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AUDIT OF ADVANCED LABORATORY INVESTIGATIONS

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Background: Advanced laboratory investigations at reference laboratories play a key role in the diagnosis of the disease, but misuse of this precious and expensive tool may misguide the physician in patient management. This study was carried out as an audit of investigations performed at a reference laboratory, in order to assess their cost effectiveness, to identify various errors, the degree of correlation of requested tests with the clinical diagnosis and benefit to the patients. **Method:** A four phase audit of 337 laboratory investigation prescription was performed from April 2012 to March 2013 in the Medical Administration in collaboration with Department of Medical Laboratory and various Clinics at the King Salman Armed Forces Hospital in Northwestern Region - Kingdom of Saudi Arabia. All the information was recorded on a questionnaire *Pro forma*. **Results**: On data compilation and analysis it was found that 174(51.63%) test results were within normal reference range, while 163 (48.37%) test results were reported as positive. Also 218 (64.69%) investigations results correlated with clinical assessment by the physician, while 119 (35.31%) investigation results did not correlate with the clinical assessment by the physician. The expenses incurred Euro 12868 were spent on non-correlated tests while on correlated tests were Euro 31831. In terms of benefit to the patients 243 (82.09%) patients were reported by clinicians to have benefited from the reference laboratory tests, while 53 (17.91%) cases did not benefit from the reference laboratory tests as assessed by the clinicians and 41 (12.16%) cases in which even clinician did not respond regarding the benefit to the patients. Three categories of errors were identified (26.40%), i.e., at the level of clinicians (12.75%), at the level of hospital lab (5.04%) and at the level of reference lab (8.60%).**Conclusion**: Thorough clinical assessment and judicious utilization of available preliminary laboratory tests are the keys to precise diagnosis and are instrumental in reducing reliance on reference laboratory investigations.

Keywords: Reference Laboratory Investigations, Rational use, audit

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INTRODUCTION

The Laboratory (Lab) investigations are the backbone of medicine. These are essential for the precise diagnosis and management of the patients. Sometime laboratory tests are irrationally requested[1]; however their rational use is always desired. Therefore before ordering any test the physician must have a clear idea about the clinical diagnosis and the expected test outcome, a false positive or false negative test result may misguide the clinician.[2,3]

Proper diagnosis depends on detailed clinical assessment augmented by pertinent and well thought laboratory investigation. Laboratory tests serve as confirmation of the clinical diagnosis and help the clinician to arrive at the final diagnosis which is the prerequisite to adequate patient management.[4,5]

To provide adequate and rational test menu in a laboratory and to maintain it, it is imperative to utilize the laboratory investigations in a justified manner.[6] Irrational use of the reference laboratory tests not only causes delay in diagnosis but also increases the financial burden for the laboratory. In a study conducted at Calgary Laboratory Services in Alberta, Canada over a period of 12 months, it was found that when reference laboratory tests were reviewed and irrational tests or the tests for whom the physicians did not provide additional data were cancelled, there was significant (47%)saving of the expected total expenditure.[7] Physicians should first utilize preliminary simple investigations that are available in the hospital laboratory and then if required should resort to advance tests available at reference laboratories.[8] Pathologist can only interpret and comment on the test results if the clinical findings are noted on the requisition form.[9] The role of the present day laboratories is not limited to performing the tests only, but to provide good interpretation and guide the physicians for further management of the patient.[10] It is well appreciated now that thorough clinical work-up and good laboratory support go hand in hand for appropriate patient management.[11,12] The aim and objective of this study is to perform audit of investigations at reference laboratories in terms of cost effectiveness, correlation of test results with the clinical diagnosis and level of errors that happen in reference laboratory testing cycle.

MATERIAL AND METHODS

The study was based on qualitative assessment of prescribing patterns of physicians, and reporting of the results by the reference laboratory. The objective and methodology of the study was explained to all doctors

before starting this study who were requesting the advance laboratory investigations (investigations requested to the reference laboratory after utilization of in house laboratory facilities) for their patient management. The study was carried out in four phases. A questionnaire was designed which was filled by the physicians, laboratory and medical administration in different phases of the study. At the first phase the questionnaire was sent to all the physicians who were prescribing the advance laboratory investigations regarding the clinical information of patients and justification of tests based on their assessment and initial investigations done in the hospital laboratory. The samples were received in the containers of the reference laboratory in the send out section of hospital laboratory from the wards and clinics. The send out section monitored the requests as well as prepare the samples packages for the shipment to the reference laboratory by their designated courier service. The second phase was related to medical laboratory after receiving of results from the reference laboratory. The results were interpreted in the light of information provided by clinicians and correlation was established.

Data regarding any delay, other errors and the cost of the tests was also recorded. The third phase was of feedback from the physicians who assessed the impact of these results on patient management/benefit to the patient, i.e., to rule in or to rule-out certain diagnosis, treatment strategies and prevention of disease by genetic test. Fourth and final phase was analysis of above mentioned three phases by the hospital medical administration and laboratory. In descriptive analysis mean was calculated and for comparative analysis binomial z test was used to calculate *p*-value, a value of <0.05 was considered statistically significant.

RESULTS

Out of 659 questionnaires distributed, 337 were returned by the clinicians. Table-1 shows the distribution of the requested investigations with results from the reference laboratory. Number of test results of each category either normal or abnormal with their sex and age were recorded. Table-2 shows the correlations of initial assessment with the results received from reference laboratory, and their impact on patient management in the form of patient benefit or vice a versa (refer to the methods, phase 2and 3 respectively).There were still remaining cases in which clinicians did not comment (41/337;12.16%) on patient benefited in the questionnaire and even did not respond on the contacting individually they were (5/34;14.70%) in HCV RNA, (10/114;8.77%) in HBV DNA, (7/48;14.58%) in Autoimmune, (2/21;9.52%) in Thymoglobulin, (9/31;29.03%) in immune-phenotyping, (6/40;15%) in Hormonal Assay and (2/41;4.87%) in Amino/Organic Acid. The other information was the total cost spent on non-correlated results with clinician assessment was Euro 12868 and in individual category cost was Euro 2590 in HCV RNA, Euro 3145 in HBV DNA, Euro 390 in Autoimmune, Euro 165 in Thyroglobulin, Euro 3680 in Immune-phenotyping, Euro 64 in Erythropoietin, Euro 1040 in Hormonal Assay, Euro 1794 in Amino/Organic Acid. While the total cost spent on correlated results was Euro 31831 and in individual category the cost was Euro 3700 in HCV RNA, Euro 17945 in HBV DNA, Euro 2034 in Autoimmune, Euro 528 in Thyroglobulin, Euro 3450 in Immune-phenotyping, Euro 448 in Erythropoietin, Euro 2322 in Hormonal Assay, Euro 1404 in Aimino/Organic Acid. Table-3 shows the errors at clinicians, hospital laboratory and reference laboratory level.

Table-1: Distribution of advance laboratory investigation results

TEST	TOTAL NO. CLINICIAN RESPONDED TO QUESTIONNAIRE	PATIENT'S DEMOGRAPHICS				RESULT		
		Sex	N	Mean Age	Range	NORMAL /NEGATIVE	ABNORMAL / POSITIVE	P-VALUE
HCV RNA	34	Male	19	43	24 - 69	11 (57.89%)	8 (42.11%)	0.2483
		Female	15	33	05 - 62	12 (80%)	3 (20%)	0.0102*
HBV DNA	114	Male	61	41	22 - 71	14 (22.95%)	47 (77.05%)	0.000
		Female	53	38	22 - 65	16 (30.19%)	37 (69.81%)	0.002*
AUTOIMMUNE	48	Male	8	34	01 - 65	6 (75%)	2 (25%)	0.0793
		Female	40	27	01 - 70	23 (57.50%)	17 (42.50%)	0.1711
THYROGLOBULIN	21	Male	9	39	10 - 61	6 (66.67%)	3 (33.33%)	0.1587
		Female	12	27	06 - 54	7 (58.33%)	5 (41.67%)	0.281
IMMUNO PHENOTYPING	31	Male	19	23	01 - 70	12 (63.16%)	7 (36.84%)	0.1257
		Female	12	26	01 - 68	7 (58.33%)	5 (41.67%)	0.2819
ERYTHROPOIETIN	8	Male	2	46	31 - 60	1 (50%)	1 (50%)	No difference
		Female	6	39	23 - 60	4 (66.67%)	2 (33.33%)	0.2071
HORMONAL ASSAY	40	Male	21	19	06 - 57	11 (52.38%)	10 (47.62%)	0.4136
		Female	19	22	11 - 54	10 (52.63%)	9 (47.37%)	0.4093
AMINO/ORGANIC ACID	41	Male	27	22	01 - 75	21 (77.78%)	6 (22.22%)	0.0019*
		Female	14	22	02 - 55	13 (92.86%)	1 (7.14%)	0.0007*
All Tests	337	Male	171	33	01 -75	82 (53.80%)	84 (46.20%)	0.1601
		Female	166	29	01 -70	92 (49.40%)	79 (50.60%)	0.5617

**p*-Values are significant

Table-2: Correlation of advance lab investigation results with provisional diagnosis

Test	No. of cases assessed by clinician*	Result correlation with clinical assessment**			Patients benefited***		
		Yes	No	*p*-Value	Yes	No	*p*-Value
HCV RNA	34	20 (58.82%)	14 (41.18%)	0.1517	24 (82.76%)	5 (17.24%)	0.0002****
HBV DNA	114	97 (85.09%)	17 (16.91%)	Approx 0****	96 (92.31%)	8 (7.69%)	0.00****
Autoimmune	48	18 (37.50%)	30 (62.50%)	0.0416****	23 (56.10%)	18 (43.90%)	0.2174
Thyroglobulin	21	16 (76.19%)	5 (23.81%)	0.0082****	17 (89.47%)	2 (10.53%)	0.0003****
Immuno phenotyping	31	15 (48.39%)	16 (51.61%)	0.4287	17 (77.27%)	5 (22.73%)	0.0053****
Erythropoietin	8	7 (87.50%)	1 (12.50%)	0.0169****	7 (87.50%)	1 (12.50%)	0.0169****
Hormonal assay	40	27 (67.50%)	13 (32.50%)	0.0134****	28 (82.35%)	6 (17.65%)	0.0001****
Amino/organic acid	41	18 (43.90%)	23 (56.10%)	0.2174	31 (79.49%)	8 (20.51%)	0.0001****
Total	337	218 (64.69%)	119 (35.31%)	Approx 0****	243 (82.09%)	53 (17.91%)	0.00****

*Clinician assessment means clinically and also by Hospital lab facilities. ** Cost spent on correlated and non-correlated results were reported in the Result text. ***No information was received from clinician regarding benefited/non benefited and reported in the Result text and it is also not included in the table calculation. ****Means *p*-Value is significant.

Table-3: Level of errors recorded during the advance laboratory investigations

Total tests	Total errors	Clinicians		Hospital lab			Advance lab			
		Improper test nomencl-ature	Mismatch of clinical feature	Dispatching the sample with wrong request	Impro-per tube	Follow up system	Delay of results	Missing samples	Logistics error	Incorrect result
337	89 (26.40%)	2 (2.24%)	41 (46.06%)	5 (5.61%)	2 (2.24%)	10 (11.23%)	15 (16.89%)	2 (2.24%)	8 (8.98%)	4 (4.49%)

DISCUSSION

The clinical laboratory investigations have a pivotal role in patient management.[13] In recent times there has been tremendous advancement in molecular biology techniques and these techniques have been harnessed to offer an ever increasing and rapidly evolving battery of laboratory investigations for patient management. The in-house investigations offered by the present day tertiary care laboratories are protean, with an additional repertoire of reference laboratory tests. However it is beyond doubt that these reference laboratory tests are essential for the confirmation of clinical diagnoses and monitoring of the disease. In view of the ever increasing costs of the newly introduced laboratory investigations on one hand and emphasis on reducing health care costs on the other, it is imperative to create awareness regarding the judicious use of laboratory facilities with an aim to reduce abuse (over-ordering) and misuse (e.g. Order the appropriate test for the wrong purpose or vice versa) of available tests. Hence, before ordering reference laboratory investigations the following questions must be answered by the clinicians: (1) Is this test essential for diagnosis of the disease? (2) Can the disease not be diagnosed without this test? (3) How much this test will contribute to the diagnosis of the disease? (4) What will be the interpretation of the test result? (5) How the test result will impact the patient management? The answers to these questions will guide the clinician to appropriate use of extramural reference laboratory investigations. It will be appropriate to mention that some clinicians have the misconception that random or "curiosity" testing will clinch the diagnosis even if it is not suspected after thorough clinical examination of the patient. The "curiosity" testing practices will rather lead to a cascade of expensive diagnostic investigations.

Basically there are four main reasons to order a laboratory test, i.e., diagnosis of disease, monitoring of disease, evaluation and research.[14] Laboratory testing is an essential component of health care for patients in resource-limited settings.[15] Reliable, accurate, precise and rapid tests are necessary for diagnosis, to determine the aetiology, monitor treatment effectiveness and for disease surveillance. The laboratory results in reality are required to make a large proportion of medical decisions. In developed countries, approximately 60% and 80% of patient management decisions are based on laboratory data, [16] these investigations are often more sensitive and specific than clinical decision criteria alone.[17,18] In this study according to the clinical feedback 72.10% of all the reference laboratory tests, contributed strongly to the diagnosis and patient management, which is in keeping with the international studies.[15]

In the current study HCV RNA (n=34) and HBV DNA (n=114) together constituted a major proportion of all the ordered tests, i.e., 148 out of 337 (43.91%), incurring a total cost of Euro 27380 (185 Euro/test). The turnaround time for these tests at the reference Lab was 7–10 days. If the said tests were developed in-house, the turnaround time would be two working days and the total cost incurred would be Euro 5920 (40 Euro/test), saving Euro 21460 (48.01% of the total expected expenditure) for the hospital, this money

can be utilized to upgrade other patient services. This is in accordance with the study that was conducted at Calgary Laboratory Services in Calgary, Alberta, Canada over a period of 12 months, it was found that when reference laboratory tests were reviewed and irrational tests or the tests for whom the physicians did not provide additional data were cancelled, there was significant (47%) saving of the expected total expenditure.[7]

In our study the ratio of requested tests that correlated (n=218) with the clinical diagnosis to those that did not correlate (n=119) with clinical diagnosis was 1.8:1, the *p*-value being <0.05 which is statistically significant. The cost incurred on tests which did not correlate with the clinical assessment was Euro 12868. According to the clinical feedback 82.09% of patients were benefited by the laboratory investigations whereas 17.91% of patients did not benefit from these test results (*p*-value <0.05). Casual attitude of some of the clinicians was depicted in our study when they did not comment on the number of patients who benefited from the reference laboratory test or otherwise (41/337; 12.16%) even on contacting them & following individually by laboratory staff.

In most of the hospital there is an annual increase of 5–10% in laboratory investigation requests.[15] Laboratories are continuously striving to rationalize the utilization of in-house and send-out tests. Several studies have shown that between 25% and 40% of all tests sent to the laboratory are unnecessary and some laboratories in the UK have actually managed to reduce the number of such unnecessary tests.[16] However, even when such reductions were achieved, it was difficult to sustain them. Various reasons have been proposed that are probably responsible for failure to cut down on unnecessary testing.[16] These include incomplete clinical workup (associated with junior or inexperienced clinicians); lack of knowledge about the requested test, e.g., how to interpret the test result, their sensitivity and specificity; the desire for diagnostic completeness and fear of litigation. The last and major obstacle to successful test utilization management is "consumer resistance". In our setup, neither the clinician nor the patient directly pays for the laboratory investigations. Therefore the clinicians are not obliged to alter their current laboratory investigation ordering practices.[18] It is imperative that the clinicians should have sufficient knowledge of the tests that they order, false positive or false negative results in low prevalence areas can lead to a cascade of more expensive tests causing excessive financial burden and a source of anxiety to the patient.

Reference Laboratory test send-out involves multiple phases starting from specimen collection, packing and send-out through a courier service, to receipt of the report and making it available to the requesting clinician. This multiphase process makes it vulnerable to many error.[19] Three categories of errors were observed in this study; 1) errors by the clinician, 2) errors by the hospital Laboratory, and 3) errors by the reference Lab. The maximum number of errors were noted at the clinician category (48.31%), constituted firstly by; wrong test nomenclature (2.24%) which implies receiving test results which are irrelevant to the patient's disease, leading to further testing, and secondly, recorded clinical features on requisition form which were not in keeping with the requested tests (46.06%), raising questions about the necessity of the requested test and the commitment of the clinicians to diagnose the condition. The second category of the errors was recorded at the level of hospital laboratory where samples were collected and dispatched to the reference Laboratory. In 5.61% cases Laboratory sent the test with clerical errors. There were two cases wherein HCV RNA PCR was written instead of HBV-DNA PCR. These clerical errors led to wastage of time for the patient and resources for the laboratory. In 11.23% cases there was improper follow-up of the sent tests causing delay in receiving the test results. The third category of errors was at the reference Lab where most of the errors occurred. The most common error in this category was delay in the reporting of the results (16.89%, exceeded turnaround time), the affected tests included flow-cytometry, FISH analysis and cytogenetic studies. The delay of the results in such cases led to delay in initiating the treatment. The other errors noted in this category were lost samples (2.24%) and logistic delays (8.98%) causing sample deterioration, the Lab had to review the system so that such errors are avoided in the future, as all the patient samples intended for the reference laboratories are dealt with as irretrievable and precious. In 4.49% of cases reference laboratory test interpretation was ambiguous or discordant with other send-out tests for the same patient. Two such cases were for foetal karyotype and other two cases were for immune-phenotyping by flow-cytometry. Studies in the United States and Europe have demonstrated that errors occur throughout the testing process, including the pre-analytical stage (sample collection, labelling, and transport); analytical stage (testing in the laboratory); and post-analytical stage (data management and reporting results). The majority of errors occur outside of the laboratory in the pre-analytical (46–68%) and post-analytical stages (18–47%).[19] This does not include clinic-based errors that occur in deciding which tests to order and in the interpretation of test results, both areas of high error risk. The frequency of errors during the analytical stage is lower but remains significant, estimated to be between 7% and 12%,[20,21] despite years of quality management regulation. In the United States, it is estimated that 6–12% of laboratory errors put patients at risk of inappropriate care and potentially of adverse events, whereas 26–30% of errors have a

negative impact on other aspects of patient care. The magnitude of laboratory errors in resource-limited settings is not well documented. It is likely that error rates and their impact on clinical decision making and patient outcomes are greater than in resource-rich settings, but studies to evaluate this are needed.

CONCLUSIONS

This study highlights the importance of liaison between pathologist and clinician to reduce the number of unnecessary tests and to properly interpret the test results when they are received. Also judicious use of the reference lab tests can significantly reduce the financial burden of the hospital. The hospitals should develop certain high demand investigations in-house so as to save time and finances.

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AUTHOR'S CONTRIBUTION

MS Al-P, ASS, AAK and MK; designed the study, recorded and interpreted the results of their respective fields, and analyzed as mentioned in the methods. Finally all participated in the writing and final approval of the manuscript.

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