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Clinical Evaluation Of Rubrics Of Pulsatilla From Synthesis Repertory To Assess Its Validation By Bayesian Theorem

Dr. Rakhshanda Ayoub[1], Dr. Jyoti Deepak Patil[2]
Bharati Vidyapeeth (Deemed to be University) Homoeopathic Medical College,
Dept. Of Post Graduate & Research Centre, Pune-Satara Road,
Katraj, Dhankawadi, Pune, India – 411043
Department of Homoeopathic Repertory
[1]Post Graduate Department of Homoeopathic Repertory, Bharati Vidyapeeth (Deemed to be University), Homoeopathic Medical College and Hospital, Pune -Satara Road-411043.
[2]Associate Professor, Department of Homoeopathic Repertory, Bharati Vidyapeeth (Deemed to be University) Homoeopathic Medical College and Hospital, Pune-Satara Road-411043.

Abstract: Homoeopathic prescription is done on the Totality of symptoms formed by indicative symptoms and signs of the patients, but knowledge about those symptoms is not organized and controlled. Moreover, there are numerous rubrics and symptoms listed in our Repertories and Materia Medica for specific medicine which are based on their absolute frequency. There are false entries in our repertories due to this absolute occurrence in successful circumstances. To consider a symptom a keynote or characteristic of a specific medicine, the Likelihood Ratio (LR) of that symptom must be higher in the patients exhibiting good therapeutic response to that medicine than in the remaining population. Based on Bayesian statistics, likelihood Ratio (LR) may yield a better estimation of a medicine's indication than the existing method of entry of symptoms into Materia Medica and Repertories. An Observational Retrospective study was undertaken to evaluate Rubrics of prominently present symptoms of Pulsatilla by implication of the Likelihood Ratio (LR). 316 cases of prescriptions of Pulsatilla were taken for study and 20 most prominent symptoms of Pulsatilla were selected for the study. Pulsatilla for 1 Rubrics (Company desire for) could be upgraded for **BOLD CAPITAL** and 1 Rubric (Fullness sensation of, Epigastrium) could be upgraded for **bold small** typeface, for 4 rubrics (Consolation amelioration, Timidity, Fear-alone being of, Eructations; Type of-sour), the typeface is analogous to the existing typeface in Synthesis Repertory, for others (Weeping-tearful mood, Thirstlessness, Menses-suppressed menses, Eruptions acne, Menses before-aggravation, Heartburn-fat food-after, Head-pain-pulsating, Cough-Dry night at, Warm-agg) rubrics, the typeface could be downgraded but with caution while as 1 rubric (Leukorrhea- cream like) is still doubtful.
(Keywords: Homoeopathy, Bayesian Theorem, Materia Medica, Pulsatilla, Retrospective study, Likelihood Ratio, Conditional Probability)

Introduction:

In Homoeopathy we use Repertories showing which medicines are indicated when specific symptoms are present. But the meaning of typefaces in Repertory is not very transparent.[1] Dr. Fredrick Schroyens in Synthesis Repertory used four grades for Rubric entries.

1. BOLD CAPITAL (4 marks)/ 1st grade
2. Bold small (3 marks)/2nd grade
3. Italics (3 marks)/3rd grade
4. Romans (2 marks)/ 4th grade

Hitherto repertory entries have largely been based on single observations of a symptom occurring in proving or in a "cured" case: that is, the absolute occurrence of symptoms, and eventually, that too, based on expert opinion, usually of very few experts. Moreover, their experience is seldom systematically collected and mostly memory-based. Even experienced homeopathic physicians have a limited number of successful cases concerning one medicine.[2] This is a systematic and serious bias. This system of absolute grading of medicines in rubrics is fundamentally problematic. These are not relative statements; so, the more a medicine is prescribed, the more frequently corresponding symptoms will be confirmed and verified. Thus, the frequently used "polychrests" become over-represented in repertory rubrics.[3] Besides, the size of repertory rubrics varies much more than expected from the prevalence of symptoms. Large rubrics tend to have

superfluous entries, whereas in small rubrics medicines are missing.[4]

Another shortcoming is that the same Homeopathic Repertory has been used all over the world for more than a century despite huge climatological, cultural, and other variations and historical developments. Homeopathic practitioners in cold and in warm countries use the same repertory rubrics for being warm-blooded or cold-blooded and for influences of weather.[5] Apparently, Homoeopathic practitioners use their clinical expertise to correct for such confounders, but it is uncertain how much bias these confounders could cause.

Evidence–based medicine[6] is a challenge for the future years of Homoeopathy, within which we are further inspecting for evidence of the effectiveness of the Homoeopathic treatment which indeed could be done through clinical evaluation of the symptoms.[7] Clinical evaluation indicates the process of reviewing and confirming the symptoms that were already documented and noted in the literature of Homoeopathic science as the proving symptoms and the cases cured. If the documented symptoms are further seen in the cases which give a good therapeutic response to the relative medicine, this assures the pertinence of that symptom in association with that medicine.

These types of inadequacies and misrepresentations can be addressed by reconsideration of Repertorial entries by Baye's Theorem,[8] that is, mathematically expressed as a Likelihood Ratio (LR).

Likelihood Ratio is one such modern epidemiological tool and also a modern Bayesian translation of the expression as "characteristic", "peculiar" or "keynote" symptoms in Homoeopathy.[9] If the symptom is peculiar, the prevalence is lower and LR will be high.[10]

Thomas Bayes, the 18th-century English clergyman, and mathematician, described "conditional probabilities" in terms of beliefs and degrees of uncertainty:

- Posterior odds = Likelihood ratio (LR) X prior odds
- Odds = Chance/ (1 - Chance)
- LR = prevalence of symptom in target population/prevalence of symptom in the remainder of the population.
- Target population = population responding well to the medicine.
- LR can be denoted as LR (+) if the symptom is present, or LR (–) if the symptom is absent.

The practical implication of Bayes' theorem is that if LR (+) > 1, the odds/chance increases that the medicine will work. This odds/chance increases more if LR is higher: that is if the difference between the target population and the remainder of the population is larger. The opposite is true for LR (–) < 1: odds/chance decreases if the symptom is absent; more so if LR is lower. Thus, LR provides a better indication of the prognostic value of a homeopathic symptom than the present repertory entries. Odds become greater when LR >1 and smaller when LR<1 (between 0 and 1); higher is better to include and lower is better to exclude. As a rule of thumb, per symptom or rubrics, LRs<1.5 with corresponding medicines are discarded from the pick listing, also because LR values between 1.0 and 1.5 hardly change posterior probability.[2,4]

LR is the modern epidemiological tool for determining the characteristic and keynote symptoms of medicines.[11] In this retrospective study, the investigators intended to estimate the prevalence and LRs of 20 symptoms of frequently

prescribed Homoeopathic medicine, "Pulsatilla Pratensis". This study may help in better understanding the symptoms of the medicines.

Materials and Methods: A retrospective observational study in already registered cases with Pulsatilla prescription by various Homoeopathic physicians in various OPDs of Bharati Vidyapeeth Homoeopathic Hospital within the time span of 5 years was taken after taking permission from the Hospital administration. All the cases were handled and examined by experienced Homoeopathic physicians working as teaching staff along with a group of students assisting them. Inclusion of the cases was done on the basis of patients within the age group of 18 – 65 years, prescriptions with only a single remedy were considered, and all the cases whether acute or chronic were taken into contemplation, wherein the acute cases outcome at the last follow-up recorded is considered and cases with minimum 2 follow-ups were considered in the chronic cases. Repertorization was done through the RADAR 10 software, using the Synthesis Repertory.

The assessment of the cases and their follow-ups have been done following the GHHOS (Glasgow Homoeopathic Hospital Outcomes Scale) or ORIDL (Outcome in Relation to Impact on Daily Living) scale. The outcome of the cases was calculated by using the 9-point scale of the above-mentioned. If a symptom is vigorously present, the degree is considered to be "2", if the symptom is present in mild form its degree is considered to be "1", and "0" is considered if there is the absence of the symptom. The calculation of LR+ and LR- was done through a 2 x 2 contingency table including a, b, c, and d represented in table no 1.

a: aggregate of patients with a symptom, with positive results from Pulsatilla

b: remaining population with the presence of a symptom

c: the aggregate of patients, symptom-absent, still improved by Pulsatilla

d: remaining population with the absence of symptom

	Medicine worked	**Rest**	
Symptom present	a	b	a + b
Symptom absent	c	d	c + d
	a + c	b + d	a + b + c + d

Table no 1:

In order to suggest the addition or omission of a rubric for Pulsatilla, divergent cut-off values are used.

Statistical Techniques & Data Analysis: The comparison was conducted among 2 groups – Patients with a positive response (improved and cured) to Pulsatilla and the remaining population (Patients who did not respond to Pulsatilla). For all the 20 rubrics which were verified: the Prevalence, LR + with 95% Confidence Interval, and LR- with 95% Confidence Interval were calculated. All the calculations were attempted with the help of MS Excel and MEDCALC (medcalc.org) and the "p" value was calculated using SPSS-IBM software.

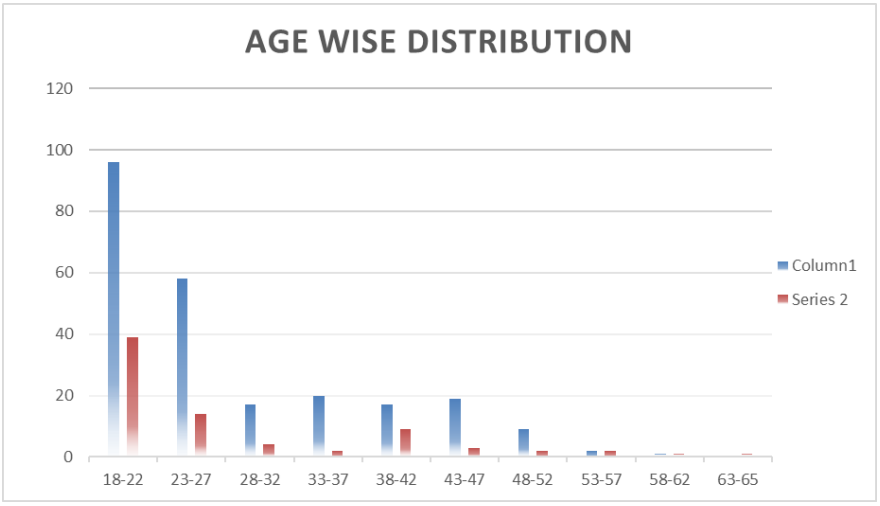
Result: 316 cases were assessed after excluding the cases which did not follow the inclusion criteria for the purpose of the retrospective study. The distribution regarding the total number of cases per year, age distribution pattern in all the 316 cases along with a description of the number of patients suffering from complaints of different systems. The outcome of cases was done through the 9-point scale of the GHHOS scale.

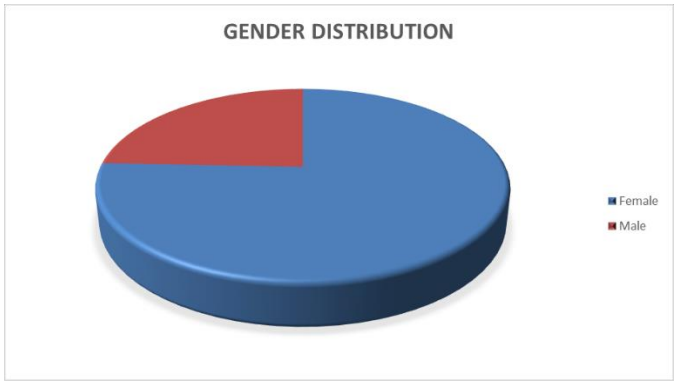
Characteristics of the patient: Case records of the patients were taken from the year 2018 – 2022. Case-taking with Anamnesis was done by the physicians in the Bharati Vidyapeeth Homoeopathic Hospital, Pune. The maximum number of cases was recorded in the age group of 18-22 years, covering 42.08% of the total population under study. Age-wise distribution of cases is represented in Figure 1.

Figure 1: Clustered column representing the age wise distribution along with gender wise distribution in respective Age groups.

Pulsatilla was more frequently prescribed to the female 239 (75.63%) population than the male population 77 (24.36%). The gender-wise distribution is represented by a pie diagram in Figure 2.

Figure 2: Pie diagram representing female and male distribution in the population.





From the total 316 cases, 243 (76.9%) cases were observed as excellent therapeutic responses while 73 (23.1) cases were observed for not responding to Pulsatilla. A significant majority of the patients suffered from ailments of the Reproductive system (74.7%), Multiple systems (32.9%), Respiratory system (27.8%), Integumentary system (19.7%), G.I (16.6%), where remarkable results were found after the prescription of Pulsatilla.

S. NO	SYSTEM INVOLVED/ COMPLAINTS	SUM OF CASES	%AGE
1	C.N. S	12	5.90
2	G. I	38	16.60
3	Resp.	42	27.83
4	Reproductive	121	74.71
5	Integumentary	27	19.74

6	**Multiple Systems**	**52**	**32.90**
7	**Psychological**	**10**	**6.99**
8	**Endocrine**	**1**	**0.41**
9	**Genitourinary**	**1**	**0.41**
10	**Skeletal**	**4**	**4.52**
11	**Urinary system**	**4**	**4.52**
12	**Immune**	**1**	**1.37**
13	**Musculoskeletal**	**2**	**2.74**
14	**Vestibular**	**1**	**1.37**

Table 2: Representation of the system(s) involved/ complaints with the sum of cases with their percentage.

The intensity was noted on the basis of the degree with which they were present, 0: denotes the absence of the symptom, 1: denotes the presence of the symptom in low intensity, and 2: denotes the presence of the symptom in higher intensity.

For "Company desire for", Pulsatilla is present in italic typeface. Following what our assessment suggests, Company desire for (LR+7.26, 95% Confidence Interval [CI]:1.81to29.06), Pulsatilla should be placed in the **BOLD CAPITAL** typeface. For the Rubric "Fullness sensation of, Epigastrium" Pulsatilla is present in italic typeface. After assessment, it is suggested to be placed in a **bold small** typeface as it is higher than cut- the off value (LR+ 4.84).

Pulsatilla for the rubrics "Consolation amelioration" (LR+ 8.54, 95% Confidence Interval[CI]:2.14to34.05) and "Timidity" (LR+ 7.11, 95% Confidence Interval[CI]:1.78to28.51) qualify for the **BOLD CAPITAL** typeface as they cross the cut-off value (LR+ >6) and also the rubrics "Fear, alone being of" (LR+ 3.14, 95% Confidence Interval[CI]:0.83to14.10), and "Eructations; Type of, sour" (LR+ 3.98, 95% Confidence Interval[CI]:0.97to16.31) stands by the cut-off values (LR+ >3 for italics) which states the presence of the medicine in italic typeface. All 4 rubrics with their respective and required values mentioned above for the medicine Pulsatilla justify the existing typeface in the Synthesis Repertory.

For Rubric "Warm-aggravation" (LR+3.47, 95% Confidence Interval [CI]:1.93to6.25), Pulsatilla is present in bold small typeface, but according to our assessment, it must be downgraded to *italic* typeface. For Rubrics like "Eruptions acne" (LR+1.85, 95% Confidence Interval [CI]:0.82to4.19), "Menses-before-aggravation" (LR+1.81, 95% Confidence Interval [CI]:0.90to3.64), "Heartburn-fat food, after" (LR+1.87,95% Confidence Interval [CI]:0.88to3.96) Pulsatilla is present in **bold small** typeface in Synthesis Repertory, but as per our assessment Pulsatilla for these rubrics must be downgraded into roman typeface. Whereas for rubrics "Weeping" (LR+1.36, 95% Confidence Interval[CI]:0.90to2.07), "Thirstlessness" (LR+1.37,95% Confidence Interval[CI]:1.04to1.80), "Menses, suppressed" (LR+1.33,95% Confidence Interval[CI]:0.81to2.17), "Leukorrhea-cream like" (LR+0.88,95% Confidence Interval[CI]:0.46to1.71),"Head-pain, pulsating" (LR+1.19,95% Confidence Interval[CI]:0.65to12.17), "Cough-Dry-night at" (LR+1.05, 95% Confidence Interval[CI]:0.55to2.01).

Rubrics	Gradings	Sample size	a	c	b	d	LR+	95% CI	LR-	95% CI	X^2 value Yates	p- value
MIND-weeping	3	n=110	91	155	19	51	1.36	0.90-2.07	0.86	0.73-1.03	1.9156	0.1663
MIND-Company desires for	2	n=53	51	195	2	68	7.26	1.81-29.0	0.86	0.76-0.88	11.2250	0.0008
MIND-Consolation – Amel	4	n=62	60	186	2	68	8.54	2.14-34.0	0.78	0.72-0.84	14.6854	0.0001
MIND-Timidity	4	n=52	50	196	2	68	7.11	1.78-28.5	0.82	0.76-0.88	10.8577	0.001
MIND-AILMENTS FROM-anger	1	n=97	79	167	18	52	1.25	0.81-1.9	0.91	0.78-1.08	0.7698	0.3803
MIND-Fear-alone of being	2	n=26	24	222	2	68	3.41	0.83-14.1	0.93	0.88-0.98	2.5820	0.1081
STOMACH-Thirstless	3	n=186	154	92	32	38	1.37	1.04-1.80	0.69	0.53-0.90	5.7394	0.0166
FEMALE GENITALS/SEX-Menses-suppressed menses	3	n=85	70	176	15	55	1.33	0.81-2.17	0.91	0.79-1.05	1.0343	0.3091
Female genitalia\sex-dysmenorrhea(painful)	2	n=81	67	179	14	56	1.36	0.82-2.27	0.91	0.79-1.05	1.1412	0.2854
FACE-Eruptions-acne	3	n=45	39	207	6	64	1.85	0.82-4.19	0.92	0.84-1.01	1.8076	0.1788
FEMALE GENITALIA/SEX-LEUKORRHEA-cream-like	3	n=41	31	215	10	60	0.88	0.46-1.71	1.02	0.92-1.13	0.3267	0.5676
GENERALS-Menses-before-agg	3	n=59	51	195	8	62	1.81	0.90-3.64	0.89	0.81-0.99	2.5235	0.1122

STOMACH-Heartburn-fat food; after	3	n=53	46	200	7	63	1.87	0.88-3.96	0.9	0.82-1.00	2.3639	0.1242
Stomach-Eructations; Type of-sour	2	n=30	28	218	2	68	3.98	0.97-16.31	0.91	0.86-0.97	3.6704	0.0554
STOMACH-Fullness sensation of -Epigastrium	2	n=18	17	229	1	69	4.84	0.66-35.72	0.94	0.90-0.99	2.1135	0.146
HEAD-Pain, pulsating pain	3	n=57	46	200	11	59	1.19	0.65-2.17	0.96	0.86-1.08	0.1575	0.6914
HEAD-Hair, falling	2	n=40	34	212	6	64	1.61	0.71-3.68	0.94	0.86-1.03	0.9250	0.3362
COUGH-Dry-night,at	3	n=47	37	209	10	60	1.05	0.55-2.01	0.99	0.89-1.11	0.0011	0.9731
GENERALS-HEAT-lack of vital heat	2	n=104	94	152	10	60	2.67	1.47-4.85	0.72	0.63-0.83	13.0651	0.0003
GENERALS-WARM -agg	3	n=132	122	124	10	60	3.47	1.93-6.25	0.59	0.50-0.69	26.4971	0.0000

Table 3: Rubrics for the medicine Pulsatilla with a, b, c, d values for LR+ with 95% CI, LR- with 95% CI, X^2 value and, p-value.

The only accurate and practical technique is to express the relative incidence of the rubrics as LR. Only after converting the LRs of the relevant rubrics into typeface can, we get an idea of how many patients would benefit from the medication under consideration. Table 6 for the Pulsatilla shows the same information along with prevalence as a percentage.

Rubric	**Prevalence**	**Type**	**Expected LR**	**Assessed LR**
MIND- Weeping	35.1%	Bold small	>4	1.36
MIND- Company desire for	16.8%	Italics	>3	7.26
MIND- Consolation Amel	11.4%	Bold capital	>6	8.54
MIND- Timidity	87.0%	Bold capital	>6	7.11
MIND- AILMENTS FROM, anger	30.6%	Roman	>1.5	1.25

MIND- Fear, alone being of	8.2%	Italics	>3	3.14
STOMACH- Thirstlessness	61.0%	Bold small	>4	1.37
FEMALE GENITALIA/SEX - Menses-suppressed menses	27.8%	Bold small	>4	1.33
FEMALE GENITALIA/SEX - painful, menses	25.6%	Italics	>3	1.36
FACE-Eruptions, acne	14.2%	Bold small	>4	1.85
FEMALE GENITALIA/SEX LEUKORRHEA-cream-like	13%	Bold small	>4	0.88
GENERALS-Menses-before-agg	18.7%	Bold small	>4	1.81
STOMACH-Heartburn-fat food; after	16.8%	Bold small	>4	1.87
STOMACH- Eructations; Type of sour	9.49%	Italics	>3	3.98
STOMACH-Fullness sensation of Epigastrium	5.37%	Italics	>3	4.84
HEAD-Pain, pulsating pain	18.0%	Bold small	>4	1.19
HEAD-Hair, falling	12.7%	Italics	>3	1.61
COUGH-Dry-night,at	14.8%	Bold small	>4	1.05
GENERALS-HEAT-lack of vital heat	37.7%	Italics	>3	2.67
GENERALS-WARM-agg	41.8%	Bold small	>4	1.36

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Discussion:

A retrospective assessment for 20 Rubrics of a commonly and frequently prescribed homeopathic medicine pulsatilla is done in order to evaluate the typeface assigned for the medicine for these rubrics in Synthesis Repertory (one of the most reliable and most commonly referred repertory by the homeopathic physicians). It is an attempt to evaluate and assess the presence of a relationship between pulsatilla and its symptoms. The study aimed at investigating the LR and prevalence of the symptoms which are commonly assigned to the frequently prescribed homeopathic medicine pulsatilla. A total of 316 cases from the records of 5 years were assessed, excluding the cases which were not matching the inclusion criteria. Female domination was observed in the target population with a percentage of 75.6% and the male population covered the remaining 24.3%%. Two age groups (18 - 22 years) and (23 - 27 years) with almost 42.08% and 22.78% respectively were found to be treated with pulsatilla.

316 cases were prescribed with Pulsatilla, out of which 246 cases showed tremendous results, and 73 cases were assessed as not responding to the treatment given (prescribed with Pulsatilla). The majority of the cases prescribed with Pulsatilla were presented with complaints of Female/Male

Reproductive system, Gastrointestinal system, Respiratory system, Integumentary, and Multiple system involvement.

The likelihood ratio and prevalence of symptoms responding well to Pulsatilla were done.

For entering and discarding the entries in Synthesis Repertory, different cut-off values were used.

According to our evaluation and assessment of the 20 rubrics under research, Pulsatilla for the rubric "Company desire for" must be upgraded to **BOLD CAPITAL** typeface, and the rubric "Fullness sensation of, Epigastrium" must be upgraded to the **bold small** typeface. While for 4 rubrics it was found to be relevant with its existing typeface in Synthesis Repertory. And 9 rubrics could be downgraded but cautiously, while 1 rubric is still doubtful.

Discrepancies were found between Kent's Repertory and our evaluated result, as in the earlier times the chance influence was not taken into account for adding and discarding entries in a rubric. The shortcomings of the Repertories could be handled by adapting this methodology but this does not mean that it will solve every shortcoming, few may be solved by implication of LR and some might not.

Conclusion:

This study's objective is to investigate and assess the prevalence of symptoms in those who respond well to Pulsatilla. This study intends to improve the precision of the prescription of Pulsatilla rather than making a diagnosis of the condition. A few Rubrics in medicine need to be given more weight. There are problems with both our repertories and the synthesis repertory that can be further fixed and improved by applying the likelihood ratio. Physicians are familiar with the primary symptom and the symptoms that point specifically to Pulsatilla, but this depends more on the illness's frequency than its level of rarity. A prospective study's symptom selection may be improved by retrospective verification and evaluation of symptom prevalence and LR in patients who have responded well. The study's findings indicate a possible relationship between the typeface used in Synthesis Repertory for Pulsatilla under Rubrics.

Accepting a prospective study would be more beneficial than a retrospective study, for carrying out research of this kind.

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