhood cancer in India evaluates the ranges from 38-124 cases per million children per year [8]. Incidence and mortality rates are higher in boys than in girls, while long term survival is almost similar [9,10]. However,

cancers like retinoblastoma, Wilms' tumour, osteosarcoma, and germ cell tumour usually show a little female preponderance.

Most common cancers in children are acute lymphoblastic leukaemia (26%) and, CNS tumours (21%) [11], neuroblastoma, Wilms' tumour, germ cell tumor, hepatoblastoma. But lymphoma is the most common abdominal tumour in paediatric age group [12]. The differential for an abdominal mass can be extensive and quite challenging, as it incorporates many systems including the gastrointestinal (GI), genitourinary (GU), and endocrine system etc [13]. Majority of the patients presented with abdominal mass are below 5 years of age. In patients with resectable renal mass role of FNAC is limited [14], however patients with unresectable Wilms' tumor requiring

neoadjuvant chemotherapy, or children with metastatic disease at the time of presentation may benefit from a FNAC diagnosis [15,16].

Hepatoblastoma is the most common primary hepatic malignancy in children. Rhabdomyosarcoma and Ewings sarcoma less commonly present as abdominal mass. Only few cases of pancreatoblastoma are reported. Childhood germ cell tumours (GCTs) are rare in children younger than 15 years [17-19]. Teratoma accounts for 32% to 66% of extragonadal germ cell tumours [20]. In the neonatal age group, most extracranial GCTs are benign teratoma occurring at midline locations, including sacrococcygeal, retroperitoneal, mediastinal, and cervical regions [21,22].

The management is very specific for each neoplasm and its stage and hence accurate diagnosis and staging is essential [12]. Imaging techniques cannot always accurately distinguish between benign and malignant masses. Serum tumour markers offer great promise in the diagnosis and prediction of treatment response [23]. The pathologist plays a crucial role in the management of paediatric abdominal tumours by giving a rapid, accurate diagnosis for these potentially treatable tumours.

Fine Needle Aspiration Cytology (FNAC) guided by ultrasonography (USG) is now being considered as a valuable diagnostic aid because of its high diagnostic yield, rapidity, safety and low cost. The risk of malignant cell implantation within the abdominal cavity is an extremely rare complication.

The present study has been undertaken in the tertiary care hospital to assess the efficacy of Fine Needle Aspiration Cytology as a diagnostic tool in paediatric abdominal tumours by comparing cyto-histological samples.

MATERIALS AND METHODS

A one and half year's prospective study from February 2014 to July 2015 was undertaken on children

aged below 12 years in the department of pathology and paediatric surgery of Nil Ratan Sircar Medical College & Hospital. Patients with suspected neoplastic abdominal mass underwent ultrasonography (USG) guided FNAC after initial assessment of platelet count and prothrombin time. Patients having severe coagulopathy, in acute hypertensive crisis and those who have received any chemotherapy or radiation for that mass were excluded from the study. Clinical details like age, sex were recorded. Biochemical parameters, serum alphafetoprotein (AFP), human chorionic gonadotrophin (hCG) etc & urine test for vanillylmandelic acid (VMA) were done appropriately.

Leishman-Giemsa, Haematoxylin-eosin (H & E), Papanicolaou stain and Ziehl-Neelsen (Z-N) stain were done on cytology smears. Histological examination of the biopsy specimens was done with H & E stain and special stains like Periodic acid Schiff (PAS) and relevant IHC were used where necessary.

FNAC findings of abdominal tumour were compared with the histology of same tumours along with the patients profile as well as giving special emphasis on assessing the diagnostic efficacy of FNAC.

RESULTS

USG guided FNAC was done in 52 patients and biopsy specimens were available in 50 cases. In other 2 cases without surgical specimens were excluded from the study.

There were 5 benign cases and 45 malignant cases out of 50 cases [Figure-1]. Most common diagnosis found in this study was Wilms tumour (20/50=40%) [Figure-2a & 2b] followed by neuroblastoma (11/50=22%) [Figure-3a & 3b]. Other tumours were primitive neuroectodermal tumour (3) [Figure-4a & 4b], hepatoblastoma (1), pancreatoblastoma(1), rhabdomyosarcoma(2), non hodgkins lymphoma (1) [Figure-5a & 5b] and adrenocortical carcinoma (1).

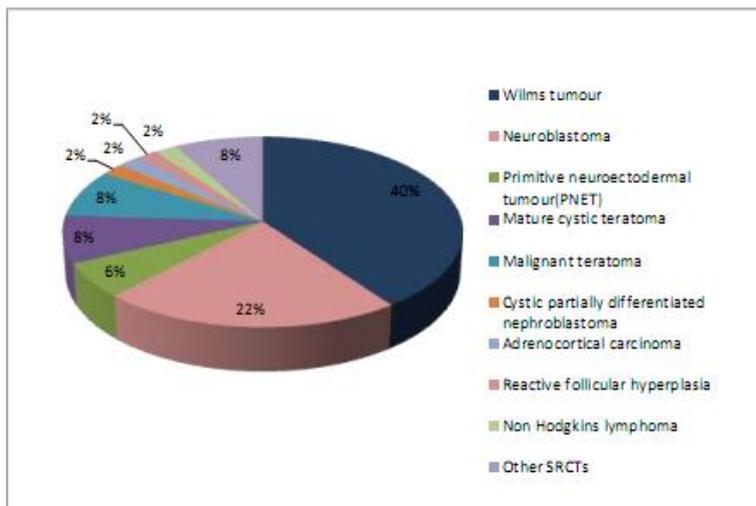


Fig-1: Pie diagram showing distribution of tumour according to histological diagnosis

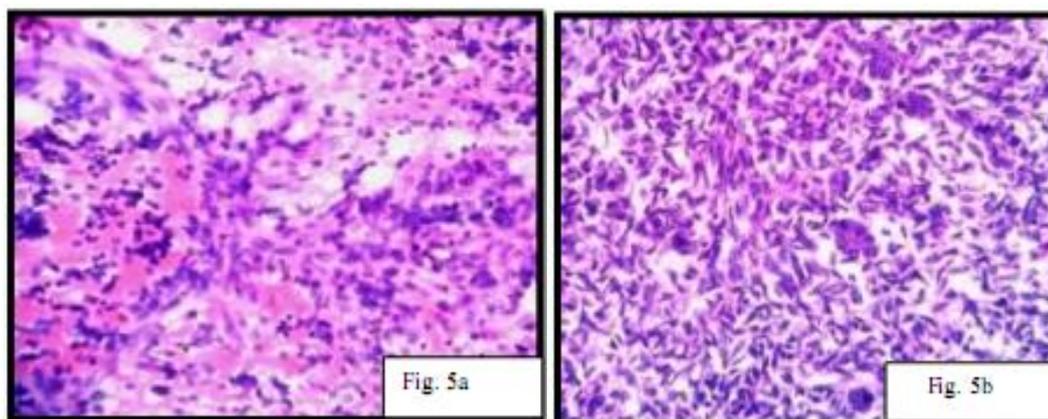


Fig-2: Triphasic wilms tumour (a) Cytology picture showing stromal and blastemal elements [LG,100X] (b) Histology picture showing epithelial and mesenchymal differentiation [H&E,100X]

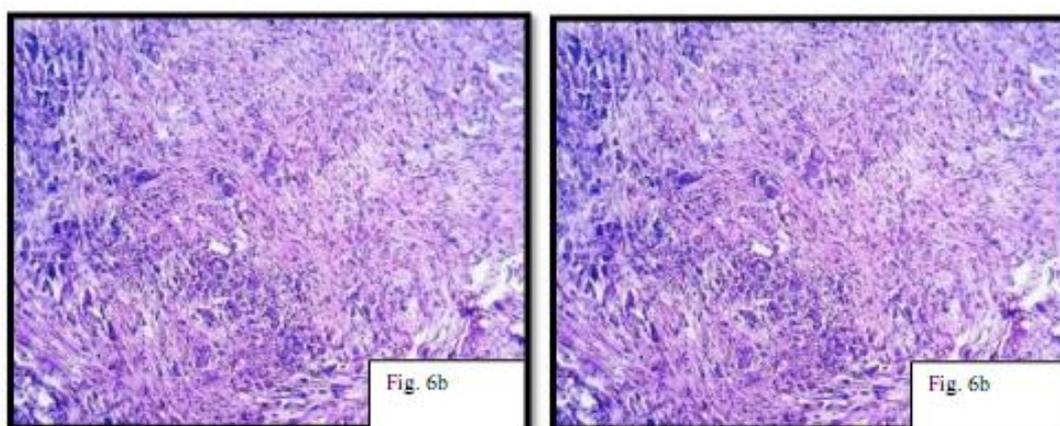


Fig-3: Neuroblastoma (a) Cytology picture showing small round cells forming rosettes and fibrillary intercellular material [LG,400X] (b) Histology picture showing blastemal cells with ganglionic differentiation [H&E,100X]

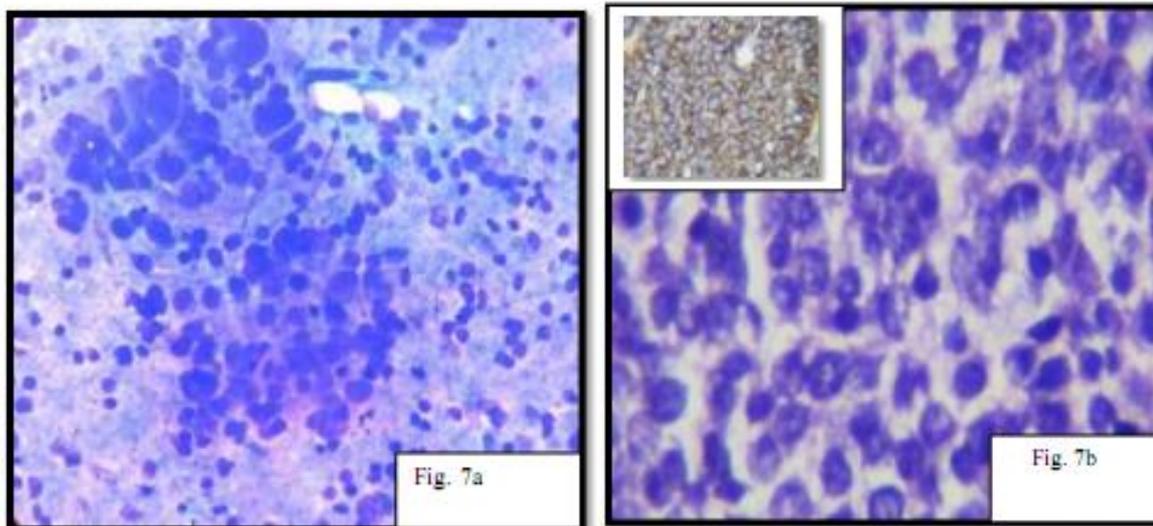


Fig-4: PNET (a) Cytology picture showing small round cells occasionally forming rosettes [LG, 400X] (b) Histology picture [H&E, 400X] with inset showing CD 99 membrane positivity

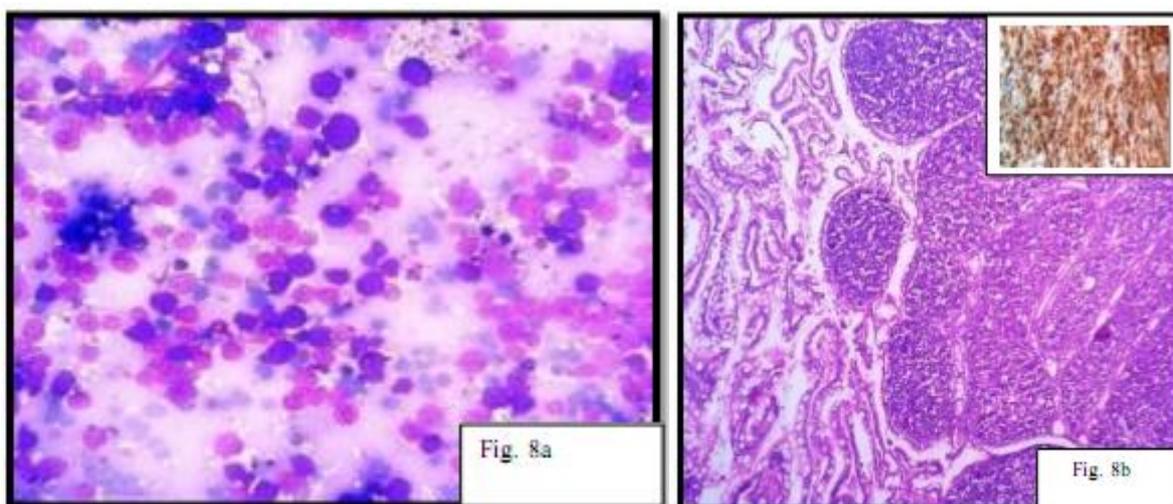


Fig-5: Non Hodgkin lymphoma (a) Cytology picture showing monomorphic population of medium sized cells with vacuolated cytoplasm [LG, 400X] (b) Histology picture [H&E, 100X] with inset showing BCL 6 positivity

Table 1 describes age distribution; 82% cases, 41 out of 50(41/50) were below 5years of age group. Very few cases were seen at above 10 years of age group. Predominant population in the study is male accounting for 28 cases (56%) with male: female ratio 1.27:1. In majority of cases, Wilms tumour showed male predominance whereas neuroblastoma, primitive

neuroectodermal tumour (PNET) and mature cystic teratoma cases seen slightly higher predominance in females. In this study population, the most common presenting symptom was abdominal lump which was found in 94% cases followed by features of compression which is seen in 72% cases.

Table 1: Distribution of tumour according to the age of the patients

Type of diagnosis	0-5 years	6-10years	11-12years	Total
Wilms tumour	17 (34%)	3 (6%)		20
Neuroblastoma	11 (22%)			11
PNET	1 (2%)	2(4%)		3
Mature cystic teratoma	4 (8%)			4
Malignant teratoma	3 (6%)	1 (2%)		4
CPDN	1 (2%)			1
Adrenocortical carcinoma	1 (2%)			1
Reactive follicular hyperplasia			1(2%)	1
Non Hodgkins lymphoma		1 (2%)		1
Other SRCTs	3(6%)	1(2%)		4
Total	41	8	1	50

Various tumour markers were like serum AFP, HCG, LDH and urinary VMA analysed. Hepatoblastoma and most of the malignant teratoma showed elevated levels of AFP. It was observed that 11 cases of neuroblastoma had a mean value of 38.532mg of urinary VMA level in 24 hours of urine.

FNAC was inconclusive in only two cases due to scanty material obtained from deep seated lesion which was difficult to reach and due to cystic nature of the lesion. Overall definite diagnosis was possible by

cytomorphology in 84% (42) cases, while in 12% (6) cases only a diagnosis of small round cell tumour could be made. Concordance with final histological examination was done in 48/50 (96%) of cases [Table 2]. it was found that USG guided FNAC was both sensitive (98%) & specific (80%), and it had a high positive predictive value of 98% and negative predictive value of 80% for diagnosing abdominal tumours of childhood. Overall diagnostic accuracy was found to be of 96% [Table 3].

Table 2: Concordance between cytology and histological diagnosis

Histological Diagnosis	Cytological Diagnosis	Inconclusive Cytology	Concordant Cytological Diagnosis
Wilms tumour(20)	Wilms tumour(20)		20/20
Neuroblastoma(11)	Neuroblastoma(11)		11/11
Primitive neuroectodermal tumour(PNET)(3)	Neuroblastoma(1) Undifferentiated sarcoma/ Ewings sarcoma(2)		3/3
Mature cystic teratoma(4)	Mature cystic teratoma(4)		4/4
Malignant teratoma(4)	Teratoma with yolk sac components(2) Germ cell neoplasm(2)		4/4
Cystic partially differentiated nephroblastoma(1)	Benign cystic tumour(1)	1	
Adrenocortical carcinoma(1)	Adrenocortical carcinoma(1)		1/1
Reactive follicular hyperplasia(1)	Lymphoproliferative disorder(1)	1	
Other SRCTs(4)	SRCT of childhood(4)		4/4
Non hodgkins lymphoma (1)	Non hodgkins lymphoma (1)		1/1

This table shows that out of 50 cases, FNAC was inconclusive in only two cases. Overall definite diagnosis was possible by cytomorphology in 84% (42)

cases, while in 12% (6) cases only a diagnosis of small round cell tumour could be offered. Concordance with

final histological examination was subsequently obtained in 48/50 (96%) of cases.

Table 3: Detection of malignancy by cytology

Statistical Parameters	Values
Sensitivity	98%
Specificity	80%
Positive Predictive Value	98%
Negative Predictive Value	80%
Accuracy	96%

DISCUSSION

Fine-needle aspiration cytology [FNAC] under radiological guidance is helpful for intra-abdominal mass lesions. FNAC is a rapid and cost-effective procedure for early diagnosis and has become an indispensable tool for cancer management in developing countries. Due to its relatively uncomplicated outcome, FNAC has been widely used in the diagnosis of childhood tumours over the last few years [24]. Overall cancer in childhood is more common among males than females; the reported incidence in India in males (39-150 per million children per year) is higher than in females (23-97 per million children per year) [25]. In the present study on paediatric abdominal tumour, majority of the study population is male, with male: female ratio 1.27:1. It is similar to the overall rate of malignancy in childhood tumour in India [10,26].

Most patients presented with abdominal lump, in 94% cases, followed by features of compressions like hydronephrosis which is seen in 72% cases, similar to the study done by Ansaar Tanq Rai *et al.* Abdominal pain and other gastrointestinal symptoms (nausea, vomiting and/or diarrhoea) were present in 34 (64.1%) cases [27].

In this study it is observed that AFP level of all cases of mature cystic teratoma is within normal range whereas patients of hepatoblastoma and most of the cases of malignant teratoma specially having yolk sac tumour as component of germ cell tumour are showing raised level of AFP. Most of the cases of neuroblastoma showed raised level of urinary VMA level. But few cases of neuroblastoma especially with ganglionic differentiation showed normal range of urinary VMA level.

In the present study, male preponderance was seen in Wilms tumour in 60% (12/20) cases which is similar to K Alam *et al* [28] as well as Joshi VV *et al.* and Sharma S *et al* study [29,30]. Further K Alam *et al*

[28] and Stiller *et al* [10] showed bilaterality in presentation of Wilms tumour in 3-6% cases whereas Joshi VV *et al* study showed bilaterality in 5% cases. This is in contrast to the present study which showed only unilateral presentation. FNAC revealed varying combinations of blastemal, stromal and epithelial elements consistent with observation made by other authors like K Alam *et al* [28] & Akhtar M *et al.* Quijano G *et al.* and Dey P *et al* [31-33]. In the present series, anaplastic Wilms' tumour was not encountered. Its presence is an indicator of poor prognosis [34]. K Alam *et al* [28] did not report anaplasia in their series whereas Mishra *et al* [35] reported anaplasia in 1.5% of cases in a series of 125 North Indian children while Beckwith [36] reported it as 5%. Blastemal component was seen uniformly in all cases on both histology and cytology. We found one case of Wilms tumour with rhabdomyoblastic differentiation. Lawler *et al* [37] and Wigger *et al* [38] reported that presence of extensive tubular and glomerular differentiation along with rhabdomyoblasts in large number carries a better prognosis. Differentiating Wilms' tumour from rhabdomyosarcoma may pose a problem since rhabdomyoblasts can be found in both lesions [39] but the presence of bimodal population of cells in smears and localization of tumour in kidney by imaging techniques would favour a diagnosis of Wilms' tumour.

The differential diagnosis of cystic nephroma and partially differentiated cystic nephroblastoma (CPDN) should be considered especially if fluid is aspirated [40]. CPDN, rare neoplasm is a multilocular cystic neoplasm composed of epithelial and stromal elements, along with nephroblastomatous tissue within the septa. It is commonly seen in very young children. When no nephroblastomatous tissues are found, it is called as "cystic nephroma". In the present study, out of 50 cases neuroblastoma was found in 11(22%) cases and all the cases are presented within 5 years of their age group. Among 11 cases, 2 cases were found with ganglionic differentiation. Here radiological features and characteristic rosettes with pink staining fibrillary

centre helped to diagnose them as neuroblastoma on cytology. They were later confirmed on histology giving cytological concordance of 100%.

Out of 3 cases of PNET in the present study, there was one case which originated primarily from kidney. ESPNET lesions of the kidney are exceedingly rare tumour with poor prognosis and were first reported by Seemayer and his colleagues in 1975 [41]. As the imaging signs of this tumor are often nonspecific, immunohistochemical and molecular studies played a critical role in differentiating EWS/PNET from other small round cell tumours. In our study we also took the help of CD 99 to differentiate PNET from other SRCTs.

We found one case of adrenocortical carcinoma in this study period. Percutaneous FNAC of adrenal mass is known for significant morbidity due to dangerous complications like septicaemia and haemorrhage in 8-13% cases [42,43]. Complications can be reduced with correct technique. However the FNAC procedure was uneventful in our single case. Cytological features of both adrenocortical adenoma and carcinoma are quite similar to each other. According to Saboorian *et al* [44]. Wu *et al* [45] and Fassina *et al* [46] loosely cohesive cells having vacuolated cytoplasm and sometimes having naked nuclei are seen in both adenoma and well to moderately differentiated AC carcinoma. But enlarged, hyperchromatic, multilobated and multinucleated nuclei, mitosis and prominent nucleoli favours adrenocortical carcinoma.

There was one case of non-hodgkin lymphoma found in the study period. Both cytology as well as histology were suggestive of Burkitt's lymphoma which was confirmed on immunohistochemistry (IHC) on the biopsy specimen. IHC showed CD 20 +ve, bcl-6 +ve & bcl-2 -ve.

Out of 50 cases, there were 4 cases of mature cystic teratoma and 4 cases of malignant teratoma; all of the tumours originated in the sacrococcygeal region. In Isaacs H Jr *et al* [21] study revealed sacrococcygeal teratoma as the leading teratoma (214; 40%) out of 535 foetal and neonatal GCTs. In our study, female preponderance was seen in mature cystic teratoma. Yolk sac tumours are seen as predominant component of malignant teratoma in this study. Rescorla FJ *et al.* pointed that malignancy rates of sacrococcygeal tumours in the older infant and child are reportedly very high, most commonly due to yolk sac tumor [47].

In the present study the total cases we found were 5 benign lesions and 45 malignant lesions. One case was inconclusive in benign lesions and one case was incorrectly diagnosed in malignant lesions by FNAC. Wilms tumour and neuroblastoma constitute the highest number of total cases in this study. This is consistent with the Geisinger KR *et al* [15] and Joshi VV *et al* [48] study. Out of 50 cases, concordance of cytology with histology was found in 96% cases. The overall sensitivity, specificity is quite high i.e. 98% and 80% respectively with high positive predictive value and negative value of 98% and 80% respectively. Diagnostic accuracy was found to be of 96%.

Florentine BD *et al* [49] in their study showed that overall sensitivity of FNAB in case of palpable abdominal masses was 93%, and the specificity was 100%. Using histology or clinical follow-up, the positive predictive value was 100%, and the negative predictive value was 99%.

In B. Geramizadeh *et al* [50] study mentioned FNA cytology as a sensitive tool for diagnosis and typing of most common malignant intraabdominal tumours of children. The sensitivity and specificity of FNA cytology were found 97.2% and 81.2% respectively and its accuracy for diagnosis of the tumour type of malignant ones was 86.5%.

In Indian scenario a few studies are available on this matter. One was conducted by Viswanathan S *et al* [51] showed that definite diagnosis could be offered on cytomorphology in 74.7% (62) cases, while in 25.3% (21) cases only a diagnosis of round cell tumour could be offered. Concordance with final histopathology and biochemical parameters was subsequently obtained in 79/83 (95.5%) of cases.

Similar studies like Veena Maheshwari *et al* [52] and Razack R *et al* [53] studied revealed high degree of sensitivity, specificity, positive predictive value, negative predictive value with high degree of diagnostic accuracy to diagnose paediatric neoplasia.

In spite of plenty of advantages, there are some limitations due to tumour spillage during FNAC [54]. Tumour cells in the needle tract may not be able to manage to grow into a local tumour, but a cell that is seeded in the needle tract may gain access to the systemic circulation through ruptured microvessels or lymphatic in the vicinity causing iatrogenic metastasis [55]. But this complication of needle tract seeding is very rare [56-58].

CONCLUSION

FNA cytology under the guidance of ultrasonography, with clinical history, physical examination and imaging studies and other ancillary investigations such as immunocytochemistry, is a very effective method for earlier accurate diagnosis of abdominal masses in children. Although overlapping of cytological features between various neoplasms produce hindrance to reach at diagnosis in few cases. This method obviates the need for a more time-consuming biopsy procedure in critical situations and in stage II nephroblastoma where it is contraindicated.^[15] Furthermore, FNA cytology can provide rapid and reliable provisional diagnosis in many cases and allows clinicians to instigate further where needed and commence proper treatment without delay.

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